Japan and Taiwan in the Wake of Bio-Globalization: Drugs, Race and Standards

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ABSTRACT

This is a study of Japan and Taiwan's different responses to the expansion of the global drug industry. The thesis focuses on the problematic of "voicing," of how a state can make its interests heard in the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The ICH is a unique project that facilitates the formation of a single global market by creating universal standards for clinical trials and drug approvals. Tracing, through "slow motion" ethnography, step by step, why Japan claims a racial difference requires additional local clinical trials with "Asian bodies," this thesis rejects conventional interpretations of protectionism for Japan's resistance to globalization. It argues that more than protectionism is involved, and that a rich ethnographic understanding of Japan's medical infrastructure is required to understand the claim of biological, cultural, and national differences, as well as biostatistical arguments about the ambiguities of "extrapolation" of clinical data from one place to another.

The inherent ambiguities of efforts to create "bridging" studies as a temporary solution to these problematics created a deadlock in the ICH, and provided an opening for Taiwan, another Asian state, which does not enjoy formal recognition from the world, to speak for itself to this conference, and to create the fragile, but politically critical, possibility of becoming a clinical trial center for Asian populations. The language of genomics and biostatistics become in the more recent period the vehicles for both Japanese and Taiwanese efforts at "voicing" their concerns. Both genomics and biostatistics look different in these contexts than they do from the United States or European Union.

In sum, (1) Japan's and Taiwan's response, as well as "global ethnographic objects" such

as the ICH, provide important tools to rethink the comparative method as well as universalizing claims of harmonization. (2) Race, culture, and the nation-state are transformed as categories through the contemporary reworkings of genomics and biostatistics. (3) The thesis demonstrates that abstract accounts of the spread of clinical trials and resistance in various parts of the world are not to be trusted unless they include detailed probings of local understandings, identity issues, and problems of voicing.

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Acknowledgements

It is a long journey to write a thesis like this. I am grateful to many people who helped me, and I will thank them all. First of all, I want to thank the STS program, my intellectual home, which granted me the freedom to try something unconventional and interdisciplinary. Almost all of the issues and concepts discussed in this thesis are derived from either the fruitful discussion in classes or colloquia I attended. Just to name some occasions. My first paper about Taiwan was written for Professor Peter Perdue's class on methodologies in history, which turned into a research paper. My first paper on Japan was for Professor Evelyn Keller's gender and science seminar, which opened my eyes to the alternative ways a non-Western culture can be approached. Professor Joseph Dumit is my encouraging yet critical guide to the world of medical technologies. In addition to the history of medicine in the United States, Professor Evelynn Hammonds showed me the complicated social and cultural dimensions concerning race, which became a key concept to probe Asian states and bio-globalization. My special thanks also go to Professor Deborah Fitzgerald, my student advisor, Professor Rosalind Williams, the program director, and to many others I met in this community—Rachel Prentice, Hannah Landecker, Christopher Kelty, Adriana Petryna, Kaushik Sunder Rajan, Aslihan Sanal, Hyun-Gyung Im, David Kaiser, Livia Wick, Chen-Pang Yeang, and David Jones—for joyful discussions and generous support.

However, this journey cannot start without the intellectual inputs from the advisors of this thesis. Professor Michael Fischer, my thesis supervisor and mentor, is the first and main thinking source for this study. It is always a joy to work with him. Responsive, open-mined, clear, to the point, and keen to science and the world, he demonstrates to me how a true STS study can be achieved putting aside the clouding of disciplinary boundaries. He is also the person who pushed me to think of the meaning of the nation-state in a global era, which became the theme of this thesis. Professor Dumit is the best communicative creator I ever met. Every meeting is an exciting roaming in the network of knowledge. With Joe, theories become clear, comprehensible, and interrelated. Like playing logos, in these thinking exercises (or thought experiments) we deconstructed the world and discussed the ways to reorganize it. Further, our common interest in the politics of pharmaceuticals brought us closer intellectually. I am grateful for having Professor Stefan Helmreich join this journey. He carefully examined this thesis from very early drafts and shared with me his insights on race and globalization, which supplemented a crucial part of this challenging attempt. This is a team I could not dream of elsewhere on my topic.

Numerous individuals and organizations have helped me during my archival research/ fieldwork in Japan and Taiwan. They are not merely informants and providers of materials; they injected to this study their opinions and inspirations, which were very important for

making possible this global ethnography. My stay in Japan would not have been possible without the sponsorship from the MIT International Study Program and the help of Professor Kuriyama Shigehisa of the International Research Center for Japanese Studies. We first met in 2000 when he was visiting the History of Science Department at Harvard University, and have kept in contact in Tokyo, Shanghai, Taipei, and again Boston. In Japan my primary debts are to Professor Hashimoto Takehiko, who kindly hosted me at the Research Center for Advanced Science and Technology. My unexpected encounter with standardization in his seminar on the history of science and technology in Japan, in fact, became the stepping stone to approaching the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and the world of proprietary drugs. Through Professor Hashimoto I am fortunate to know Professor Hiroi Yoshinori, an expert on health policy. Some arguments in this thesis were created in the unforgettable talks we had in Au Bon Pain at Kendall Square, ANA Hotel Café at Roppongi, or his office in quiet suburban Tokyo. Various people and groups helped me with this study. In addition to those who generously accepted my interviews, I would like to thank Kato Shigeo, Steven Barker, Yoshikawa Miki, Nakajima Takako, Kim Boumsoung, Dan Plafcan, Ito Kenji, Nakamura Masaki, Chen Yi-Nin at the University of Tokyo, Hakoda Keiko at Kyoto University, Jerry Chiu at Nomura Research Institute, and the Japan STS Association in whose activities I participated.

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Of course, this global study cannot be completed without the voice of the experts

working on and for the ICH. I would like to thank Odette Morin, the ICH Secretariat, who introduced me to the proceedings of ICH conferences, the most reliable material concerning the project of harmonization. I want to thank also Eric Abadie, Alex Giaquinto, Elaine Esber, Yves Juillet, Etienne Labbe, Uwoi Tohru, and Naito Chikayuki, for sharing their first hand experience, in person or by e-mail, on the making of the ICH and of the E5 guideline.

The interdisciplinary nature of this study brought its early attempts to several occasions in various forms. I thank Yang Tsui-Hua at Academia Sinica, who invited me to organize a panel about institutions and science policy at the tenth International Conference on the History of Science in East Asia. Also, I am grateful to Timothy Choy, Sheila Jasanoff, and all participants in the Lively Capital conference for their useful comments. I should thank especially Kaushik Sunder Rajan at University of California, Irvine, who made my appearance in this conference possible. Some results of this study have been presented in the annual conference of the Taiwan Sociology Association in 2004; I thank all comments and feedback from my sociological colleagues. *Science Development* and *ICH-Taiwan Bulletin* are my channels to general public and policy makers; I thank them for allowing me to share these ideas, many of which are used in shaping this thesis. In addition, this thesis cannot be read the way it is without many people who have worked on my English while writing it. I should name three of them, Professor Ralph Kirby at National Yang-Ming University, Samuel Gilbert and Kenneth MacLeish. Serving not only as a polisher, Professor Kirby in fact is my fourth "reader" of this thesis, helping me to check scientific details and legal issues, on which he is an expert. It is always a joy to read his witty comments and suggestions. I am also grateful to have Sam and Ken on this project. Sam's broad knowledge on East Asia and Ken's insights in anthropology perfectly helped me to bring this piece into the English-speaking world.

Finally, my deepest thank should be reserved to my parents and brothers, who continuously support me here and there on the long "detour" at the margin between the realms of medicine and humanities studies. For their unconditional love and regards, I thank them. Lin Jin-Ann, who first appeared around the time as this thesis emerged, fulfills my life in many ways. On this journey back and forth between Asia and the United States, she is my faithful companion, colleague, critic, and soul mate. I cannot tell the invaluable contributions she has made to this project; but she deserves this credit. With her, we are ready for coming journeys, together and forever.

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Abbreviations

ACP	Advisory Committee on Pharmaceuticals, DoH (Taiwan)
APCRA	Asia-Pacific Clinical Research Alliance
APEC	Asia-Pacific Economic Cooperation
ASEAN	the Association of South-East Asia Nations
AUSFTA	U.S.-Australia Free Trade Agreement
BNHI	Bureau of National Health Insurance (Taiwan)
BPA	Bureau of Pharmaceutical Affairs, DoH (Taiwan)
CBER	Center for Biologics Evaluation and Research, FDA
CC-GCP	Cooperation Center for Good Clinical Practice (APEC)
CDE	Center for Drug Evaluation (Taiwan)
CDER	Center for Drug Evaluation and Research, FDA
CERD	Convention on the Elimination of All Forms of Racial Discrimination
CPMP	Committee for Proprietary Medicinal Product (EU)
DIA	Drug Information Association (USA)
DoH	Department of Health (Taiwan)
DPP	Democratic Progressive Party (Taiwan)
EC (EU)	European Community (European Union)
EFPIA	European Federation of Pharmaceutical Industries and Associations
EFTA	European Free Trade Area
EMEA	European Agency for the Evaluation of Medicinal Products
FDA	United States Food and Drug Administration
FMPAT	Federation of Medical Professional Alliance in Taiwan
HOWDY	Human Organized Whole Genome Database Project (Japan)
GCC	Gulf Cooperation Council
GCG	Global Cooperation Group (ICH)
HGDP	Human Genome Diversity Project
HGP	Human Genome Project
HHS	Department of Health and Human Services
ICDRA	International Conference of Drug Regulatory Authorities, WHO
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
ICSA	International Chinese Statistical Association
ICWP	International Conference on World Peace (Japan)
IEC	International Electrotechnical Commission
IFPIA	International Federation of Pharmaceutical Manufacturing Association

IRPMA	International Research-Based Pharmaceutical Manufacturers Association (Taiwan)
ISO	International Organization for Standardization
ISTWG	Industrial and Scientific Technology Working Group (APEC)
JCRR	Joint Commission on Rural Reconstruction (Taiwan)
JMA	Japan Medical Association
JPMA	Japan Pharmaceutical Manufacturers Association
JSNP	Japanese Single Nucleotide Polymorphisms Project
KFDA	Korean Food and Drug Administration
KMT	Chinese Nationalist Party (*Kuomingtang*, Taiwan)
LSIF	Life Science Innovation Forum (APEC)
MEOA	Ministry of Economic Affair (Taiwan)
MHRA	Medicines and Healthcare Products Regulatory Agency (UK)
MHW	Ministry of Health and Welfare, Japan (reorganized as MHLW in 2001)
MHLW	Ministry of Health, Labor, and Welfare, Japan (reorganized from MHW in 2001
MITI	Ministry of International Trade and Industry, Japan (reorganized as the Ministry of Economy, Trade and Industry in 2001).
MOSS	U.S.-Japan Market-oriented, Sector-selected Discussion
NDMC	National Defense Medical Center (Taiwan)
NHRI	National Health Research Institute (Taiwan)
NTE	Annual National Trade Estimate Report on Foreign Trade Barriers (USA)
NTU	National Taiwan University
OPSR	Organization for Pharmaceutical Safety and Research (*kiko*, reorganized as part of PMDEC in 2004)
PANDRH	Pan American Network on Drug Regulatory Harmonization
PBS	Pharmaceutical Benefits Scheme (Australia)
PhRMA	Pharmaceutical Research and Manufacturers of America (renamed from PMA in 1994)
PMA	Pharmaceutical Manufacturers Association (renamed as PhRMA in 1994)
PMDEC	Pharmaceuticals and Medical Devices Evaluation Center
PWPA	Professors World Peace Academy (Japan)
ROC	Republic of China (Taiwan)
SDAC	Southern African Development Community
SRB	Strategic Review Board, Executive Yuan (Taiwan)
STR	Special Trade Representative (renamed as USTR in 1979)
TGA	Therapeutic Goods Administration (Australia)

UNESCO	United Nations Educational, Scientific and Cultural Organization
UNICEF	United Nations International Children's Emergency Fund
UNIDO	United Nations Industrial Development Organization
USTR	United States Trade Representative
WHA	World Health Assembly
WHO	World Health Organization
YMU	National Yang-Ming University (Taiwan)

Acronyms

ACTD	ASEAN common technical document
ADME	absorption, distribution, metabolism, and excretion
ADR	adverse drug reaction
AUC	area under concentration (of a drug in the body)
CCDP	complete clinical data package (ICH)
c-GMP	current good manufacturing practice
C_{max}	maximum effective concentration (of a drug in the body)
C_{min}	minimal effective concentration
CRO	contracted research organization
DTC	direct to consumer
E5	fifth guideline on efficacy (of the ICH)
EWG	expert working group (ICH)
FTA	free trade area
GCP	good clinical practice
GDP	gross domestic production
GMP	good manufacturing practices
HLA	human leukocyte antigens
IND	investigational new drug application
IP	intellectual property
IRB	institutional review board (for clinical trials)
JIRB	joint institutional review board (for clinical trials)
MRSD	maximum recommended starting dose
NDA	new drug application
NIEs	newly industrializing economics
NTE	Annual National Trade Estimate Report on Foreign Trade Barriers (USA)
OTC	over-the-counter drugs
PD	pharmacodynamics
PK	pharmacokinetics
R&D	research and development
TI	therapeutic index (Cmax/Cmin)

Chapter 1
Prologue: An STS Inquiry into the Nation-State as It Encounters Bio-Globalization

> A collectivity united in a belief is a culture. That is what the term means. More particularly, a collectivity united in a false belief is a culture. Truths, especially demonstrable truths, are available to all and sundry. But errors, dramatic errors, are culture-specific. They do tend to be the badges of community and loyalty.
>
> Ernest Gellner[1]

> Who has seen the wind? Neither I nor you;
> But when the leaves hang trembling, the wind is passing thro'
>
> Christina Georgina Rossetti[2]

PART I
FORMATTING PROBLEMS

"Ridiculous Race" and "Nationalist Mania"

You may be puzzled by the juxtaposition of a quotation from the political scientist Ernest Gellner and two lines by the poet Christina Georgina Rossetti. Their connection is not apparent. I shall try to explain by introducing two scenes I happened to encounter during my fieldwork on the pharmaceutical industry.

The first scene took place at midnight. After a long day of writing, I sat before my computer, idly clicking through some e-mail. One was from an American (a Caucasian) anthropologist I am acquainted with. He had been browsing through a website devoted to the pharmaceutical business and had come upon a PowerPoint presentation that illustrated, he said, the "irrational" insistence of many Japanese that they differed from all other races. The tone of this e-mail message gave me the impression that I had been added to the list or recipients in the middle of a long discussion between some anthropologists, copied when the topic moved to Asia. The way the Japanese evaluated race fascinated the message's author: he was bewildered by the extremely long list of so-called extrinsic and intrinsic factors that appeared in the PowerPoint presentation. So Andrew, as I shall call him, wrote:

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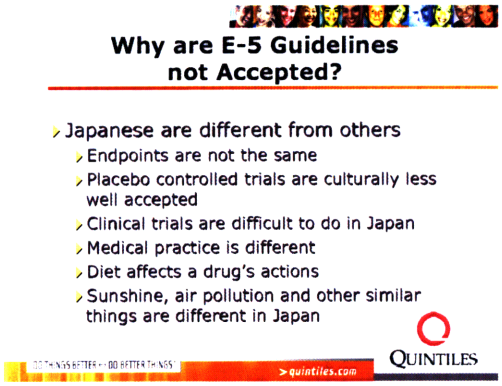
1 "The Coming *Fin de Millenaire*," in Ernest Gellner. 1996 [1995]:244.
2 "Who Has Seen the Wind?," in *Sing-song: A Nursery Rhyme Book* (1893 [1872]).

i [sic] find [it] an interesting complication of the meaning of ethnic/race differences. They have approximately 20 slides full of factors that may account for "ethnic difference" in clinical trials. With the following conclusion [Andrew inserted here the original presentation slide, as shown in fig. 1.1]:

Fig. 1.1 Why Are E5 Guidelines Not Accepted? Japanese Are Different from Others



Source: Trygstad 2003.

Andrew was fascinated by the Japanese definition of race. But when we go back to the original presentation,[3] which was made by the executive director of Japan Hawaii Alliance, Quintiles Transnational Commercialization Group,[4] we can better understand Japan's racial discourse. It is real but absurd, absurd but real. From biological ethnicity and medical practices to lifestyle and culture, including even sunshine, everything is different in Japan. What strikes us as ridiculous and funny is the use of "different" (and its synonyms) as the key concept in understanding the Japanese race, with race extended to include everything found on the Japanese archipelago.[5]

Moreover, the form in which they appear makes these criteria look funny. This is not idle gossip but a summary of how racial difference was manifested in clinical trails performed by Japan's Ministry of Health, Labor, and Welfare (MHLW). It participates in a scientific discourse, or at least, it is written in scientific terms, which have immediate

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[3] The presentation was made at New York Pharmaceutical Forum on November 5 2003. See Trygstad 2003.

[4] It is one of the biggest contract research organizations (CROs) in the world. Founded in the United States in 1982, Quintiles has grown into a global giant in the area of clinical trials; it now has branch offices, laboratories, and research sites in every continent except Oceania.

[5] In fact, on Quintiles' world map, Japan and Korea are separated from other countries in the Asia-Pacific region. I will return to this point later in this chapter.

practical implications, namely, whether a drug should be granted official approval for sale in Japan. Andrew's reaction casts doubt on the practicality of the Japanese definition of such a sensitive concept, on the very assumption that race exists.

I assume that this is why the presentation was brought to my attention. Race, in the American scene, is a troublesome term. Didn't the American Anthropological Association urge census takers to stop collecting statistics based on race, saying that the concept of race was based on pseudoscience? The group stated that if biological information were not the objective, terms with a biological resonance added nothing to the precision, rigor, or factual basis of information being collected. If biological terms are confusing, now the Japanese have added to the confusion by bringing in non-biological terms. The message Andrew read in the PowerPoint presentation was not how advanced our current understanding of racial differences was; Andrew was just fascinated that, in a global era, Japanese people might imagine that they were racially different from others and would express this idea so naïvely.

But after replying to Andrew's e-mail message I asked myself whether there was any way to make sense of Japan's approach by working from the assumption that it was rational and not a strategic ploy in international trade. After all, when I interviewed Tominaga Toshiyoshi, an officer of the MHLW who had translated the E5 guideline mentioned in that slide from English to Japanese, he admitted that he did not see any difference between race and nation. He recalled that he had originally translated the term *race* as *jinshu,* which is more biological and closer to the original meaning of race, but his supervisor had changed it to *minzoku*, a term referring broadly to both the state and race.[6] This change provides a key insight into the Japanese attitude, since they see no significant difference between *race* and *nation-state.*[7] And I recalled Gellner's reflections on the long entanglement of anthropology and politics, which I quoted at the beginning of this chapter. According to Gellner, a nation is a constructed artifact,

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[6] In Japanese there are two sets of terms roughly corresponding to the concept of race and ethnicity in English: while *minzoku* and *shudan* refer to cultural and social factors, jinshu and *shuzoku* refer to biological factors. But for our purposes I will use the term *minzoku* as a shorthand for that which is considered the base of the Japanese nation.

[7] *Minzoku*, like its Chinese equivalent *minzhu* and *minjok* in Korean, reflects a complicated process of translating terms and concepts from one part of the world to another during modernization. Even so, concerning the uses of minzoku in the making of modern Japan, Hiroshi Yasuda's historical study clarifies the inseparable relationship of *minzoku* with the state (1992). According to Yasuda, *minzoku* is a cultural device used as the foundation when Japan transformed into modern state. Within this process, the emphasis on different aspect of its meaning varied in different periods, from a certain set of relation between the state or the emperor and its people to a biological one that facilitates the imaginary construction of a homogeneous Japanese race. At the end, as the author suggests, the tradition of *minzoku* has, on the one hand, a clear racist meaning, but on the other hand, it can only considered with the state that legitimatize its existence (72).

inseparable from culture, itself another construction. In addition, he suggested that a culture's collective specificity resided in what it considered false. If, instead of hastily rejecting such preconceptions we consider them seriously as one aspect of the nation-state, we might be able to explain Japan's attitude toward its race. The indexes used by the Japanese to differentiate themselves from others may seem strange, but they provide a starting point for thinking about the state that supports such ideas and the race, according to the Japanese definition, that supports such a state.

The second scene had taken place some months earlier in a hotel shuttle on the way to the University of California, Irvine, where an anthropological workshop on global capital was being held. I was there to present a paper about the standardization of pharmaceuticals and its impact on East Asia. Since there were no other passengers on the shuttle, I had a relaxed, pleasant chat with the driver, an immigrant from Mexico, who had just started this part-time job. "Mike" kindly described his experience as a foreigner and a minority — exciting, yet definitely not easy. He talked and I listened. After a while, Mike asked my nationality, possibly out of simple courtesy (I look distinctively East Asian and speak English with a noticeable accent). Having run into many people who confuse my homeland with the People's Republic of China (PRC) and Thailand (*Thailand* certainly sounds like *Taiwan*), I decided not to test his knowledge of world politics or my English. I replied, slowly, taking care with my accent, letter by letter: "*T-a-i-w-a-n.*"

To my surprise, Mike was familiar with Taiwan and immediately responded with a sharp and straightforward question: "Huh. Do you believe that your country is independent?" Maybe he wanted to show that he was quite familiar with Taiwan. In any case, I was intrigued. Let me say that my academic experience in the United States has convinced me never to touch this topic on any public occasion. Of course, it is, in itself, a difficult topic. Area studies specialists have their own way of connecting the island's society and culture to the web of knowledge. Those in science studies, who prefer science and technology's universal effects, do not accord Taiwan any special importance. For them, an industry or a laboratory is a more valid research subject. But what really prevented me from discussing Taiwan in academic circles was a fear of becoming confused by a peculiar political grammar. In the question "Do you believe that your country is independent?" nearly every word is troublesome. Who, for instance, is able to determine Taiwan's political status? What is meant by believing in a state's political status? The very expression *your country* assumes a great deal, possibly too much. When can we say a state is independent? Independent from what?

Somehow, without realizing how "wrong" and how complicated some might think his question, the shuttle driver knew that asking it was the most direct way to enter into a close relationship with a Taiwanese person. This was not the conventional greeting that Americans who know something about Taiwan tend to offer on first meeting a Taiwanese person here. To be greeted with a "*Ni hao*" or a "*Xing hui*" ("How are you?" and "Nice to meet you" in Mandarin) does nothing for me, though no doubt these phrases are meant kindly. It seems to me, a Taiwanese native, that the most moving greeting is not a confirmatory sentence but a question.[8] So I said to Mike, not at all answering his question, "You must know about this from a Taiwanese." And he admitted that he had discussed the subject with a Taiwanese immigrant who had helped him get his job. And he told me the story of this Taiwanese immigrant, whom I will call Hu.[9] Like many immigrants, Hu moved to the United States for economic reasons — and for economic, cultural, and social reasons was marginalized by American society. But what amazed me was the topic he chatted about with his friends — apparently he talked nonstop about building a Taiwanese nation; Mike must have ended up thinking that all Taiwanese have a mania for politics and that all are devout nationalists. Hu had often spoken with him about Taiwan's politics, Taiwan's relations with the PRC, Taiwan's failure to get a seat at the United Nations, and so forth. Mike might not have felt a need to belong to a nation, but he sympathized with Hu's desperation.

Mike's comment revived my own reflections on Taiwan's national problem, which I had forgotten. I can understand his ignorance about the nation. In a world of nation-states, the state is everywhere yet barely felt in our everyday lives. This is why Christina Rossetti's image of wind is appropriate for understanding nation-states in the modern world. Just so, political scientists are forever trying to give the nation and nationalism a definition, but in vain: it is so abstract that it can be seen only in how people live and react to it. No matter how artificial and contingent they are — or perhaps because they are — the nation and the state have become an inseparable part of the constitution of the modern world. Gellner has even said that it is obvious that now an individual must have a nationality, just as she or he must have a nose and two ears (Gellner 1983: 6).

But what of those born without an internationally recognizable nationality? Gellner failed to take into account this tricky situation, which is the starting point for the present

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[8] This question can be interpreted in another way, namely, as in inquiry into the gap between a generally recognized political status and the aspirations of the mass of the people. Later in this thesis I will return to this alternative.

[9] This fictitious name is inspired by the main character in Jonathan D. Spence's historical investigation, *The Question of Hu* (Vintage, 1989), a tragic tale of a sixteenth-century Chinese man, John Hu, thought to have lost his mind after being brought to Europe by Jesuit missionaries.

study. Hu's manic longing for a nation (or, for him, a clear nationality) should be reassessed. Is every Taiwanese a nationalist? Why don't the Taiwanese take their nationality for granted, as others do? If the state is remote from most Taiwanese, as it is from most of the Earth's inhabitants, why is Taiwan's nationhood a part of their everyday conversation? Whether or not the cry for a nation is a valid inquiry in global politics or international relations, it seems to me that it is already an anthropological phenomenon deserving of serious study.

After sending Andrew my reply, I sat in my room and started thinking about whether questions about the state should carry more weight in my study of the pharmaceutical industry and globalization. I could not help recalling the moment when I got off that shuttle in Irvine. I thanked Mike and asked him to send my regards to his friend Hu. But he told me he couldn't: a month after learning that his wife had an ovarian tumor, Hu had returned with her to Taiwan, where his wife, otherwise uninsured, had health insurance. For Hu, the nation is not the purely imaginary artifact described by academics. I asked myself: How is Taiwan's statehood presented and, given this peculiar statehood, what does Taiwan fail to give its people as ordinary citizens in the world?

An Interdisciplinary Inquiry into STS: Bringing the State Back into the Technoscientific World[10]

Perhaps my readers are having trouble seeing the relationship between the two vignettes and the present thesis. As I hinted above, my study began long before I met Mike and got a note from Andrew. My topic had been decided in 1999, when I learned about Viagra (sildenafil citrate), then just approved for use in Taiwan and Japan after having been developed in the United States. From 2001 to 2002 I did archival research at the Research Center for Advanced Science and Technology in Tokyo. I was hoping to trace the social and cultural influences of Viagra, from the global level to the level of individual users. During my stay in Japan I noticed abnormalities in the reviewing process for the drug and interviewed a handful of people who provided useful comments. I also heard about other Western-developed products that had run into problems when

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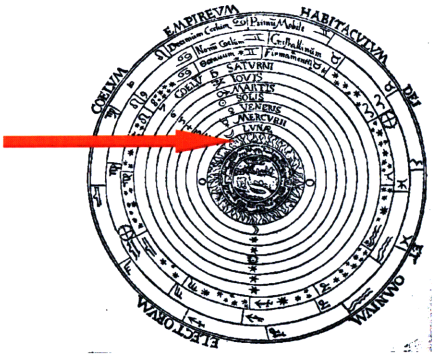
[10] This abbreviation refers to the academic field devoted to "science, technology, and society" and to "science and technology studies" and even to a certain research agenda devoted to "social studies of science and technology." Examples of the last would be the program devoted to the sociology of scientific knowledge at Edinburgh University and the actor-network theory proposed by Bruno Latour at the Centre de Sociologie de l'Innovation, École Nationale Supérieure des Mines in Paris. Rather than cling to any one of these schools of thought, the present thesis is my attempt to include every approach and discipline that might be useful in dealing with the issues.

their manufacturers tried to export them to Japan. However, this material could not be accommodated by my original plan.

Let me explain the above situation through an example from the history of science. My previous conception of the world of pharmaceuticals can be described as an Aristotelian-Ptolemaic model of the universe, in which the state functions as the lunar sphere that demarcates the "empirical" and "abstract" worlds (fig. 1.2). Below the state level, the world of pharmaceuticals is observable and experience-based. In contrast, beyond the state lies a purely abstract world that nothing except theories can enter.[11] So far, this is fine. Relating abstract theories about the world to local experiences can be a challenge, but certainly there has been excellent research on how science and technology have affected American people's lives. This does not mean that I could not simply apply this to what I observed in East Asia, but over time I came to see this approach as unconvincing.

Fig. 1.2. Model of the Aristotelian-Ptolemaic Universe, in Which the Lunar Sphere (indicated by red arrow) Is the Boundary Separating the Empirical World from the Abstract One



Source: Galileo Project website at http://galileo.rice.edu/sci/theories/ptolemaic_system.html.

The problem was that everything depended on the position from which observations were made. In my original plan, the United States was regarded as the center of the world. Like the Earth in the Aristotelian-Ptolemaic model, the United States not only has geographical importance but also ontologically preempts all other claims; from this position researchers can only elaborate the universe as they conceive of it.[12] In studies of

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[11] An anthropological version of this situation can be found in the "crisis of representation" described in Marcus and Fischer 1999, Chapter 1, esp. 11–12.

[12] This criticism was accepted among some Western scholars after the appearance of Edward Said's

the United States, the state itself, like the Moon in the Earth-centered cosmological model, does not play a crucial role in practice. The material sphere, according in medieval theories, was "gradual," starting in the lunar area and ending in the starry dome. The lunar sphere is attenuated and imperceptible, existing only in theories.

To return to my situation. When I tried to use this model to describe individuals living outside of the United States, such as those in Japan and Taiwan, I found inconsistencies among local concerns and outsiders' concerns. The Asian states do not present a neutral interface through which our ideas about the world can be easily projected. It could be said that what I learned in the United States was an "Americentric" view of the world; I have since switched to a "local-centric" one (an anthropologist on Mars). Traveling back and forth between these states and the "center of the world" has enabled me to "see the wind" by watching the "trembling leaves." For me, the state is a lens that refracts the anthropologist's view.

My exchanges with Andrew and Mike did not change the field I had been working in — I still work on East Asia and the pharmaceutical industry — but they did change my subject and my viewpoint. I began to wonder whether the state, which has long been considered merely an intermediate between the global and the individual, really matters in a technoscientific world empowered by science and technology and unified by shared ways of living and thinking.[13] I decided to expand my field to make it international and I took as my topic the interactions between the state and the world.

This provoked a range of conceptual problems. The first is related to the meaning of *global* in this study. In conventional anthropological discourse, the world, if mentioned, functions largely as the background for local activities. As a result, the world tends to be portrayed in an abstract manner. There may be sound questions about whether the whole image of world can be obtained from selective observations, but if one shifts the scale of research from the individual to the state, this criticism can be dodged. Then one can pose questions about the world itself, such as, how can we find a world we are able to describe? Obviously, if I cast the world as one of my main characters and not merely as background

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pioneering work on the Western view of the Islamic world, *Orientalism* (1979). Said evaluated and criticized the long tradition of writings about the Middle East generated by Western travelers, scholars, and colonizers who had created a set of fantastical images of their "Other." These fantasies assumed a palpable form in the capital circulation of knowledge and material, becoming an integral part of European material civilization and culture. Although my project deals with how Asia is misinterpreted by some American scholars, I have refrained from adopting a Saidian perspective.

[13] For a brief review of the term technoscience and its meaning in the context of science, technology and society studies, see Fischer 2003: 416 n. 3. Later in the present chapter I will explain why biology should be considered a new and challenging realm in my project.

in this anthropological discourse, one solution might be to draw up a self-contained theory about it that is convincing enough to its readers, but since I am interested in something else I set myself the task of defining a world that is restricted yet can be empirically described, only to wonder whether such a world exists.

Another problem is how to treat the state as a workable subject. Although the scenes I observed over the course of my fieldwork have some shared characteristics, this does not mean that the state is the appropriate level of analysis. Here Gellner's argument on the formation of nations is useful. It is the attributes of nation-states that configure the world: French cuisine, Japanese bonsai, Taiwanese tea. Using a computer metaphor, we can say that the world is a hard disk that is conceptually "formatted" by nation-states. Though political scientists offer formalistic definitions that clarify the difference between nations and states, in practice one may speak of them in terms of the subjects they assume: there is the entity that international organizations can deal with and there is the different entity that allays the anxiety of an individual like Mr. Hu.

Even if the state can be a subject for study, we still have to figure out how it can be represented. To put this question more precisely, how can we cast a state as a person? We are often told that the world is a global village and states are residents. We read in the international section of newspapers that "Germany and France finally signed the agreement," "the United States attacked Iraq," "Russia is involved in a territorial dispute with Japan," and so forth — the grammar implies that the state functions and behaves like a person. Even so, we need to go beyond the explanations provided by studies of international relations, which simply render the state synonymous with government. In addition, the presumed predictability of governmental behavior, subject to universal rules of rationality and describable through game theory, may make governments seem like political scientists' understanding of people, but it only makes states seem less human by anthropological standards. Gellner has shown us that sometimes the state is not rational — he ascribes this to culture and thus to nationalism. My project, then, is to explain why Japan looks "irrational" in a scientific field such as biomedicine, which supposedly acts independently of politics. My tasks are as follows: first, to search out the logic of nationalist discourses in the technoscientific world; second, to see how this logic is presented through the state.

After these tasks have been accomplished, a third task, possibly the most challenging, remains: writing a single and comprehensible narrative describing more than one state and more than one worldview. In other words, I need a method. Certainly, this would not be a problem if I believed that the world could be objectively conceived. Like Copernicus, I could write a new book on the world by abandoning the

Aristotelian-Ptolemaic model and putting the sun in the middle of things, filling my literature review with complaints about how stupid my predecessors were to believe in any other model. I could even add a meta-analysis about this switch of worldviews, as Thomas Kuhn did in his pioneering *Copernican Revolution* (1957). Unfortunately, recent science, technology, and society (STS) thinking frowns on such a progressive narrative. The argument offered by anthropologist Michael Fischer in "Modules for a Science, Technology, and Society Curriculum: STS@the-turn_[]000.mit.edu" suggests some of the complexity that is being sought in the contemporary discourse on science (2003: 334–39). Over the course of explaining why he begins his history of science with the scientific revolution, Fischer notes that the main reason is not "its temporal priority or presumptive content, but because the seventeenth century had become within the world of STS a central arena for social theory and mutual borrowing between historians and anthropologists" (334). Indeed, the scientific revolution is a period that is much studied, especially by those with an interdisciplinary disposition. However, this pedagogical statement also reminds us that there is more than one way to understand a period like this. Fischer then uses a series of examples to show how the scientific revolution should be considered not as a universally agreed upon historical fact but rather an event ontologically located, for historians, in the context of periodization, and for anthropologists, in cultural encounters. According to Fischer, the scientific revolution deserves an interdisciplinary narrative, which is possible since "the presumptive division between the work of historians and anthropologists ha[s] already broken down" (339). If I want to develop a thesis describing not one state but many, featuring not one viewpoint but many, my main challenge would be that of describing a world where many "local-centered" schemes coexist and, on the level of narrative, synthesizing these conflicting views into an understandable narrative.[14]

Fischer has suggested a practical way to initiate such an interdisciplinary discussion. He asks, quite simply and straightforwardly, "What is at stake" (339)?[15] As for the interaction between states within the context of globalization, two interrelated questions should be kept in mind. First, part of my subjective analysis concerns how the voice of the state comes to be heard through research. This question is crucial because it determines the characteristics of my narrative. International studies are not new to the

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[14] I do not admit the existence of a "standard" worldview acknowledged by all other worldviews. I prefer to think in terms of a "pre-paradigmatic" period in which no model dominates.

[15] In writing the present STS study, I have tried to avoid the debates within cultural anthropology on writing and the representation of culture, though they are related to my project. Those who are interested in this topic and recent related work in the STS field, see *Late Edition Series* edited by George Marcus and Michael Fischer (University of Chicago Press) and Fischer 2003.

field of the social sciences, where comparative studies are common. Though comparisons can be powerful, they imply a non-historical, non-ethnographic approach that removes the subjects in question from their contexts, setting them in an artificially determined grid and collecting everything the grid demands, in order to compare them. The current practice in STS will not tolerate this sort of decontextualization. This thesis has to consider how the voice of the state can be heard and I have to be selective in a study of globalization — although it is equally important, in light of anthropology, to notice what is missing from what the state tells us.

The second question is about the structure of narrative. In response to globalization, cultural anthropology has developed a "multisited" approach. Though attractive and useful for capturing synchronic changes, only a small number of multisite studies have been successful. In other words, though such an approach has much to recommend it, everything depends on how the sites are related to one another. On the other hand, grand theories remain taboo. Thus, in order to make the juxtaposition of voices (worldviews) possible, it is necessary to identify a locus outside of national boundaries where the voices of states can speak, converse, quarrel, debate, and achieve consensus.

In the remainder of this chapter, I will introduce the requirements imposed by globalization, the Asian states I have chosen to study, and a range of methodological issues. For each, I will review the related literature, assessing achievements, identifying what remains to be done and explaining what I hope this study will achieve.

PART II
AT THE INTERFACE BETWEEN STATES AND BIO- GLOBALIZATION

Bio-Globalization: Why "Global" and Why "Bio"?

In the literature review that follows, I discuss the two principal themes addressed in the present thesis —the state under globalization and the place of race in the state and in nationalism. Narrative technology and methodological problems I will discuss in Part III.

Globalization is a burgeoning field in social studies. Although the term lacks a precise definition, the dynamic notion of globalization help us to depart from a static, descriptive one of the "global," thinking a process in which we conceive the formation of this world or how it operates. Political scientists David Held and Anthony McGrew (2001) point out the following four types of activity it features. The first is the increase in social,

political, and economic activities across frontiers, regions, and continents. Second is the growing interconnectedness of the various increasing flows of trade, investment, finance, migration, culture, and so forth. Third is the acceleration of the processes through which ideas, goods, information, capital, and people freely diffuse. Fourth is the increasingly fluid boundary between domestic matters and global affairs. Distant events can have significant consequences close to home and specific local developments can come to have global consequences.

The origins of globalization can be traced back to the so-called age of discovery when the "modern world-system" was formed (Wallerstein 1974, 1989). But not until the mid-twentieth century did globalization became a tangible political reality for social science researchers. This was when the gap between the developing and the developed —both economical and political — first appeared in the landscape of global political economy. In response to this trend, some cultural anthropologists integrated Marxist cultural perspectives into their ethnographic works (e.g., Taussig 1983). As Marcus and Fischer (1999) commented, such works suggest that "ethnography is an effective medium for representing the range of moral and cultural responses to capitalist penetrations. [. . .] [W]hat is new about these works is the demonstration of the sophistication of these responses" (90).

Globalization gave birth to bio-globalization in the context of a cultural critique that rose up to reconsider the value of life science. As thinkers struggled with the trajectory that led from Voltaire, Diderot, and Hegel to the horrors of the first half of the twentieth century, the relations among life, the body, power, and control provided a new matrix for understanding the past, as Michel Foucault (1970, 1973, 1979) brilliantly demonstrated in his critique of the European Enlightenment through studies of insanity, structures of knowledge, sexuality, and self-discipline. In addition, quite a few works critically reexamined the rise of science in the context of the manipulation of modernity and power (e.g., Kay 1993), considering how it has governed our conception of life (Doyle 1997; Keller 1996, 2000). This line can be extended even to the cultural criticism of other forms of life, such as the birth and development of cybernetics and artificial life (Helmreich 1998; Keller 2000; Mindell 2002).

The most influential works that emerged were those that treated the operation of the world as technoscientific. The impact of modern biology went far beyond the realm of science proper: the new metaphors of life became mighty enough to shape our perception of the world. A classic is Evelyn Fox Keller's study (1992) of the language scientists used in the development of nuclear weapons, and Donna Haraway has done much to show how life and the world are conceived in light of technoscience. Formerly a biologist, Haraway

has shown how the world has come to be understood in terms of the metaphors and insights of biology. Two of her most frequently cited books, *Simians, Cyborgs, and Women* and *Modest_Witness@Second_Millennium. FemaleMan©_Meets_Oncomouse*™ provide us with a new way to conceptualize globalization. Emphasizing globalization's fluidity, she obliges us to dwell on our new subjectivity in this world, arguing that new relations between humans and machines, men and women, human beings and mice should be redefined: technoscience is rewriting biology as biology rewrites our world.

Echoing the critical approach of Foucault, Keller, and Haraway, more and more anthropologists include science among the subjects they study, considering how it changes our lives and bodies. As Michael Fischer (Marcus and Fischer 1999) noted, science is one of the strategic terrains being explored by ethnography. He later expanded these musings into a rich review article, describing scientific practice, the subjects of this practice, and the philosophical underpinnings of the practice as "emergent forms of life" (Fischer 2003). Thanks to Fischer's broad grasp of anthropology, he is able to show how the contemporary life sciences and biotechnologies have engaged with the technoscientific world, serving as the intermediary between the individual and the global (45–48). Medical practices have become a favorite subject for anthropologists, with a rash of studies have been devoted to medicine in American society as well as in democratic societies around the world (Davis-Floyd and Dumit 1998, Lock et al. 2000). These works, in my opinion, reveal a crucial aspect of bio-globalization depicting how our understanding of life and personhood was shaped in the light of bio-power and the mechanisms it introduces.

In addition to the philosophical perspective, Fischer reminds us of how the life sciences have become enmeshed in the changing relations of state, academia, and the market, just as physics and engineering did long ago (2003: 45). This is the social aspect of bio-globalization that links to the production of knowledge and capitalism Science is now a powerful culture that, as Emily Martin (1997) suggested, it is as if it were dispersed and entangled like rhizomes. This is my intention for the present study. The field is pharmaceuticals, a business that has thrived at the intersection of science and globalization. For millennia human beings have traveled considerable distances to trade in drugs. The word "drug" can refer to either a healing medicine or a poison. As a cure, the history of drugs is closely bound up with the development of scientific medicine (Weatherall 1990). But as a dangerous material that can intoxicate or kill, drugs have a different history, connected to crime and political power (Inciardi 1986, 1992, 2001). A lucrative commodity and balm for the ill, pharmaceuticals promise an interesting story.

Even so, the literature on drugs varies a great deal, depending on whether the focus is on the local or global level. Ethnographic studies of chemotherapy, AIDS, and psychiatric agents have all dwelt at length on drugs (Dumit 1998, Lock et al. 2000). Scholars have examined the intimate interactions between the medicine and the patient, or the conflicts between patients' perceptions of the medication they are taking and the more official interpretation offered by modern medicine. Some research that deals with public health may extend this concern to take in national policy or social movements (for example, studies of responses to oral contraceptive pills). But few anthropological studies have taken on the globalized pharmaceutical industry.

Among the handful of studies of globalization and the pharmaceutical industry,[16] the dissertations of Andrew Lakoff (2000) and Kaushik Sunder Rajan (2002) demand attention. Lakoff looked at how Argentinian psychiatry changed upon the introduction of new drugs from France, while Sunder Rajan traced genomic research from laboratory to industry in the United States and India. Although Lakoff and Sunder Rajan worked on different parts of the pharmaceutical assembly line and did their fieldwork in difference places, the two studies share three traits. First, both scholars were aware of the colossal scale of the pharmaceutical industry and of the importance of understanding its operating logic, which is complex and multilayered because of the need to combine scientific realities and marketing strategies. Second, like Marx 150 years earlier, both were critical throughout their studies, particularly as they examined the fight against the co-production of capitalism and modernity. Although their dissertations were developed at top American universities, both authors also displayed a rare level of self-reflexivity in conducting their investigations. Their studies devote nearly as much space to discussing themselves as ethnographers as they do to the subjects that they work with. Third, and most important, Lakoff and Sunder Rajan tried to describe a global ethnography or an ethnography about globalization. Unlike those who study people in a developed society, such as the United States, or in a remote, well-defined site, they attempted to capture a critical moment when no single site can escape from globalization and ethnographers cannot isolate themselves from their fields. Theirs are not just studies of modernity, the peripheries of modernity, or alternative modernities: these are ethnographic studies of that which is specifically global.

Though these pioneering ethnographies exhibit remarkable sophistication, the

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[16] Though the number of publications remains small, more anthropologists have recently shown an interest in the pharmaceutical industry and its global impact. Ongoing projects include: Adriana Petyrna's study of the CROs in the United States (some of her findings appeared in Petyrna 2005), Joao Biehl's study of Brazil's pharmaceutical industry, and Nancy Chan's study of China's.

relationship between the sites they chose to compare provokes real methodological problems. As Marcus and Fischer pointed out (1990: 90–92), a knowable community, the traditional unit of ethnographic study, may not be suitable for understanding a system of political economy. So they suggested two strategies, seeking relations between the subjects and providing an interpretive frame for the phenomena observed; as it happened, these strategies were, entirely coincidentally, used by Lakoff and Sunder Rajan. The subjects Lakoff decided to present in his story — bipolar patients, Argentinean psychiatrists, and young reformers at Buenos Aires's Hospital Pinero — were linked to one another by the intended and unintended consequences of specific activities: "pharmaceutical reason" is the thread that unites his narrative.[17] For Sunder Rajan, a site is nothing but genomic research and its use in the research and development of drugs. In other words, it can be anywhere in the world. The main concern of his study is not some entity, such as a patent advocacy group in India or a genetic laboratory in the United States, but a set of concepts, including speed, ownership (intellectual property), vision (the potential of a commodity), and subjectivity (of a patient or a nation).

Though they are fascinating, these narrative strategies are not without problems, as Marcus and Fischer pointed out. While they claim to take local culture into account, these works are not interested in the problems of interpretive anthropology. But this is reasonable because when globalization is a theme rather than a vague background, the scale of the writing has to grow to match its subject. (After all, no atlas of the Australian continent includes a street map of every small town.)

To create a meaningful global ethnography of the pharmaceutical industry while maintaining the possibility of a detailed representation of the local, I propose a third narrative strategy: choosing a truly global site as one's field. This is definitely not a return to descriptive realism or a backlash against the abstract approaches that have recently appeared in cultural anthropology. Instead, it is an honest search for new sites and subjects in an age of diversity and global connectivity (Fischer 2003).[18] According to Fischer, creating big interpretative frames is not the only way out when anthropologists have lost their energy (and motivation) by exhausting every distinct, geographical field in the world. Indeed, new fields and subjects are emerging through several mechanisms,

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[17] This approach is explored further by Marcus (1998), whose multi-sited methodology interrogates the distinction between life-world and system. He believes in exploring not only the life-world of his subjects but also some aspects of the world system, by tracing the paths of connections and associations that the anthropologist delineates among sites.

[18] This is related to Marcus's multisited ethnography. In his view, the world system can be ethnographically portrayed by connections and paths decided by the anthropologist. Accordingly, it becomes "integral to and embedded in discontinuous, multisited objects of study" (1998: 81).

such as the new technologies of cyberspace, new medical practices involving surrogate mothers and organ donors, new social relationships among AIDS activists, new media for film and art, and new ways for institutions to communicate and negotiate. Obviously, the pharmaceutical industry benefits from the last. As Marcus and Fischer point out, "Markets and capitalist modes of production, distribution, and consumption are the most obvious views of systems as objects for experimentations with multilocale ethnographies" (1999: 93).

Since drugs are a global phenomenon, we do not have any excuse to reject an emerging site that belongs to our traditional taxonomy of local, regional, and global. The global locus this dissertation will deal with is the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), a unique project that brings together the regulatory authorities of Europe, Japan, and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration. Since I will introduce the ICH in some detail in Chapter 2, here I will simply make some points about the conference that are related to the issues already discussed.

The first issue is about the meaning of this conference in globalization. Despite its global characteristic, the ICH distinguishes itself from two kinds of meetings that deal with the consequences of globalization—one involves the commercial negotiations to decide the price of certain pharmaceuticals or the amount of their production, and the other concerns scientific explorations of new drugs and their uses. The ICH is a conference that attempts to set up universal standards upon which these advanced pharmaceuticals are made and accepted as such. In other words, it presents the origin or the "backbone" of globalization where a standard or set of rules has to be set in order to make the flow of knowledge and capital possible.

The second issue concerns the form of this gathering. Although people from around the world attend this conference, the ICH is not a permanent organization such as the United Nations. It has a clear mission to standardize all requirements for drug approvals and has a clear goal of minimizing the number of clinical trials. In short, the ICH is a locus by globalization, of globalization, and for globalization. When all of its missions have been accomplished, it will cease to exist. It is not located in a place; it is everywhere. Even so, the ICH is not a market, an exhibition, or a trading zone where people gather by chance and talk. This is a locus with a concrete structure. It has rules for negotiation, agendas, and formal guidelines. It has its own official scientific language, and only those who are selected and invited may join. As I will discuss later in the present chapter, this

conference faithfully reflects the power structure of the capitalist world, thus makes it an excellent site for this project.

The third issue raised by treating the ICH as a global site is its ability to act. The ICH is a discursive site with the ability to turn discussions into reality. These are not loose gatherings, but a model of globalization in general, with participants representing selected organizations or states. Every word said in conference is transcribed and the individuality of participants is somewhat regulated by the state or organizations that send them. The acts of the ICH are guidelines, rules for corporations as well as commandments for participating states and their people. Given the function of the ICH, it is important to distinguish among the voices of participants, who include experts, regulatory officials, industry representatives, and the many observers.

Two problems remain. The bigger one, which I will address in the next chapter, is whether the ICH is in any way typical of global institutions. Since it is no simple matter to distinguish the ICH from the world as a whole, I feel obliged to clarify what in the world this conference refers to. The other problem, which is more immediate, is how to interpret the statements made at the ICH. This is the subject I will address over the remainder of this section.

State Transformation in Global Context

There have been so many studies of the nation-state that it is virtually impossible to review them one by one. I will focus on studies that relate to examining the state in the context of globalization.

I want to clarify first why the state is the subject, at least in this study of globalization. I have several reasons. First, as with many international meetings, the state or regional political entity is the basic unit of the ICH. The European Union, Japan, and the United States each reserves the right to send delegates to any given committee meeting; at the same time, attendance makes it that much more likely that the results achieved at the conference will be fully obeyed by all entities. Thus, the regulatory authorities that attend the ICH are accredited by central governments: the United States sends the Food and Drug Administration (FDA), the European Union (EU) sends the European Medicines Agency (EMEA), and Japan sends the Ministry of Health and Welfare (MHW).

The second reason why I've taken the state as my subject is that the ICH's interest

is state-oriented. The three interest groups selected to attend this conference — the Pharmaceutical Research and Manufacturers of America (PhRMA), the Japanese Pharmaceutical Manufacturers Association (JPMA), and the European Federation of Pharmaceutical Industries Associations (EFPIA) — represent the interests of their home states. They are indubitably business groups, entities infamous for ignoring national identity, but at the conference they must act in the interests of their states: they must defend domestic markets from foreign competitors. The universal desire among pharmaceutical companies to sell more drugs encounters resistance at state borders: the aim of the ICH is to subsume the state to the world. Because the ICH needs a juridical body to execute its guidelines and because the only such body that qualifies is the state, the ICH must draw its legitimacy from the states that participate, and their interest has to be part of the system. The third reason for foregrounding the state is related to the scale of my project. I am not intent on studying a small area of the cosmos by adjusting the focus of a telescope. Instead, in order to establish a basic understanding of the sky, I propose a star map in which galaxies indicate the structure of the universe. I am not questioning the significance of microsystems, the operation of trade, negotiations, and exchanges within each state, but mine is a study of macrosystems.

The existence of the state is complicated by the puzzles created by social science researchers. To begin to understand the main trajectories followed by previous studies of the state, I propose a simple two-by-two matrix. One axis is defined by how the state is viewed, reducing the choices to the international and the domestic perspective. The former, as classically declared in the Montevideo Convention in 1933, defines the legal attributes of the state as an entity possessing the following attributes: (1) a permanent population; (2) a defined territory; (3) a government; and (4) the capacity to enter into relations with other states. The domestic view of the state focuses on the relationship between the state and its people; according to this view, the state can be defined as an organization with a monopoly on legitimate violence in a particular geographic area.

The other axis is defined by the source of the state's authority, which is either popular or tyrannical. In the popular model, a social contract affirms the role of the state as serving the people and their interests. The tyrannical model recognizes the dominant role that the state plays in people's lives. Some assail this dominant state for using force to defend the existing system of class domination and exploitation, while some praise it for preserving traditions and hierarchies that benefit society as a whole.

This simple analytical matrix can be used to classify all studies of the state. Unlike political scientists, anthropologists assign the state an important yet remote position. The distinctive quality of the state, as anthropologist Elman Service says, "is the presence of

that special form of control, the consistent threat of force by a body of persons legitimately constituted to use it" (1975: 163). Thus, state control over the people is addressed in works of cultural anthropology or of the anthropology of science and technology, many of which I have cited in the previous section — they emphasize the centrality of the state. To get at how the modern state functions, anthropologists look at how it is constituted, subjecting to critical examination educational and policing systems, medical facilities, bureaucracies, systems used to keep track of individuals, social statistics, culture and ideology, and so on. Such works fall into the category of people-centric studies approached from the domestic viewpoint. The state is cast as the sum of hegemonic apparatuses — apparatuses, it is implied or declared, against which a social movement can struggle. Some researchers extend their critical arguments across national borders, seeking the ultimate origin of systems of coercion in the ideology of colonization and post-colonization (Anderson 1998), dependence and modernization theory, or a diffused yet powerful global government (Gupta 1998; Lakoff 2000).

But the image of the state as a social actor is vague. Even political anthropologists, who study the origin and evolution of early states, present the state as a point of reference, a fixed entity rather than an object of inquiry. As Ted C. Lewellen (2003) has shown, many political anthropologists choose a primitive society for their fieldwork, trying to identify factors, such as food production or population pressure, that foster the earliest steps taken toward a centralized political system. On the other hand, those who study civilization and modern states shift their focus from the state itself to its impacts on its people. As Lewellen pointed out, the concept of the political field was applied with an awareness that "political structures overlap but do not coincide with other social structures and [. . .] they tend to wax and wane over time. [. . . A] political field is nothing less, or more, than the wider area of political activity defined by a particular researcher" (87–88). In anthropology in the modern world, the state seems to be a reference, a fixed grid rather than an object of inquiry.[19]

From the 1960s to the end of the 1980s, political anthropologists were able to create their own terminology, systems of classification, and theories without referring much to what was going on outside of their field. However, by the 1990s it was clear that these tools were no longer sufficient to explain an increasingly complex world, a world "in some ways more integrated and in other ways more fragmented than could be accounted

[19] An exception to this generalization is Michael Fischer's *Iran: From Religious Dispute to Revolution.* Thanks to the intensive fieldwork he carried out before the revolution, we not only appreciate the religious tensions created by the Shiites' denial of the legitimacy of the Pahlavi regime, we also see that these tensions were located in a complicated context of dualistic dynamics involving global politics/state politics, Capitalism/Islam, and modernity/traditionalism.

in either paradigm" (Marcus and Fischer 1999: 203). This opened up a gap between anthropologists and political scientists. While many anthropologists still see globalization as precipitating the decline of the state-centric system, political scientists have rediscovered the state (Keyman 1997, Chapter 3; Evans, Rueschemeyer, and Skocpol 1985; Weiss 2003, Part 3). Although recently some anthropologists have shown increasing interest in cultural diasporas, immigration, the international labor market, and global business (Lewellen 2003: 221–22), these works tend to isolate an individual agency, treating the state as part of a global collectivity rather than an object of analysis (an example is Aihwa Ong's interpretation of "flexible citizenship" in Ong 2002).[20]

This dissertation is dedicated to filling this gap by trying to make sense of the state's behavior from an international viewpoint. In what remains of the present section I will discuss the three kinds of studies on which I have drawn. The first kind of studies presents an interest of policy that can be seen in James Scott's *Seeing Like a State* (1998). Scott looked at the tension between state authorities and various "unstable" individuals throughout history. Numerous scholars have interpreted individual responses to a particular political system is not new (see, for example, Roful 1999); Scott casts the state itself as his object of study, analyzing the failure of some authoritarian states to take into account "the indispensable role of practical knowledge, informal processes, and improvisation in the face of unpredictability" (Scott 1997). The evolution of modern states into flexible organisms capable of responding to requests — Emily Martin (1998) creatively relates this organism to the human body and its immune system — has made it necessary to treat the state as a subject. In the present study, the request made by various constituencies is the provision of high-quality health care.

The second kind of studies concerns the responsiveness of the state, which has already been considered by Marc Swartz, Victor Turner, and Arthur Tuden (1966), all anthropologists determined to go beyond both structuralist and functionalist approaches. The political system gets its "life" when researchers notice the interactions taking place beyond social or ethnic boundaries, allowing this system to change with time. As these authors wrote in their introduction to *Political Anthropology,* the study of politics "is the study of the processes involved in determining public goals and in the differential achievement and use of power by the members of the group concerned with these goals" (7). The importance of Turner in cultural anthropology, as we all recognize, resides in his

[20] A few historians of science have begun to look at global scientific enterprises. An excellent example is Sharon Traweek's work (1996) on Japanese high-energy physicists and their relations with the international community.

emphasis on process and his studies of social drama and liminality (1969, 1974). The subject of my thesis is not a static state but a dynamic one that changes over time. My method involves showing practices as though seen in slow-motion, trying to grasp the moments when the ICH first came to an agreement over universal standards for drug approval. At the interface between the national and the global, we can expect that this encounter will yield more than a simple acceptance or rejection.

Finally, as will deal with two East Asian states, this study is drawn into a substantial literature on Japan and Taiwan, the third kind of studies I would mention here. It is not my intention to introduce them here. I call attention to the characteristics of these two countries to echo policy researcher Sheila Jasanoff's recent comparative study of biotechnology in Europe and the United States (2005). In her study three main arguments are advanced concerning different states' attitudes toward biotechnology. First, current democratic theory cannot satisfactorily explain certain political behaviors if it fails to examine the details of the politics of science and technology. In addition, the policies concerning life sciences have become a more or less self-conscious project of nation-building at a critical juncture in world history. Lastly, political culture does matter to contemporary politics. Following that trajectory, the present dissertation supplements this theme with cases from East Asia, where Japan is suspected for the resurge of military nationalism and Taiwan is anxious for its political visibility.

Table 1.1. Considering the Nation-State: An Analytical Frame

	Civic-territorial (Political/territorial map)	Ethno-cultural (Cultural/cognitive map)
Global level	Interstate system International organization International law Transnational arbitration system	International cultural grammar of nationhood International epistemic communities
National level	State sovereignty, territoriality, and citizenship Signifying symbols (flag, national anthem, etc.) Diplomacy Military Border control	"National culture" Language Cultural patrimonies "Nation-view" and knowledge systems (history, literature, etc.)

Source: Wang 1999: 51.

In order to study the problem of the nation-state in the global scene, political sociologist Horng-luen Wang has proposed an interdisciplinary approach (1999, 2000,

2001). He suggests first that the nation-state be understood in relation to the world. In a context broader than straight politics, Wang defines a nation-state as a political and cultural product derived by demarcating a territory within the networks of the global. The related fields can be variously categorized as civic-territorial and ethno-cultural (table 1.1). According to Wang, no clear line can be drawn between culture and politics, or between nationalist reality and pure nationalism, when dealing with a modern nation-state. Instead, "it is an institutionalized form [of life] whose existence relies on the operation and context of a given institution" (Wang 2001: 197). From this institutional perspective, traditional attributes of the "imagined community" might not be enough for global institutions; furthermore, a nation-state can be recognized in fields not limited to politics. Wang has argued that tourism, fashion, popular culture, and sports are all part of everyday life and are places where nationalism can arise (224–25); I would like to add medicine to this list.

A study of pharmaceuticals seems to fit perfectly into the above matrix. In the left column of civic-territorial, which is state-related, we have the ICH as the international field and a regulatory authority for drug approval as the domestic counterpart. Taiwan's national problem becomes a crisis of representation, fulfilling all that is expected of a state at the national level (lower left cell), yet failing to show its proper existence at the global level (upper left cell). However, shifting to ethno-cultural concerns, it is not clear that race will help us understand state in globalization (right hand cells). I shall discuss this in the next section.

Reading Race into the State: Toward Nationalism and Globalization

Questions about race have recently given rise to heated discussion in the social sciences and the life sciences. As the anthropologist Ashley Montagu (1942) sets the title of his study of race (1942), race is human beings' "most dangerous myth." Indeed, race is a socially conceived category rather than a scientifically measurable phenomenon. In his well-documented *Race: The History of an Idea in the West,* Ivan Hannaford traced the conceptual roots of modern race theory to natural philosophy, early anthropology, and the search for national characters, continuing the historical narrative with the late nineteenth century's systematic pursuit of the biological and historical origins of the racially pure state (Hannaford 1996: Part 2). Race was all and the state was the political tool to regulate it. Montagu published his plea during the heyday of Nazism in hopes of delegitimizing the Third Reich's racist political doctrine.

Even so, neither Montagu nor Hannaford rejected research on ethnic variations;

they were opposed to the perpetuation of myths and ideologies based on race. As Montagu reasoned, "There are numerous differences between ethnic groups, and even regional segments of such groups, in many bodily and genetic traits. These differences are real enough, and they are of the greatest interest to the student of variation. [. . .] Differences are not denied where they exist. What is denied is that they are biologically either great or significant enough to justify men in making them the pretext for social discrimination of any kind" (1942: x–xi).

But progress in medical research and social changes — if not polarization or stratification — complicate the landscape. The distinction between the medical and the social has already become blurred. Bodily differences have become bio-information that predetermines people's lives, while social distinctions have evolved into delicate controls deep in the disciplines of body and mind. In modern societies, the nation-state is no longer at the top of the guilty list for exercising racist ideology. Scholars devote considerable effort to recognizing and negotiating the cultural and political tensions among ethnic groups whose geography defies national boundaries. As Hannaford pointed out, "Ethnicity is essentially an idea introduced in modern times, and it has prospered in proportion to the decline in political ideas concerning the disposition of civil affairs" (1996: 398). As researchers try to comprehend a complicated society, ethnicity becomes an analytical variable, along with other items such as gender, age, and class.

As this happens, the biologically oriented concept of race is gradually replaced by a broader, socially constructed concept of ethnicity. Today anthropologists study the social assumptions that construct the image of "the other," and the study of anatomical variation has halted. I want to say this more clearly: while differences in cultural heritage, religious beliefs, and linguistic characteristics are noted, biological differences are largely ignored. This is especially so in the field of STS, which has been deeply affected by social constructivism. As they try to counterbalance the prevailing biological determinism found in medical research, social constructivists tend to argue against the suggestion that biology affects complex social behavior.

Let me cite two recent examples. In June 2003 *Technology Review* published an article describing a debate over race that accompanied the emergence of genetic medicine. The HapMap project, an international project aimed at building a huge genetic database that would help scientists make comparisons among different ethnic groups, is one of the latest targets of critics' concern.[21] They worry that these data will be manipulated to give credence to ethnic stereotypes or to revive discredited racial classifications. Scientists

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[21] For a detailed introduction to the HapMap project and its role in the ICH, see Chapter 8, Part 2.

have fought back by simply calling the critics "nihilists" because they did not come up with alternative methods for carrying out this genetic research.

My second example is drawn from the clinical side. Observant physicians are reminded frequently of the ethnic differences among their patient pools: as Sally Satel admitted in the title of her *New York Times* article (2002), "I am a racially profiling doctor"; she went on to say, "Certain diseases and the approval of treatment responses cluster by ethnicity." Drug companies are also aware that special treatments for different ethnic groups constitute an emerging market. But they know that caution is necessary, as has been shown in a furious debate over the clinical trials targeting African-American heart failure described in the May 2001 issue of the *New England Journal of Medicine* (for a more detailed report on this controversial case, see April 2005 *Technology Review*). Robert S. Schwartz, one of the journal's deputy editors, wrote that taking race into account when prescribing medication was both morally and scientifically wrong: "Race is not only imprecise but also of no proven value in treating an individual patient" (Schwartz 2001). As serious discussions take place, the agenda is silently and steadily moving toward individual, gene-based medication guided by racial categories.

Most anthropologists prefer to leave these problems to physical anthropology, the anthropological counterpart of evolutionary biology. They know that there has never been such a thing as a pure race; they know that there is no causal linkage between physical and behavioral traits (AAPA 1996). However, no alternative has exactly replaced the category of race, no matter how crude it may be, in the production and circulation of anthropological knowledge. It may be possible to achieve a lot by criticizing the approach scientists are taking from *outside,* as the American Anthropological Association did in the statement cited earlier, but in my opinion, such arguments amount to hollow warnings rather than constructive suggestions, calls for an ethical line that medical experts and clinicians must not cross. Such arguments usually conclude by asserting that medical practices are part of a range of modern institutions that aim to control people, as if these critics are living in a paranoid universe.

The problems are many and the present thesis will not answer them all. I will not try to criticize the idea of race *outside* the medical arena, but I will try to show how it cannot work *inside.* The ICH is a perfect locus for such a project. The issue of racial difference appeared early in the history of this conference, in the context of whether the data from clinical trials conducted in foreign countries or regions should be accepted as universally valid. Some scientists from Japan and Europe insisted that racial differences should be taken into account, because the distribution of reactions to certain drugs among Japanese

patients differs from that among Caucasians. A scientific understanding of race was required and an expert working group was assigned to work it out. Although from 1993 to 1997 these experts met many times and drew up over twenty drafts of a guideline on racial differences, no consensus was reached. The Japanese delegates thought that the racial differences between Japanese and Caucasians were fundamental and that thorough studies would need to be carried out before any guidelines were completed. But the delegates from the United States and the EU — which are the site of over 80% of the world's clinical trials — did not think that there was much variety among the peoples of the world. They accepted the existence of some differences between Asians and Caucasians, but they firmly believed that, in the end, all human beings should be considered the same, rendering a universal standard possible, so long as it included some local modifications. This disagreement was never resolved, and though a vague guideline was implemented in 1998 the situation was still a nightmare for drug companies: almost every drug had to undergo long and expensive clinical trials wherever it was going to be marketed.

This is a problem both familiar and strange to anthropologists. Familiar, because it concerns racial difference in medical research and clinical trials, and because it has clear social implications, such as people's access to the latest drugs. Even so, it is also strange because, uncharacteristically the Western medical mainstream acted as if all racial differences were bridgeable. What can be prescribed to Caucasians should also be prescribed to Asians. The opposing group, arguing for "race-based medicine," is Japan, an Asian power infamous for its racist nationalism during World War II. That old purveyor of racism, the nation-state, seems to have returned, but anthropologists have forgotten how to deal with it. I would like to remind readers of the scene I mentioned at the beginning of this chapter, when that anthropologist spotted something interesting in the Japanese conception of race but did not know how to make sense of it. Indeed, in the global era, when interactions among races and huge waves of immigration shake the traditional definition of race, the relationship between the state and race has become a very tricky research topic, but it certainly should not be skipped. To pursue this topic, old models of race and nation have to be discarded.

Hannaford (1996: Chapter 5) has reviewed how race played a part in the creation of nation-states (or race-states) in the nineteenth century. However, if we review the idea of race in the context of nationalism, we find that remarkably few biological characteristics belonged to the academic discourse. Although nationalism can be historically defined as the combination of several factors, including lineage ties, shared language, religion, cultural heritage, and life and historical experiences (Hobsbawm 1990), much as we

expect a discussion of race it just isn't there. It may have played a part in building a nation, but it soon lost its position to political institutions, which became the arbiters of difference (Giddens 1985).[22] Although nationalism tends to be ethnic in character, this is not necessarily the case.

But East Asian states are virtually unique in terms of the relations between race and state. Eric Hobsbawm has connected the racial homogeneity of Japan, Korea, and China to their citizens' sense of national identity and political loyalty (1990: 66).[23] This topic has been much discussed among Asia scholars. They all note the distinctive discourse built on the idea of a single origin for the Japanese race, identifying that race with the surrounding polity. The discourse was crystallized when developed ideas about the modern state were introduced to Meiji Japan (1868–1912). As the state pursued the goal of "a rich nation, a strong army" (*fukoku kyohei*), a naïve set of ideas about common descent and shared biological traits evolved into the complex *nihonjinron* (theories about the Japanese). These theories described relationships among the Japanese (developed out of the dyad self/others) and with foreigners (insider/outsider), while also erecting a collective goal for the entire "race" based on social Darwinism (Weiner 1995). The Japanese *minzoku* emerged as an ontologically unique existence that defines itself through itself. It can be seen in the individual pursuit of pure self, but the collective enterprise of building a wealthy nation is just as significant. Race and the state are in Japan two sides of the same coin.

The above belief does not disperse when Japan has more contacts with outside world. In fact, the notion of *kokusaika*, which can be roughly translated as "internationalization," closely linked to ideas about nationalism. *Kokusaika* and *minzoku* occur in close proximity to such terms as *kokumin-shugi* (civil nationalism), *kokusui* (national essence) and *junketsu-shugi* (pure-bloodism). Let us return to Japan's "ridiculous" insistence on its racial uniqueness. In her study of how people think about death and organ transplants in Canada and Japan, anthropologist Margaret Lock (2002) has reminded us that the point of such an investigation is not to adjudicate whether Japan

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[22] Benedict Anderson (1983) assigns virtually no weight to biological factors in the construction of an "imagined political community." Racism and myths based on race are, according to Anderson, rather a consequence of the formation of a community and an internal affair among the dominant race and minority groups.

[23] The idea of "one race, one nation" has influenced political relations between the PRC and Taiwan. When the former denies the political sovereignty of the latter, the reason is often that both are of the "same language, same race" (*tong wen tong zhong*) and so must act as a single nation. This idea has affected Taiwan's domestic politics: some political parties cite the same argument when they insist that Taiwan should be a part of China. On the invention of Han "race" and the Han nation, see Kai-wing Chow 1997.

should accept the definition of brain death in its medial practice, but to gain an appreciation of both Japan and North America through continuous reflections on the debate over this issue. Adorned with culturally and socially specific attributes, death, according to Lock, "will not be pinned down once and for all" (377).

As Lock's thesis implies, anthropologists cannot make sense of Japan's ideas about race without considering its ideas about the state. Moreover, because these ideas are manifested most clearly in Japan's relations with other countries, any assessment ought to be made in a global framework instead of a national one. The key to understanding Japan's resistance to Western standards is a reassessment of race and an abandonment of the idea that all nations subscribe to the same universal beliefs. Nancy Stepan's historical study has successfully demonstrated that the idea of Latinity is different from the Anglo-Saxon view of race: while the latter is monolithic and excessively biological, the former is multiple, reflecting the divided nature of politics in Latin America (1991: 190).[24] In fact, Stepan showed that even science is not universal in her story. As she asserted: "The adoption of a specific scientific theory within scientific circles and elsewhere is not a purely empirical, logical, or evidential matter but a historical and political one. [. . .] Science that get taken up by particular groups or attached to specific institutions cannot be explained solely by reference to their purely factual character or truth states" (197). Echoing this idea, this thesis will not address whether Japan has "misunderstood" the meaning of race. Instead I examine the similar concept of *minzoku,* showing how advanced sciences, such as genomics and biostatistics, are incorporated into Japan's agenda on racial difference at the ICH.

Consider Horng-luen Wang's analytical frame, introduced in the previous section and illustrated in table 1.1. Let us call *minzoku* the sum of all national ethno-cultural institutions (lower right cell); politically these correspond to the Japanese state (lower left cell). However, this mingled identity is challenged by the ICH through two global institutions: one is the civic-territorial institution of the conference (upper left cell) and the other is the ethno-cultural institution of universal standards where the operational definition of race is determined (upper right cell). Thus, we find that Japan's attitude toward its race and its state is always hard to capture. I will state, as my own "uncertainty principle," that Japanese race and state cannot be simultaneously measured with any degree of precision. Rather, these have to be monitored as elements of a diachronic process viewed from a global perspective — this is exactly what I try to do in the

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[24] Of course, race and nation building in Latin America are parts of a complicated process. The creation of a hybrid race, known as *mestizo,* implied a racial politics that rejected the Anglo-Saxon race on the one hand and excluded "undesirable" groups of Chinese, African, Syrians, Jews, and Gypsies on the other.

following chapters.

Before ending this section, let me comment on two statements frequently made about Japanese race and nationalism, which I jointly refer to as state determinism. One is in the field of international trade. Since race is considered a fictitious category, it is often said that Japan's insistence on the uniqueness of the Japanese race is a hypocritical defense of protectionism, a means of protecting a share of its national market against global partners. Though this is interesting, it fails to explain why even the world's top scientists cannot solve this problem by just giving a workable definition of racial difference. The other statement is political and more widely known: in response to recent nationalist claims by the Japanese Right, many foreign observers have spoken of the coming revival of nationalism and militarism. At times statements from the Right seem one short step away from calls for a pure race. But I think such a conclusion is too hasty. Although the concept of race does figure in contemporary Japanese political thinking, it is not always connected to nationalism. I agree that race is an important parameter when considering the state in the modern world; however, the old model of the nation-state may not be able to accommodate the complicated relationships that have arisen during the global era. Although anthropologists no longer participate in discussions of the biological construction of race, I will try to show here that in the context of state and global politics, particularly in East Asia, ethnography is still the best critical tool for getting at state policies on race from *inside* its practices.

PART III
WRITING ON THE ETHNOGRAPHY OF STATES: AGENCIES, SITES, AND VOICES

States as Anthropological Agencies

In my discussion of methods I will address three related issues: (1) whether the state can be an agency for anthropological inquiry; (2) what characteristics a site must have for states to be recognized as active and responsive; and (3) how to identify a state's institutional voice. The intrinsic relations between these topics will be shown in the order of their appearance.

The thorniest of these questions is perhaps how to treat a state as a workable agency

(character) in an ethnography.[25] States are everywhere personified. This is especially true when talking about the state within an international context, where one never even thinks about the implications of such passages as "In the global village, Japan is uncooperative, always carefully protecting herself" or "Because of its long isolation, Taiwan is an orphan in the global community." But what do such statements mean? Are they merely analogies, or are they something more? Political scientists tend to think of the state as a person and they construct knowledge based on this analogy; an extreme case is the scholars committed to "bringing the state back in," who are fond of terms like "state actor," "state's behavior," and so forth (Evans, Rueschemeyer, and Skocpol 1985). Certainly we live in metaphors; still, it is different to talk about the role metaphors play in the construction of a systematic body of knowledge. For instance, Evelyn Fox Keller has shown (2002) that molecular biology — a specific way of explaining life — was created by the metaphors and models borrowed by biology from cybernetics and mechanics. While I am opposed to the view that the state possess a personality that scholars can study, what is at stake is not whether one can accurately speak of the agency of the state, but rather whether this metaphor can generate (guide, shape, evolve) a systematic knowledge.[26]

This perspective leads us to look at this question from another angle, namely, whether the state is represented as a person in anthropological texts — the answer is of course positive. Clifford Geertz reminded us that the core of anthropology is a cultural institution. He wrote that anthropologists are constantly trying "to convince us what they say is a result of their having actually penetrated (or, if you prefer, been penetrated by) another form of life, or having, one way or another, truly 'been there.' And that, persuading us that this offstage miracle has occurred, is where the writing comes in" (1988: 4–5). Two questions about the author and the text immediately arise: "The first question, call it that of signature, is a matter of the construction of a writerly identity. The second, call it that of discourse, is a matter of developing a way of putting things — a vocabulary, a rhetoric, a pattern of argument — that is connected to that identity in such a way that it seems to come from it as a remark from a mind" (9). Writing and written must be considered together; anthropological agency is defined as that which generates a

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[25] For example, Michael Fischer is evidently uncomfortable when referring to an anthropological or ethnic unit higher than the individual. See Fischer 2003: 11–12.

[26] Lily Kay explains this standpoint clearly in her understanding of the genetic sequence, or the "book of life" (2000). Differentiating her approach from the objectivist, constructivist, and deconstructivist vantage points, Kay situates her post-structural understanding of genomics as "the presentation itself that guides the imagination and reasoning, as was the case with the idioms of 'information' and 'knowledge.'" From this viewpoint, "it is the writing itself that writes" (xviii).

strategic text addressing the relationship between this writerly identity and others. If we extend this argument to all of the identities appearing in an anthropological text, our question becomes: can the state be a writerly agency in a given ethnographic text, able to write and to be written about?

Though clearer, this question is still difficult to tackle. Perhaps it should be asked as a negative: why cannot the state be a writerly agency? Two immediate answers, or the same one doubly claimed, occur to me. One, which is a quite intuitive and true, is that the state is not an ontologically existing individual that the ethnographer can interrogate; the collectivity of the state makes it a conceptual term rather than a concrete object for anthropological inquiry. The other answer relates the state to its artificiality: it is a subject conceivable only through the actual agencies that stand in for it: the people concerned. These prevent a state from taking an active part in an ethnographic text. I will try to respond these assertions, focusing more on the issue of artificiality, since the problem of collectivity has haunted ethnography from its earliest days and I have little to contribute there.

Even after identifying a manageable unit for study, ethnographers run into problems. The difficulty of examining all of the components of a subject is often disguised by narratological devices. The question is not whether the ethnographer has successfully solved this problem, but whether the text generated is conventional enough to convince the audience. A typical example is Marjorie Shostak's acclaimed *Nisa: The Life and Words of a !Kung Woman* (1983). The book takes the form of a series of conversations between the ethnographer and an exceptional and outspoken !Kung woman named Nisa. In order to convince her readers of the reliability of the description, Shostak wrote an extensive introduction to !Kung culture before presenting her informant's narrative. Shostak also opened each chapter with a description of a specific stage in the lives of !Kung women, based on other sources. At a dramatic moment in the book, Nisa's peers warned the author that her informant was a liar; only when Nisa told an impressive story about herself was the truth revealed.

Shostak's story is so compelling that readers generally find themselves deeply moved. But the problem of the relation between the whole and its parts remains. I am not concerned with the question of Nisa's veracity; rather, I am troubled by how this work of ethnography was made. More exactly, I wonder about the conceptual gap between the word "a" in the title (*a !Kung woman*) and the presumed "the," the entirety of the !Kung tribe. Whether Nisa told the truth has no bearing on whether all !Kung women can be presented by this single person. In fact, in reading Nisa's narrative, we are not considering only her; instead, we are imagining a whole group of people, with a writerly

identity, speaking though her.

Though this thesis steers clear of this epistemological problem, I am aware of it and to bridge this potential gap I have used the most conventional narrative styles, such as plain descriptions supported by statistical data and examples. Still, in studies of an ontologically conceivable group (tribe, community, society, etc.) we tend to accept the slippage between individual informants and an imaginary writerly identity without any good reason. If this problem occurs in all attempts to relate the parts to the whole, it is certainly true of an ethnographic consideration of the state.

Anthropology is about human beings. Certainly the state is anthropogenic, an apparatus that fits into no category in traditional anthropology.[27] But this does not mean that this thesis cannot find allies among recent cultural ethnographies, especially studies of science and technology. The works I would like to discuss here are Joseph Dumit's *Picturing Personhood* (2003) and Stefan Helmreich's *Silicon Second Nature* (1998). In my opinion, these very different works not only extend the interpretative power of ethnography to the technoscientific world, they radicalize — silently and perhaps unwittingly — the discipline of anthropology by reminding us of its original aims, which so many of its practitioners have forgotten. They both ask what on earth human beings, life, and personhood are and how they are to be represented.

Dumit studied positron emission tomography (PET), an imaging technology now widely used in psychological research on the brain. His method involved tracing the "social life of things" surrounding PET: how the experiments were designed, how human categories were defined, how the results were created and interpreted, and how these results became part of the circulation of knowledge and social relations. The object of analysis is not just a machine or a technology applied to it but a lived relation among cultural actors: "To the extent that things such as images and technologies are attributed agencies [. . .] they, too, participate in cultural exchanges" (10–11). Let us look more closely at the idea of "attributed agencies." If we consider the difference between an ontological existence and an identity exhibited in the narrative, inconsistencies start popping out of this ethnographic text. While the ontological existence of PET is always that of a nonhuman actor, the focus the author writes about shifts from PET to the inventors who developed the idea of this technology, to the images that can be interpreted in a particular way, and, in the end, to a biomedical personhood able to replace our true personhood. The more of *Picturing Personhood* we read, the further we depart from the

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[27] As mentioned previously, political anthropologists tend to base their insights on an awareness that

argument that PET is a merely a nonhuman actor of no importance. This change always depends on the context involved; in the end, it gives readers a feeling that it is the writerly identity called PET that initiates various relationships and discourses in this narrative.

Perhaps this shift began at very beginning of this book, when the author spoke of multiple interpretations of the history of PET (Chapter 2). When the editors of a science encyclopedia invited Dumit to produce "an objective, historical narrative [about PET], in the third person, past tense," his research unearthed a variety of deterministic historical narratives, written from different perspectives, having different focuses, which even contradicted each other. He abandoned the original plan to write a simple historical explanation of PET and instead composed an analytical text in which readers came to understand the social relationships among inventors through PET. Fine. But what I am interested in is the creation of a writerly identity as his project changed. I agree that scientific history is a genre where clarity of subject is achieved by sacrificing the messy, intercontextual trajectories that propel the subject's development. But when PET is shifted from the subject to a factor entangled in social relationships, a writerly identity is formed and, for readers, a new narrative network is created.[28]

This writerly identity keeps changing and growing as readers move to the so-called biomedical personhood introduced in Chapter 5 and 6. Assuming that readers would see PET images as reflecting personhood, Dumit describes the most striking situation where this problematic personhood produced by this writerly identity usurps the position originally occupied by intuitive personhood in our cognitive web. The differences between the two personhoods illustrate the effect scientific research has had on our conception of our minds. Meanwhile, at the representational level, this full-grown writerly identity completes the narrative of this change. Dumit even projects this personhood back to the real world by showing a "scientist" and an "anthropologist" on his book's cover, both appropriately labeled. Perhaps this provides the key to Dumit's larger project: in the modern world, where only biological signals can be recognized and justified, biomedical personhood should be the fundamental agency we deal with, not the personhood anthropologists take for granted. On the narrative level, biomedical personhood should be considered an active writerly identity able to generate meanings by exploiting human supporting actors.

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behind the political system in question is a group of human beings.

[28] One example of the change in writerly identity can be found by comparing two quotations: "the history of PET is still under construction" (49) and "one kind of ideal PET machine would have a resolution small enough to show each neuron" (78). The distinction between the subject and the actor is clearer in some languages than others: in Japanese the former is used with an auxiliary *wa* while the latter takes a *ga*.

Silicon Second Nature exhibits a set of concerns that overlap with Dumit's, but Helmreich headed in the opposite direction. Unlike Dumit, who started his inquiries with a machine said to produce faithful images of personhood, Helmreich started with a computer that created artificial life, an existence by definition totally different from that of human beings. Like Dumit, Helmreich looked for answers in the social, thus his first task was to bridge the difference between the artificial creatures and their creators. Referring to Hegel's notion of first and second nature, Helmreich identified artificial life as second natures: "They are rule-ordered human constructions, but they are meant to mirror first nature. And they are second natures in still another way: they not only ape first nature but also offer to replace it, to succeed it as a resource for scientific knowledge." When researchers "embrace the logics of synthetic vitality, they come to possess a new sort of subjectivity, a silicon nature that may be increasingly common among humans inhabiting a world in which computers are haunted by 'life'" (Helmreich 1998: 11–12).

Though inclined to set it in quotation marks, Helmreich made artificial life a writerly identity all the way through his book. He approached this in-between position from a different direction than did Dumit. While the latter detached the socially constructed personhoods he created from real ones, Helmreich tried to show how close artificial forms of life were to real ones. As a writerly identity, artificial life is humanly alive; more accurately, artificial life functions as a miniature of the human species. From this viewpoint, Helmreigh's book is a record of the evolution and civilization of artificial life: it has primitivity; it has competitions and slaughters; it has problems of heredity; it has tensions surrounding gender and sexuality; it connects to the spiritual. It pursues an anti-Durkheimian agenda of forming a society by religion; it cries out for salvation; it even thinks of the meaning of life, as Nietzsche and Schopenhauer did in the nineteenth century, and the meaning of self, as Sartre did in the mid-twentieth century.

But this narrative project was not complete without the coda Helmreich added at the end of his book. There he described his interaction, as a narrator and an author, with a quite childish artificial life form made in Japan called Tamagotchi. He treats this dialogue as a sign that human beings are about to be swallowed up by the world of artificial life both without and within (the scene of the meeting with Tamagotchi is a thoroughly cyberneticized New York City). Citing one of the scientists he interviewed, Helmreich commented that the future of artificial life is not simulation-as-we-know-it but simulation-as-it-could-be (1998: 256). Concerning this observation, I would say that what is most frightening is not the competitiveness of this form of life, but rather the absence of a notion of "we" in its future. Possibly at stake is the disappearance of the

ethnographer: a biomedicalized personhood could produce its own ethnography.

I think I have answered why the state, even recognized as a collective and artificial entity, can function as a writerly agency in ethnography. In the present dissertation, I treat Japan and Taiwan as writerly agencies. As the optimistic discourse of globalization dominates the globe, Japan worries that the racial characteristics believed to be the foundation of the state may disappear, while Taiwan views globalization as an opportunity to gain international recognition.

Two works in the field of science and technology provide insights into the narrative context in which such writerly identity is located and functions. The first is Donna Haraway's masterpiece, "A Cyborg Manifesto," which catalyzed countless debates on the concept of the cyborg and its possible implications in the social studies of science (for example, Downey and Dumit 1997). But in the original text the cyborg was not an isolated entity in the real world, nor was it a fictional illusion: it was a writerly identity. To be exact, the cyborg must always be thought of as a cyborg *in context.* Haraway was fully aware of the power of a text and of reading, so she intentionally seduced her readers into seeing themselves as reacting to the real world *as if* they were cyborgs. This goal cannot be achieved without constructing a textual world that playfully mimics the real one while reorganizing it according to science and technology studies, socialism, and feminism. Only through the continuously intertransforming processes, which switch back and forth between the two worlds, can these cyborgs (or readers) come to understand (or be misled about) why they are not allowed to march in the ranks of Marxism as well as feminism, realizing finally where they should go. The tools she uses are "stories, retold stories, versions that reverse and displace the hierarchical dualisms of naturalized identities" (Haraway 1991: 175). As Dumit and Helmreich did with their writerly identities, at the end of this text Haraway presented herself as a cyborg author devoted to subverting Western culture, a "central myth" that had long dominated our intellectual lives. All textual identities, which have shown the way for new connections and relations in the text, have to project themselves into the real world. The link between the real and the fictional is the act of reading. Writerly identity determines its own appearance in a text; genre and context determine how it will be linked to reality. Fully aware of this, Haraway identified her text as both provocative and constructive, a blasphemy that "protects one from the moral majority within, while still insisting on the need for community" (149).

The final methodological requirement for making such an ethnographic text is that we liberate ourselves from the idea that such a text may treat only human beings as actors.

Anthropologist Bruno Latour (1993) provided an alternative approach in his acclaimed study of Aramis, an effort to design an automatic transit system that ultimately failed. In response to the criticisms raised by social constructivists, and others who attacked him for his alleged relativism, Latour carefully developed his ethnographic text around social networks rather than any objective entity.[29] Calling this approach both "distributed monism" and the "anthropology of objectivity," Latour warned scholars against trying to explain a stable object whose voice was socially constructed; the alternative he proposed was following the social network (in other words, the context) in which all humans and nonhumans interact. Applying Durkheim to science and technology, Latour claims that there is no basic difference between ontological entities and socially recognized entities: both have to be unified in a comprehensive text that he proclaims as ethnography. Any action away from this locus of inquiry, according to him, is a waste of time (395). This powerful argument obliges me to identify the context for my own writerly agencies.

Conferences as an Experimental Field for Ethnography

The second methodological issue here is the way the global and the national present themselves. Until now I have mentioned my field of inquiry only fleetingly. I have mentioned several institutions and organizations, but I have told my readers nothing about the context in which these entities interact. I hereby propose an experimental field for ethnography: conferences.

I call this site experimental because, although the conference is not an institution that first arose within modernity, almost no anthropological attention has been paid to it.[30] This does not mean that people think that the conference is nothing but a formal gathering. All who attend them, especially *Homines academici,* intuit immediately which role they are assigned to play.[31] However, here it requires an analytical scrutiny. For those involved, conferences are all about social relations and the accumulation of capital (cultural/social/economic) in a given milieu. The organizer of a conference would like to optimize its value by lining up the most impressive list of participants. These key figures work sessions into their schedules, which are full and tight. Special events, such as

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[29] The debate between Latour and scholars from the Edinburgh school over the ontology of science studies was played out in volumes 30 and 31 of *Studies of History and Philosophy of Science.*

[30] Among few ethnographies using international conferences as a working site, see Riles 2000.

[31] In *Homo Academicus,* Pierre Bourdieu notes that participation at scientific conferences is an important indicator of academic capital (1988: 46). He points out that conferences may be used to analyze the power structure of an academic system (241).

keynote speeches, special lectures, or round-table discussions, are scheduled. Those who are not featured speakers largely function as spectators, and while they are not the main characters in this social drama, by attending they are able to collect the latest useful information, which for them is certainly a form of capital. Sometimes they add to their academic capital by asking an impressive question or by meeting one of the big names. In addition to cultivating such relationships, for outsiders conferences are a "ritual of institution" that bestows value and authority upon the words spoken (Bourdieu 1991: 117–26).

I see three principal dynamics functioning at conferences. First of all, the conference is the site of a conversation, a formal discourse. If we acknowledge Jacques Derrida's differentiation of writing and speaking as central to the development of our logocentric civilization (1976: Part 2), the conference resists progress. Unlike the bazaar in anthropology and the trading zone in the history of science (Galison 1997: Chapter 9), the conference is a locus for discursive performances with a clear procedural structure. Just as important, at its conclusion the results of the conference are written up, and while the framework of the conference suggests that ideas can be worked through on the spot, improvised, reformulated, the playful aspect is always subordinated to the need for a stable final result. This makes the conference an interesting site. A modern version of the panorama or the universal exhibition, the conference visualizes and verbalizes the desires and the relations of dominance and submission among their participants (in the case of this thesis, the states). Words and actions are directed toward agreement, yet most of them are unstable, lacking any regulations and yielding no publications. I believe that conferences can be understood as a collective, dramatized action that turns speech (thoughts) into writing (representation carries symbolic power): they constitute a space that deserves an interpretative ethnography.

The conference brings people together for an exchange of opinions, which is its second dynamic. But there are two ways to think about this. On the one hand, people gather and work together toward a goal by exchanging opinions. On the other hand, different opinions are recognized by consultation and comparison. In short, the conference is an arena where both controversies and consensus are expected; tensions and conflicts provide punctuation marks on which a cultural interpretation can be built. Consider the debate over racial difference at the ICH as an instance of controversy within a context devoted to finding consensus. The social drama of racial difference and its resolution at the ICH provides two scenarios illustrating the paradoxical dynamics of the conference. The ICH is devoted to creating a universal standard for drugs and among its guiding principles is the importance of neglecting racial differences as much as possible.

However, this issue assumes differences among races. The tension thus comes about because the ICH has to recognize all the differences on one hand — that is the reason for having this conference — yet its goal is to unify them by means of scientific tools. In order to achieve this goal, the ICH allows a range of possible interpretations of racial difference, but these interpretations would be melted into a consensus, no matter how limited it may be, as a result of communicative skills and political manipulation. The ICH is a promising site for observing the merging of a range of opinions into a single standard.

The third dynamic can be observed over a series of conferences. Although the goal of conferences is to achieve consensus — or, at worst, conclusions — this is rarely achieved in a single meeting. When issues are complicated, opinions tend to be at odds, and no number of sessions will suffice to resolve differences: resolving the disagreements must be postponed until the next conference. Often such postponements arise out of a practical need: more can be done through informal exchanges of ideas after a recess has eased tensions. To ensure the next conference can pick up where the last one halted, records are needed, either formal documents (memorandums, minutes, announcements, proceedings) or informal notes (participation reports, memoirs, presentation slides, news releases).

These materials create a living archive — living because of the two ways one conference can link to another ethnographically. Until a formal conclusion can be reached, the archive cannot stop expanding. Conferences have long adopted a rule governing the use of this archive: it calls for reading the minutes from the previous meeting when a new round starts. Additionally, through various written and visual technologies, even informal materials can be indefinitely preserved and disseminated. The second way to consider these materials as living is the use the participants make of them. Although oral interviews can be of great utility in anthropological studies, my field experience convinces me that recorded materials themselves are more reliable. Burdened by everyday routines, many experts rely heavily on this kind of material as an aide-mémoire: these memories represent the nature of the conferences, both fragmentary and periodic. Participants base important decisions on these materials, and these decisions will be presented at the next conference. Observers find that these materials are the only record of actions inside a conference: they can be traced and counted, both serially and sectionally.

My concern is the debate on racial difference at the ICH, and several series of meetings on the subject have built up a rich deposit of materials. In addition to regular meetings of the Steering Committee and the Expert Working Group, many conferences

and symposiums not organized by the ICH have addressed this topic. For example, the CMR International Institute for Regulatory Science organized some technical workshops and conferences on ethnic factors, which collected early opinions from the European Union and Japan. Conferences and panels continued to be held even after a guideline was established; the annual meetings of the American Drug Information Association (DIA), for instance, are attended by experts in regulatory science and industry. Other meetings, such as the most recent International Organizations of Medical Sciences meeting on pharmacogenetics, addressed related topics and are reviewed here. The Quintiles presentation I cited at beginning of this chapter is just one other example.

Many conferences and meetings were held in East Asia and neighboring areas concerning the ICH and racial difference. In 1996 the DIA held its Asian meeting in Tokyo and since then meetings have been held in Taipei (1998), Seoul (2000), and Singapore (2005). The International Federation of Pharmaceutical Manufacturers Associations (IFPMA) held a series of conferences, the first in Hong Kong in 1997 and subsequent ones in Singapore (1999), Thailand (2001), and Beijing (2004). Regional meetings are also relevant. The most important is perhaps the APEC pharmaceutical network on bridging studies, which originated in 2000 and is held annually in either Japan (Tokyo in 2002), Taiwan (Taipei in 2000, 2001, 2003, and 2005), or Korea (Seoul in 2004). Also worth mentioning is the Kitasato-Harvard symposium organized jointly by Harvard's School of Public Health and Kitasato University's Division of Biostatistics, and held annually in Tokyo since 2000. Despite their academic orientation, these annual symposiums are closely watched by government and industry groups, especially since genomics will certainly dominate future pharmaceutical research. The latest series of meetings to be announced is the Life Science Innovation Forum (LSIF) initiated by the United States and the ASEAN member states in 2003 under the APEC scheme. The backing of the Bush administration, which clearly wants to extend its influence in Asia through this channel, has put the spotlight on this newly launched conference.

While the ICH will be at the center of my discussion, I have adopted a multisited approach that includes material from the other conferences I have just listed. George Marcus has declared the multisited approach a new mode of ethnographic research predicated on the idea that mobility and circulation are embedded in a world system and are therefore constitutive of cultural formations. This approach permits us to "examine the circulation of cultural meanings, objects, and identities in diffuse time-space" (Marcus 1998: 79). My method is basically the same as Marcus's. Given the spatial/temporal/cultural separation of sites from each other, Marcus suggested some subjects on which a comprehensive ethnography can be constructed, such as following

one group of people, a thing or a metaphor, stories and myths, or issue-oriented conflicts. My focus is on the last.

The conferences I examine are not conventional single sites: they are single sites with multisited characteristics. Let me reiterate: these are not sites naturally formed by culture, race, or society that can be taken for granted. They are artificial constructions that cross every temporal and spatial boundary that anthropologists can imagine. They are not located anyplace but can be found anywhere; they take place in a specific moment but their effects can be eternal. Although their artificiality can be partially explained through the anthropologist's use of deployment, I need to try to explain why this site is important for ethnographers and why we should recognize and describe it.

In conceptualizing sites of anthropological inquiry, Fischer has offered the concept of "ethical plateaus," which he defines as "the strategic terrains on which multiple technologies interact, creating a complex topology for perception and decision making" (2003: 30). Such a terrain might be that described by Michael Hardt and Antonio Negri as a new form of sovereignty that effectively regulates global exchanges. The empire they describe is a pyramid of global constitutions structured by international companies and nation-states and energized by the global economy (2000: 310–16). As a part of this larger phenomenon, the conferences surrounding the ICH are not merely of academic interest: they are ethical plateaus where the nation-state and its governmentality, the life sciences, capitalism, and the politics of representation are mashed together. By studying them we can trace the formation of the pyramid, with the United States and Asian nation-states interacting on the first level, and the international pharmaceutical companies negotiating with both on the second. The tensions between the world and the states can also be also understood as part of this empire, and the ethnographer may well hear a moral call to document them.

Bourdieu posed an important question that is relevant here: "Could rites of institution, whatever they may be, exercise their power [. . .] if they were not capable of giving at least the appearance of a meaning, a purpose, to those beings without a purpose who constitute humanity, or giving them the feeling of having a role or, quite simply, some importance, and thus tearing them from the clutches of insignificance?" (1992: 126). This above question suggests that a certain Danish prince might find succor at the ICH. However, it also suggests that we might question the conference's ability to present all of the voices ethnographers want to hear. Possibly those who fail to be heard in conferences are either insignificant or unimportant: they need not be incorporated into the story. However, as critical ethnographers, we have to concern ourselves with those who speak

but are not heard. That is the last methodological issue we should deal with.

Anatomy of the Institution's Anthropological Voice

The human voice is a metaphor often used in anthropology. It refers to both what anthropologists listen to and what they deliver to their audience. Anthropologist James W. Fernandez indicated the role voice plays in anthropological works: "An important part of our vocation is 'listening to voices,' and our methods are the procedures that best enable us to hear voices, to represent voices, to translate voices. [. . .] Anthropology is paying attention to the voices of those among whom we live and study" (1987). Although recognizing voices seems to be just as important as synthesizing them into a single, comprehensive voice, more attention is now being paid to the formation of the anthropological account than to "listening to voices."

There are two reasons to give careful thought to the voices I have studied. First, while I have already made my case for calling a state a writerly agency, such an agency can make more anthropological sense if one explains how a state can have a voice and how the ethnographer is able to hear it. Second, and more important, in the previous section I mentioned that a conference is not a given, well-defined territory but an ongoing global field that constantly refreshes itself. Not every voice is able to be present and not all voices get the hearing they want. For such a site, ethnographers must to be very careful to define the field they are looking at, paying attention to who is unable to express themselves in such a field.

Regarding the anthropological voice of an institution, I will provide a three-fold analysis based on Fischer's reading of autobiographies as ethnographic material (2003: Chapter 6). Fischer classified autographical voices, calling the self-contained process of finding an identity finding voice one, the dialogic process of "mirroring" and "cross-cultural critique" voice two, and the process of making networks by triangulating subjective voices and voices of rationality voice three. This classification (with minor modifications) is useful when applied to institutions such as the states I discuss in the chapters that follow.[32] I shall call voice one "instrumentality of voicing" and in my investigation of this voice I will focus on the set of mechanisms by which one institution expresses its opinions (this is the primary source ethnographers use to recognize that

[32] Fischer creatively probed the anthropological voice by looking at three kinds of text. For voice one, the identity process, he considered autobiographies; he found that when they were read along with biographies a new voice appeared. However, scientists are not wont to distinguish these voices, thinking instead of a universal voice of science, ruled by the career path that more or less controls the way the other voices are represented.

institution's identity). Voice two of an institution I call "functionality of voicing" because the voices are themselves dependent on the context for their interactions. Voice three of an institution, in the field of science and technology, is where scientific rationality dominates, defining the ability to generate a scientific discourse by, for instance, hosting conferences.

It is not difficult to imagine the state as an instrument than is able to voice its opinions. The government is the instrumental representative of the state, its formal voice on policies, laws, announcements, and so forth. And in democratic polities one can trace the mechanisms for generating such voices. Of course, political scientists have shown how complicated these mechanisms are as a result of the conflicts among interest groups and the interests of the government itself. In the realm of science, however, these mechanisms address relatively technical issues, which tend to be less politically driven.[33] In the case of the ICH, the voice of the United States is perhaps the simplest to analyze. The Center for Drug Evaluation and Research (CDER), which handles the approval of new drugs at the FDA, is the mouthpiece for United States policy at the ICH. Meanwhile, the PhRMA is a typical lobbying group for global capitalism based in the United States. Every year the headquarters of American pharmaceutical companies collect complaints from local subsidiaries around the world and submit them to the PhRMA. It then writes its annual report, which is used to pressure Congress as well as trade representatives.

The situation in Japan is a bit more complicated but still understandable. Within the MHLW are departments corresponding to the FDA. However, unlike the FDA, which also deals with scientific issues, the MHLW deals exclusively with administrative issues. On pharmaceutical matters, Japan has a consultative committee of senior scientists, whose opinions are usually taken as that of the government; the committee funds studies and routinely issues official statements. The delegates sent to this committee's meetings by the Japan Pharmaceutical Manufacturers Association (JPMA) do not play a leading role in discussions. Meetings are highly technical and the scientists are not that interested in business. Before each ICH meeting, industry representatives are provided with opportunities to consult with the MHLW. Disagreements are not rare, but traditional Japanese negotiation techniques generally resolve differences and produce consensus.

Taiwan's relations with the ICH are ambiguous, for the simple reason that it is not invited to the party. Although it formed an ad hoc committee to monitor ICH conference

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[33] I am not saying that science is of no political interest. Many cases studies by members of the Edinburgh school have revealed that science cannot be separated from policy decisions. Furthermore, in modern science, scientists are even "normally" involved as a crucial part in the process of policy making. See Jasanoff 1990.

results and later a technical organization for new drug reviews, their functions are limited. Similarly, Taiwan's drug industry plays almost no part in the ICH. Unlike the United States and Japan, Taiwan has virtually no domestic pharmaceutical production of any size; most local businesses are subsidiaries already represented by the PhRMA. Even so, the voices of Taiwanese scientists and officials do crop up in ICH records. In order to tell in what contexts these voices are counted, we have to take a look at the interactions of these voices inside and outside of the ICH; they are related to what I call voice two, the functionality of vocing.

As I have already mentioned, researchers tend to reproduce conventional images of the states they study. Since Japan is commonly described as "conservative" and "protectionist," there is a tendency to expect that representatives of that country will resist globalization. Though it is almost invisible internationally, Taiwan is thought of as an economic leader — one of the "four dragons" — and a political troublemaker due to its relations with the PRC and the Unites States. In international forums, many fear that Taiwanese delegates will upset the proceedings with political declarations. The tendency to cast nations in certain clichéd parts contributes to capturing a voice in a context, but it does not entirely account for it. Such factors play almost no role in science, where ethnography enters the frame.

The functionality of voicing, I insist, should be defined in a particular form of narrartive; let us consider how it would work in opera. Opera buffa is full of formulaic characters: cunning servants, parsimonious fathers, passionate lovers, wayward daughters, and arrogant soldiers — these provide the backbone of the comedy. But what brings the audience to the theater is the music, the exquisite melodies, the transcendent voices. Each voice performs two functions: its statements contribute to the progress of the story; its purely musical qualities can be recognized and appreciated separately. Not every actor on the stage gets to sing a solo at the front of the stage. Depending on the dramatic effect he hopes to achieve, the composer may assign a character only spoken lines or some offstage singing. Different people may react differently to these devices. While opera lovers are fully aware of the crucial functions these characters have in the story, for the uninitiated the failure to sing or to appear turns these players into vague memories.

Let us continue to rely on the analogy of opera as we consider the range of institutional voices debating racial difference at the ICH. With developing countries serve as the audience and occasional walk-on roles, only a handful of actors enjoy the glory of standing at the center of the global stage and belting out an aria. The FDA plays a judge and the PhRMA a czar; the former seeks the universal virtue of public health while the latter, accompanying the former, promotes the most advanced drugs to achieve this goal.

A special role is written for Japan in this opera, a non-Western role in this Western opera: certainly the dark baritone is talented enough to sing an aria or two. Stubborn and conservative, always protecting her traditional values, Japan's determination to cling to antiquated notions of racial identity will, like the plans of Amonasro in *Aida,* fail. Taiwan is only a voice, singing from offstage. Though this soprano has a promising idea about how to recognize racial difference even while ignoring it via a carefully designed scientific agenda, this does not finally prove sufficient to win her a role on stage. Few can identify her contribution, her role in the global text — this will be voice three in my analysis.

Voice three is concerned with creating a scientifically justifiable, globally recognizable voice. This voice can be a scientific argument or a policy, but it must be considered together with a discursive vehicle or channel by which this voice can be conveyed to listeners. For the case of ICH, this would amount to satisfying a simple yet challenging set of criteria: becoming a presence in a globally recognized conference, hosting such a conference, and recording these events in an archive so that they can be revisited over and over. The first criterion is more closely related to the voice in context, or voice two, but the other two pertain to voice three, which I shall explain here. It is not difficult to host a scientific conference and have a say in it; the difficulty lies in winning global recognition of such a conference. To host a conference modeled on the ICH means proving oneself an adept in both science and political economy. Bourdieu reminded us that conferences tend to concentrate certain types of capital, but this is not an effortless process. Many concerns have to be taken into account, depending on the types of capital available to the organizer: the selection of topics (issues of concern), consumptive power (market), political influence (superpower), and qualified science (curiosity and politics of knowledge).

Let us briefly evaluate both Japan's and Taiwan's voices. In terms of hosting well attended and generally respected conferences and forums, Japan and Taiwan are utterly asymmetric. While its huge domestic pharmaceutical market is sufficient justification for Japan to host such conferences, it suffers a broad perception of being protectionist. This is an impediment to talks with its main economic rival and political partner, the United States. Taiwan, on the other hand, stands at a distinct disadvantage in several areas. While Taiwan's medical research is superb, its reputation as a troublemaker excludes it from almost all governmental gatherings, and hosting its own events is out of the question.[34]

[34] According to the Thomas ISI data of scientific index Taiwan's performance in producing medical

In order to create a forum where its voice can be fairly heard and documented, these Asian states have to modify the rhetorical strategies they use in their communications with the Western mainstream. One can look to studies of gender in science to get some idea of why. The history of discussion of women's role in science has been divided into two stages (Harding 1991). The first stage was "equality feminism": activists asked for fair treatment and wanted outstanding woman scientists to be judged by the same norms applied to men. The second stage was "difference feminism," developed once some women had succeeded according to the standards of equality feminism. The new demands were radical: not only did proponents demand that their voices be heard, they criticized the norms by which these voices were selected.

A similar type of development can be seen in the case of Japan and Taiwan's relationships with the ICH. Although the ICH was determined to have Asian participation from the outset, Japan had to deal with the established Western norms from the outset. Taiwan lagged far behind, cruelly rejected by almost every international organization. In other words, while Japan is now at the second stage, questioning the universal standard, Taiwan is still at the first stage, hoping to be incorporated by being outstanding according to existing standards. As we will see in the following chapters, Japan used every opportunity to negotiate with the United States over what it considered its unique values. The more tightly Japan becomes enmeshed in globalization, the more desperately it clings to these conferences as forums for its unique voice. While the voice of the Japanese state is repressed, Taiwan's state voice remains inchoate. Like the women's movement, Taiwan can point to a few "successful individuals" but it is determined to see the entryway to legitimacy opened wider, so that these individuals cease to be the exception. For this reason, Taiwanese politicians view the creation of conferences as crucial. Like the women of the feminist movement, Taiwan keeps hoping that someone will hear its voice, its cadences distinctive and unlike any other.

The present study is dedicated to presenting the complexity of the interactions among voices in the era of globalization. As Donna Haraway did for feminist socialist cyborgs, I would like to propose an ethnographic interpretation of and for the non-Western world, not only to create a fairly representational identity, but to ensure that in international settings non-Western opinions enjoy parity. Echoing Geertz's reading of Levi-Strauss's *Tristes Tropiques,* where the foundation of these "strange-looking lives" can only be appreciated by "subjecting the cultural productions, the things that give these lives their immediate look of strangeness, to a universalizing analysis that, in dissolving

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papers is ranked the twentieth in the world over the past fourteen years; this is roughly the same as its

the immediacy, dissolves the strangeness" (Geertz 1988: 48). This interpretation is not a manifesto for strange Japan or outrageous Taiwan; it is, rather, an appeal for a fair multicultural world.

To bring out the state voices analyzed in my study I have relied on the institutional ethnography developed by feminist and sociologist Dorothy E. Smith (1987: Chapter 4). An important part of Smith's project was reworking theories in light of what they failed to explain, creating a "sociology for people" rather than submitting to the power of the theory to shape perceptions. In order to collect the experiences that would make possible a critique, she insisted on the performance of several tasks, which can be summarized as follows: (1) choosing a standpoint from which the institutional subject was studied; (2) achieving an understanding of how the institution functioned, especially how every individual worked with the others; (3) gaining an understanding of the institutional power structure by analyzing the institution's documentation; and (4) exploring the ideology behind this structure (167–78). Looking to discover the voice of states, I insist on a critical awareness of the incommensurability that becomes apparent when Japan and Western states discuss racial difference, and of the "off-stage" role Taiwan plays in this debate. I have interviewed the key representatives of Japan and the unofficial representatives of Taiwan at the ICH. In addition, I have collected local material, most of which is published in Japanese and Chinese, to gain a clearer understanding of the representatives' view of the ICH conference (voice one). In the pages that follow I show how the ICH functions by examining its documents and structures. I pay special attention to the tensions and conflicts surrounding racial difference, tracing there the interactions among the different states (voice two). Finally, in order to situate local experiences in a comprehensive context, I draw attention to the ideological structure that mutes the voices of the states (voice three).

The second methodology I have relied on is drawn from Latour's ethnographic studies of scientific knowledge. It is used to supplement institutional ethnography by extending its two assumptions: first, to extend its research object from a sociological category of collective individuals to a single representational agency of the state; and, second, to extend the analysis from a synchronic, cross-sectional examination of power relations to a dynamic examination that captures the changes in globalization. In Latour's *Science in Action* (1987), he showed how a laboratory orchestrated scientific facts (its voice) by various technologies. Here I will try to do the same (especially in Chapters 6

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international rank in the consumption of pharmaceuticals.

and 7) by tracing how Japan and Taiwan produce their own scientific voices in the debate over racial difference. Echoing Latour's observation that scientific knowledge is a co-product of social engineering, I describe how a state can form its own autonomous voice (voice one), or use such a voice to confirm its agency (voice two). As for the second element, the formation of a diachronic research frame, I refer to *The Pasturization of France* (1988), where Latour brings up the idea of "translation" as a way to understand the social dynamic in which actors organize and modulate density and texture. As I will argue in Chapter 5, this methodology helps me to trace a Machiavellian act of social engineering, braiding the voices of individuals into an institutional voice of the state (voice three). The book also provides a model for understanding how the FDA and the PhRMA act in East Asia, and how Japan should respond. As Latour indicates, no encounter between actors is simple; instead, it presents a social zone where clashing styles weave new connections and synapses (voice two), and various agencies trade information and visions.

I have explained the agency this dissertation will examine, the sites it will work on, and the voices it will listen to. The present chapter is designed not to convince readers but to suggest how they might approach this thick thesis — a "long argument," to use the phrase Charles Darwin modestly applied to his theory of natural selection. But one question remains unanswered. To borrow a locution from Latour, "How should we talk about all these things that hold together?" (1988: 203). In what follows I explain why and how this text is composed, and what its style looks like.

AN END NOTE: READERSHIP AND SYNOPSIS OF THE THESIS

Readership and Narrative Style

In the article "Sticking with Ethnography through Thick and Thin," George Marcus discussed the anxieties provoked in anthropologists by a multisited methodology and an interdisciplinary approach (1998: 238–49). Developed at a famous university, conceived as a hybrid of history and anthropology, this thesis shakes continuously as a result of multiple anxieties of representation. I have deviated from traditional ethnography by choosing my subject from the global politics of science; I have deviated from history and regional studies by borrowing the methods of ethnography. This puts me in danger of engaging no readership at all. Even as I consider the textual representation of science and politics, I have to ask myself, who will read this thesis? What can it offer to the lay reader,

to the academy, and to the people with whom it is concerned? In this section, I will try to answer these questions.

My narrative here is a hybrid of ethnography and history. The incubator that gave birth to it is the half-anthropology-half-history-of-American-technology academic cyborg. I expect to attract three kinds of readers, cultural anthropologists who want to understand globalization and new ways to deal with it, historians of contemporary East Asia and of pharmaceuticals, and those members of the general public interested in knowing how state and race interact in the field of medical science during globalization.

Readers with a background in science, technology, and society will easily identify the STS blood that runs through this dissertation. This is a story of scientific controversy about racial difference and about trade between East and West. Race is broken into pieces at the ICH; its operational meaning has to be found in the reconstruction performed in the conference sessions by different actors, namely government, industry, and scientists. Their interactions turn race into something that goes far beyond skin color, as the United States, Japan, and Taiwan each treat the subject with a distinctive social and cultural approach (see Chapters 4 and 5). As the sciences are called upon to serve each state's specific need (see Chapters 6 and 7), we see how science and technology function in social settings. Those who specialize in pharmaceutical policies will find in this thesis not only a description of some segments of this business on the global level (Chapter 2) and a guide to regional practices (Chapter 3), but a description of the dynamic between government and industry that produces new policies (Chapters 6 and 7).

Cultural anthropologists will have found by now that many familiar ideas provide the theoretical foundation of this thesis; the strong affiliation with ethnography is also evident. My goal has been to produce an ethnography of modernity and globalization. As a whole, this work can be considered a modern problem comedy, where conflicts take place in the domain of scientific theories and diplomatic rhetoric. Longstanding tensions and cultural misunderstandings are taken into account, as the ritual of globalization proceeds unceasingly: its progress is marked by quarrels, temporary compromises, and settlements (see Chapters 4 and 6). I have also tried to produce an ethnography of the politics of the eccentric and marginal, describing Japan's voice on racial difference with criteria of symmetry (Shapin and Shaffer 1985). Similarly, I have approached the efforts to lend Taiwan a voice through Dorothy Smith's suggestions for listening to the voiceless (see Chapters 5 and 7). Finally, this thesis is a methodological experiment in creating an ethnography of science and technology. Some of its chapters (Four, Five, Six, and Seven) may remind readers of Michael Fischer's comments on the collaboration of ethnographer

and scientist-subject in the pursuit of an ethnographic/authorial voice (2003: 149). And in some chapters (Five and Eight), I have addressed the problem of the ethnographer becoming an actor: the ethnographer must always be self-reflexive when trespassing in a foreign field.

Although this thesis is not a revival of that early ethnographic tradition of romanticizing the situation of the researcher in the field, I have found that in the era of globalization the boundaries between the observer and the observed have been almost completely eroded. As a scholarly work concerning East Asia, the present dissertation offers an interpretation of pharmaceutical business in Japan and Taiwan (Chapter 3) and one chapter has been wholly devoted to the view science takes of race and the state (Chapter 8). I have used local accounts throughout the dissertation; I feel strongly that the local should not be viewed merely as material to interpret.

It is hard to manage complicated arguments while maintaining narrative clarity. Moreover, I have run into problems of representation and authorship. Throughout the writing, my model has been *Debating Muslims: Cultural Dialogues in Postmodernity and Tradition* (Fischer and Abedi 1990). This book is a rich, creative narrative on Islamic culture in Iran and its uneasy situation in the modern world, specifically in dialogue with the United States. While the differences between that study and mine include subject matter, material, and approach, our agendas are quite close, as are our thinking about how our results can be used.

Both works address tensions between cultural tradition and modernity, and tensions between the non-Western and the Western (principally represented by the United States). On the question of tradition versus modernity, both reject the assumption that culture is a fixed, permanent heritage. And on the question of representing cultural encounters, both reject stereotyped interpretations, such as the fundamentalists' account of Islam or Japan's stubborn attitude toward racial difference. In addition, both basically share the assumption of social construction. Fischer and Abedi show that in the praxis of the state and nationalism, even the most fundamental idea about the hajj can vary through social manipulation (1990: Chapter 3). In the same manner, I argue that Japan's anxiety about globalization and Taiwan's embrace of it are interactive, if not cybernetic, social process that deserves "slow motion" ethnography, tracing it step by step.

In terms of narrative techniques, I have relied heavily on the narrative repertory of storytellers, turning this text into a story. Each chapter has a story to tell. In addition, this thesis contains multiple viewpoints created by juxtaposing stories from different informants. This is an attempt to approximate the multifaceted nature of the world that we

live in. Like Fischer and Abedi, I have made use of the structures found in folktales because of this genre's remarkable capacity for absorbing data with various characteristics; I believe that this genre also encourages more voices and interpretations to join in.

Collaborations between natives and ethnographers can produce remarkably rich results. Unlike Marjorie Shostak's relationship with her informant (in *Nisa: The Life and Words of a !Kung Woman* there is much talk of sisterhood between interviewer and subject), an American anthropologist and an Iranian Muslim coauthored *Debating Muslims* as a "cultural dialogue." I have followed this trajectory of intercultural dialogue, juxtaposing these different views, setting arguments one against another (a rational construction of the debate over racial difference), assessing the political in an international environment (Taiwan's political status and its exclusion from international settings). This approach is especially suitable here because the author is both an ethnographer and a Taiwanese native.

Finally, I have tried to write something that a wide audience can read without specialist knowledge. Readers will find comprehensive introductions to the industry of proprietary drugs (Chapter 2), to the drug business in Japan and Taiwan (Chapter 3). Fischer and Abedi said of *Debating Muslims* that it was not an attempt to show the mysterious Orient; instead, it was written in the hope that readers might "gain from it a feel for the sociological as well as cultural texture of a world" (1990: xxi). This task also implies a careful reconstruction of an understanding of non-Western culture, because, as Fischer and Abedi remind us, it is hard to appreciate Islam if it is approached only backward through the more instrumental policy categories of modernization. I have tried to provide a similar understanding of Japan and Taiwan, devoid of essentializing tags.

Synopsis

The present dissertation is divided into four basic parts; each part is made up of two chapters except for Part IV, which only has one chapter.

Part I, composed of Chapters 2 and 3, describes the creation of the ICH against a background of the world of proprietary drugs and, specifically, the drug business in Japan and Taiwan. Chapter 2 examines the logic of the production and consumption of innovative drugs. Adopting Ulrich Beck's notion of a risk society (1992), I argue that what the industry calls a high-risk, high-profit business is half-reality and half-illusion. The dangers that the body faces justify an expanding healthcare business. But the creation

of new drugs should not be considered financial risks since successful drugs have redeemed the investment in failed attempts. It has been said that the pharmaceutical business has an extremely low success rate. To better understand the ecology of this productive mode, this chapter addresses the role of regulatory science in the development of the modern pharmaceutical industry. Rising standards for new drug approval and a shrinking of the marketing period have driven big companies to expand from the domestic market to the international, creating a pressing need for a regulator-industry forum.

In contrast to Chapter 2, Chapter 3 is about local conditions. The first part covers the business outlook of Japan's and Taiwan's pharmaceutical markets. It offers an estimate of their size, an introduction to their domestic environments (ecologies), and considers how the United States has pressured the states to open up these markets. In the second and third part I try to make sense of Japanese and Taiwanese drug manufactures. Using Francis Fukuyama's ideas about trust (1995), I contend that drugs cannot be considered pure commodities in the Western capitalistic sense; they are implicated in the social relations between physicians and patients, as well as between physicians and business. Japan, a country that Fukuyama considers high trust, represents a self-contained model of health care that is not based on restrictive scientific standards and free competition but on systematic trust and collective authority; both stem from trust in the state bureaucracy and the abstract nation. Taiwan, on the other hand, is an imperfect copy of Japan, which once colonized the island and implanted various medical institutions. Despite these influences, Taiwan never developed a strong drug industry. The key to understanding this situation is, again, the concept of trust. Most Taiwanese consider drugs nothing more than neutral instruments that cure diseases, and through a combination of cultural estrangement, lack of trust, and unusually high regard for expensive foreign goods, Taiwanese society has attracted a strong foreign pharmaceutical presence while nurturing no local companies. More importantly, protracted political isolation has undermined the government's power in dealing with pharmaceuticals. The Taiwanese government is compelled to resist the intensive pressure of the PhRMA to reduce barriers to foreign pharmaceutical sales while endeavoring to maintain its global visibility in health care.

Part II, Chapters 4 and 5, describes how Japan and Taiwan separately encountered the ICH. As I explain in Chapter 4, Japan's experience was not smooth. Portraying this encounter as a quarrel between the Western and non-Western, this "slow-motion" ethnography describes two modes of negotiation used by Japan in the debate over racial

difference. The theme is the politics of standards: which standard can be accepted as universal? Answering this question proved a long and exhausting process lasting from 1986, when a bilateral agreement was reached between Japan and the United States on the acceptance of foreign data, to 1998, when a guideline was finally implemented. Instead of repeating the banal scenario about the victory of globalization, in this chapter I contest this discourse and advocate a dialogic context where there is a symmetry between the two states' interpretations. Although the meeting moved from bilateral United States-Japan negotiations to the multinational ICH roundtable discussion, and the content of the discussions shifted from trade to science, the essence of the quarrel remained an interpretative and ideological disagreement about race and the state, which could never be reduced completely to either business or science. At the end, a political compromise was reached and a single definition of race was agreed upon, but the contradictory voices were not silenced: they are quite audible in the guidelines that were drawn up.

Chapter 5 concerns Taiwan's efforts to catch up with globalization. Unlike the previous chapter, in which I depicted a defensive and combative Japan at odds with the West, here I look at how a state goes about making its voice heard in an international context. Taiwan's dealings with the ICH involve two difficulties, one commercial and specific, the other political and general. The commercial problem is simple: Taiwan was not invited to be a member of the ICH. Like many other countries, Taiwan has never had any allies that might help it resist the pressure brought to bear by the PhRMA and United States trade representatives. In addition, since Taiwan does not enjoy wide recognition as an autonomous state, it almost never participates in international negotiations, including the ICH. This results in a hopeless dependence on the United States, which further complicates the problem. Even so, this chapter is neither a lament for Taiwan's political status nor a critique of global capitalism. Taiwan's strategic embrace of globalization has permitted it to escape from the grip of the United States by sneaking into a forum where it can hope to be treated as an equal. When Taiwan's representatives began to take an active role in discussions at the ICH, it began to look very much like a state. This chapter describes the making of this institutional voice.

Part III, made up of Chapters 6 and 7, traces the second round of discussions among Japan, Taiwan, and Western countries at the ICH, after the release of a controversial guideline that attempts to cope with the intractable issue of racial difference. Chapter 6 shows how Japan tried to escape from a political deadlock while insisting on a picture of biological homogeneity. I explore the strategies that Japan has employed to unlock this impasse. Japan knows that it cannot always refer all domestic and foreign pressures to

open up its market to the ICH, and racial difference is an issue that has been tentatively "settled." It also knows that cultural values have little value in such a forum unless they are backed up by globally acceptable science. As it resists attacks from international corporations, Japan is developing a new voice to rewrite the definition of race. For the Japanese government, the way to treat globalization is not to resist but to make new standards to replace the old ones.

Continuing Chapter 5's portrait of Taiwan's institutional voice, Chapter 7 is an ethnography about voicing (*fasheng*). Though it remains formally outside of the ICH, Taiwan carefully monitors Japan's interventions on racial difference. It knows the guideline is controversial and impractical, and is aware of the cultural gap that yields these contradictions. Here is a chance for Taiwan to prove that what cannot work in Japan can work in Taiwan. Revising guidelines — which Japan is always trying to do on the racial issue — may be beyond Taiwan's reach, but Taiwan might be able to get what it needs by expanding the applicability of guidelines to other non-Western countries. Taiwan's voicing project can be divided into two strategies. To facilitate the bridging of racial differences, Taiwan started talking to other Asian countries that have not yet adopted ICH guidelines, calling for an Asia-Pacific regional network of regulatory science whose members would share clinical data. This is part of a plan to situate Taiwan's voice in regional networks to consolidate claims about legitimacy. Furthermore, in order to make the regional network a workable scientific agenda, Taiwan has drawn upon its abundant pool of statisticians to develop relevant biostatistical models. For an ignored, ambiguous political entity like Taiwan, the only way to survive globalization is neither to resist it nor to revise its operating rules; the solution is to exploit globalization to further its own interests.

Part IV is an attempt to generalize my previous findings in a broader discussion of state transformation. I rely there on the concepts of "normal" and "pathological" to contribute to the ongoing debate over race and the state. In the first half of Chapter 8 I argue that in Japan race is not a biological entity but a cultural reflection of the state. Race and the state are in fact two sides of a coin periodically flipped by globalization. Taiwan, despite the outbreak of terrific debates over ethnicity and autonomy during local and national elections, has not experienced these kinds of conflicts in its relations with globalization. Long isolation from global politics and terrible intimidation by the PRC have given Taiwan a clear national goal. What the Taiwanese really want, I conclude, is internationally recognized statehood. Though nearly all of its appeals end in humiliation, Taiwan exists as a state in those moments when it seizes center stage at the ICH. An

ethnographic study of the contemporary scene, this chapter considers what Japan's views on race and Taiwanese views on statehood *are,* not what they *should be.* The emergence of new branches of science (e.g., genomics) and new political situations (e.g., China's recent military threats against Taiwan) will continuously complicate the landscape of globalization. I want to offer a snapshot so that readers can imagine where the next move will be.

In my conclusion I offer a wrap-up of theoretical issues related to the present thesis. I review my contributions, which are: recognizing the state as an anthropological agent, showing how the non-Western functions in the technoscientific world, and conceptualizing institutional voices at the global level. I also reconstruct the story of racial difference at the ICH from three separate perspectives: those of the predominantly Western pharmaceutical industry, of Japan, and of Taiwan. These reconstructions do not constitute an ontological understanding of globalization, but they remind us that the different agents at the interface between individual lives and the world help us to imagine the effects of globalization on individuals and they give us some idea of how the state, as one of these agents, can voice.

All right. I have provided as much instruction as I can on how to read my thesis. Like Tonio's famous aria in *I Pagliacci*, which connects drama and reality, this chapter is a prologue that invites readers to the social drama concerning drugs, race, and standards that follows. I have told you my plan and how it unfolds. Without any further ado, *Andiam. Incominciate!* (Come. Let's begin!)

PART ONE
Reading the Bio-Global, Looking into the Local

It was an odd invitation for me, I have to admit, to the real world of proprietary drugs.

On a sunny winter morning, I sat in a café, enjoying my breakfast and the *Los Angeles Times*. While browsing the newspaper page by page, a column attracted me. It is about the more rigorous measures the U.S. Food and Drug Administration (FDA) intended to use to monitor drugs in response to two recent safety debacles, including the national withdrawal of Vioxx (rofecoxib), a COX-2 (cyclo-oxygenase II) inhibitor manufactured by Merck, in September 2004. The withdrawal followed Merck's acknowledgment that Vioxx was linked to heart attacks and strokes. The article quoted a comment by Steven Galson, the acting director of the FDA's Center for Drug Evaluation and Research: "We don't always understand the full magnitude of drugs risks prior to approval" (November 6, 2004, A11). At that time I had been doing archival studies on the profiles of some proprietary drugs, which are often opaque to the public. I know that these medications seriously affect millions of lives in the U.S. and around the world; however, they were only names to me until this news was released. It was so vivid and visible a case that it prompted me to think of two things that lie outside the conventional discourses of "consumers' rights" and "public safety."

First, as one of the most effective painkillers available, Vioxx has been sold for five years since its approval; an estimated twenty million American people have taken this drug and its annual sales exceeded $2.5 billion, making it the thirteenth best seller in the world. Its high profitability had led to several followers, such as Celebrex (celecoxib) and Bextra (valdecoxib), both developed by Pfizer. If Vioxx was suspended, these might be too, leaving no COX-2 inhibitors on the market. The Public Citizen's Health Research Group, cited in the *Los Angeles Times* article, claimed that the balance of power in the FDA "is in favor of approving a drug or keeping it on the market without warning." What I thought of was the fact that patients will suffer. Putting aside the loss of profits to these companies, which showed up in their stock prices (a loss of $27 billion within few hours of Merck's announcement), I was concerned about the millions of Americans who had benefited from these drugs. Pulling drugs from the market precludes them from being able to make risk-versus-benefit decisions. What else could they choose if they considered the risk of Vioxx is bearable? It is easy to pull a drug from market, whether voluntarily or not; however, it may result in unpredicted losses for people who have no better choices for their treatment.

Secondly, I was concerned about the level of safety we expect in pharmaceutical products. Although the article at least indicated that the risks were evident four years ago from the data that were not properly analyzed, the manufacturer claimed that its decision

was based on a three-year post-marketing study on the prevention of the recurrence of colorectal polyps in patients with a history of colorectal adenomas. In this study, there was an increased risk for confirmed cardiovascular events beginning after eighteen months of treatment for the patients taking Vioxx compared to those taking a placebo. In other words, if this drug is risky, it is risky for long-term users. According to the article, the FDA was asking the Institute of Medicine to study the drug safety system; nonetheless, what is most crucial may not be whether this system can discover drugs' safety problems before they are sold to customers. The problem, in my opinion, is a cultural one, a question of how long the public can stand to wait for care that is totally "risk-free." We drive cars; we hope they are safe all the time. We also know that there is slight possibility that they have problems that may endanger us. However, we have extremely high standards for pharmaceuticals. We take drugs, and we expect them to be "absolutely safe" before and after they are approved. Once a drug is thought of as risky, its sale is immediately suspended.

Even so, I agree that this event has flagged the problems that arise in this small yet important area, the ambiguous, rapport-based relationship between scientists and pharmaceutical companies. I started off being interested in the logic of how innovative drugs are produced and regulated. What is the relationship between the regulators and the regulated, and when and how was it established?

The issue remains heated and unsettled in the United States. *Science* warned in November 2004 that there could be a "class effect," meaning that all brands of COX-2 inhibitors could increase the risk of heart disease. Pfizer checked its Celebrex, which, like Vioxx, showed possible risks of heart attacks and stroke. It also announced that two recent studies showed that its drug Bextra increased cardiovascular events in people who had undergone a coronary artery bypass graft. A Merck plan to seek for approval for Acroxia, claimed to be the "second-generation" of COX-2, did not go forward. In the meant time, public hearings, debates and discussions were held. An advisory issued by the FDA in February 2005 suggested that Celebrex and Bextra should be kept on the market and allowed Vioxx to return to the market, but the public criticized some of the committee members for their links to the drug industry. The latest news I know of is that Bextra was yanked from the market on April 7, 2005, and the government ordered that nineteen other popular prescription competitors, from celebrex to mobic to high-dose naproxen, carry tough new warnings that the drugs may increase the risk of heart attacks and strokes.

In East Asia, Vioxx is another story. Although it was approved in the United States in 1999, Vioxx was still waiting for approval for the Japanese market, the second largest

in the world, when Merck pull it from the U.S. market. Banyu Co., Ltd., a first-rank Japanese pharmaceutical company that was completely acquired by Merck in 2001, had taken charge of the clinical trials that were conducted in Japan on Japanese subjects (trial code MK-966). After acknowledging its mother company Merck's decision, Banyu immediately stopped this clinical trial, which had reached the most costly and time-consuming third phase. A medical reporter commented that among the unfortunate delays due to Japan's slow system of drug approval, Vioxx presented an example of the necessity of this pickiness. In addition, Japan's Ministry of Health, Labor, and Welfare started to investigate other COX-2 drugs that were already on the Japanese market in case they posed the same risk.

Closely following the FDA, Taiwan approved Vioxx in February 2001 after conducting a clinical trial with forty local subjects (import number 023111), and the drug soon won popularity among patients with arthritis. However, when Merck announced the voluntary withdrawal in the U.S., Taiwan's Department of Health ordered the cancellation of the import permit for Vioxx the same day (October 1, 2004). In the meantime, Taiwan's Center for Drug Evaluation had been kept informed by the FDA about the monitoring of other drugs to see whether they should be pulled from the market. For various different reasons, Vioxx did not arouse public discussions in these two countries.

That is the starting point from which I want to investigate the intersection of the bio-global and the local.

Chapter 2

Harmonizing the World in the Name of Health: The Spread of Bio-Capitalism and the Need for Standardization

> Merck has always believed that prospective, randomized, controlled clinical trials are the best way to evaluate the safety of medicines. APPROVe is precisely this type of study—and it has provided us with new data on the cardiovascular profile of Vioxx.
>
> Peter S. Kim[1]
>
> These (innovations) should give patients waiting for new medicines confidence in the ongoing research commitment and continued discoveries emerging from American pharmaceutical research companies.
>
> Alan Holmer[2]

PART I
READING THE WORLD OF PROPRIETARY DRUGS

"New Medicines, New Hope": PhRMA's Voice on Drug Innovation

If some readers are puzzled about preceding description of the Vioxx incident, especially the complicated responses regarding the way a drug's safety should be properly evaluated, this chapter will demonstrate that the rhetoric the pharmaceutical industry uses is not obscure. The logic is simple, as shown in the quotes above: pharmaceutical companies are willing to develop new drugs because innovations give patients hope and confidence. Drug companies have extremely high standards for the clinical trials they use to evaluate their products. As the PhRMA claims in its motto "New Medicines, New Hope," everything is in the name of people's health. Without jumping too quickly to criticism, this chapter will try to understand what these people want to say to us.

Indeed, listening to the pharmaceutical industry's voice is a joy. With its optimistic tone, it sounds as if drugs are one of the world's most innovative, research-based mines of discovery and invention. The industry is characterized by

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[1] Director of Merck Research Laboratories in Merck 2004, "Merck Announces Voluntary Worldwide Withdrawal of VIOXX®."

[2] Chariman of PhRMA in PhRMA 2003, "A Monumental Decade for Combating Illness and Disease."

ever-growing investment in research and development. As the public is aware, incredible progress based largely on advances in life sciences including genomics and proteomics is being made. Indeed, new techniques for synthesizing chemicals using robotics, computer science and information systems are continuously being developed. It is what many refer to as "the golden age of science."

However, the joy comes with mixed feelings about this business, both globally and individually, because it is both beneficial and profit-driven. Let us take a closer look at the pharmaceutical business by reviewing a report prepared by the PhRMA for the United States' leading research-based pharmaceutical and biotechnology companies. Entitled "A Decade of Innovation," this twenty-page narrative begins with summary of achievements over the last decade: over three hundred new drugs, biologics and vaccines have been approved to prevent and treat over one hundred and fifty conditions. These pharmaceutical innovations, most of which were made by the PhRMA member companies, advanced the treatment of many major diseases of modern times: high blood pressure, schizophrenia, Alzheimer's disease, Parkinson's disease, high cholesterol, diabetes, rheumatoid arthritis and HIV/AIDS (PhRMA 2003).

As announced by Alan Holmer at *The Economist*'s Third Annual Pharmaceutical Roundtable in November 2003, "The advances achieved over the last decade have dramatically changed medical care for many serious conditions, including those highlighted in this report. As a result, many patients can now be treated effectively with medicines, instead of facing invasive surgery, a lengthy hospital stay, or a debilitating chronic condition." In this report, each disease has a separate profile that includes the treatments for it in development. Examples cited include the four new classes of oral medicines (sulfonylureas, biguanides, α-glucosidase inhibitors, and D-phenylalanine derivatives) that have allowed diabetic patients better control of their blood sugar levels and help prevent the devastating complications of diabetes, and three new classes of medicines (two drugs and one biologic) that improve the treatment of rheumatoid arthritis (including Vioxx). Medicines that did not exist in 1993 are now the standard of care among neurologists for patients in the mild to moderate stages of Alzheimer's disease.

Alongside this progress, what is also notable in the report are the various ways in which these diseases are presented. Except for traditional scenarios showing how new medicines powerfully treat a certain disease, the report takes an educational tone highlighting the dreadfulness of diseases such as diabetes and rheumatoid arthritis. For example, the latter is portrayed as leading to bone loss that causes osteoporosis, as well as the development of anemia, neck pain, dry eyes and mouth, bumps under the skin,

and very rarely, inflammation of the blood vessels. For some diseases the cost-effectiveness of drugs is emphasized by comparing them with hospital care: the report cites a *New England Journal of Medicine* study about AIDS treatment that states that drugs "are almost a perfect substitute for hospital care. We can afford them because, in fact, we are already spending the money on HIV care in the form of hospitalization." Sometimes cost-effectiveness is re-framed in order to compare the treatment and the restored functions, such as control of high blood cholesterol resulting in extension of life expectancy and better overall patient functioning. The report may in some cases call awareness to a certain disease that affects a particular group, such as Alzheimer's disease for the elderly. In some instances, it warns of tendencies in health problems, such as the increasing number of people who need to control their blood pressure, as judged by the new clinical practice guidelines from the National Institutes of Health's National Heart, Lung, and Blood Institute. While the report is written in a plain, scientific writing style, a richness of multi-faceted meaning seems to be embedded in these subtle expressions.

This report is not an exception—there are many publications and public lectures made by the PhRMA like it. What can we learn from reading a report like this? On the basis of our understanding of the narrative style described here, what messages can we expect to receive about the pharmaceutical industry? In the rest of this section I will discuss four issues that help construct the image of this business in the United States. They are: 1) changing concerns about illness and treatment; 2) the correspondence between diseases and the people they affect; 3) the rationale of cost-effectiveness in drug development; and 4) the increasingly important role of research and development in general.

Miles Weatherall presents a good review of the first issue in his *In Search of a Cure* (1990). Although human beings have used plants and minerals for medicinal purposes for thousands of years, he writes, no synthetic drugs existed prior to 1800. Despite the modern medical institutions that were established in the early and mid-nineteenth century, hospitals for teaching and research, the practice of laboratory medicine, and the origin of the germ theory for disease transmission, pharmacology was still primitive and alien to the emerging field of scientific medicine (Chapter 2). Modern pharmacology did not develop until the last decade of the nineteenth century, when it emerged in the form of vaccines. The research-based pharmaceutical industry and agents for chemotherapy only emerged in the 1920s. Through the use of antibiotics and vaccines, the battle against infectious disease reached an historical climax: in 1928 penicillin, the "magic bullet" against bacteria, was discovered by Alexander Fleming,

and in 1942 its medical use was identified.[3]

When Americans' memory of infectious disease faded with the eradication of diphtheria, whooping cough, measles, and polio, the targets and consumers of pharmaceutical industry gradually changed. Although chronic infectious diseases and viral diseases could still be found in some populations and in the developing countries of the world, in industrialized societies there was an increasing awareness of chronic diseases and the maintenance of a healthy status. Led by cancer research conducted by the U.S. government, more studies were made by the drug industry to discover the unknown causes or mechanisms of such illnesses, including degenerative and psychiatric diseases. Unlike infectious diseases, these other types of disease present a great gray for matters like the identification of an illness, ways to change it, and proof that the treatment is responsible for improvement.[4] In the contemporary context, the pharmaceutical industry is one of the main players in framing our conceptions of illness and ways of dealing with it. Guidelines shift; the demography of the unhealthy is changed.

The second issue refers to establishing a correspondence between an illness and a certain group of people. Michel Foucault (1978) has pointed out that in the nineteenth century, special measures were taken to discipline the sexualities of certain groups or people in order to construct a modern society.[5] The same kind of tendency can be found in recent discourses on drugs and diseases, but the expressions are different. Based on existing medical institutions, this discourse focuses not on the development process but on the degeneration of human beings. In addition, the call to take care of these degenerating bodies comes not from outside but from within. Pharmaceutical companies know clearly which people are aware of their bodily changes and would like to pay for treatment. Unlike the marginal people at the dawn of modernity, the targets for today's most advanced medicine occupy the center of health care. In order to

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[3] Although influential, this account is problematic. For example, sulphonamides, not penicillin, were the first antibacterial agent put on the market. They are not usually called antibiotics because they are not produced by a living system. In addition, penicillin was not available for general use until the end of World War II. I am grateful to Professor Ralph Kirby at National Yang-Ming University for providing the above information. For more detail about the discovery of penicillin, see Brandt 1987.

[4] This ambiguity is well illustrated by historian Charles Rosenberg's notion of "framing diseases" (1992). Rosenberg asserts that disease should be considered "both a fundamental substantive problem and an analytical tool, not only in the history of medicine but in the social sciences generally" (xxii).

[5] These "abnormal" people, including children, women, criminals, the mentally ill, and homosexuals, needed to be subjected to a process of modernization and became objects of study. Making these people "normal" required mechanisms that operated through previous and emerging power relationships, such as those between children and parents, students and educators, patients and psychiatrists, delinquents and experts. New sciences were created to serve this need, and all these elements were built into the fabric of power/knowledge and have become invisible under the disguise of modernity.

maintain their health, these baby boomers are willing to be subjected to the system in the name of public health or social welfare. The latest example of this tendency is the Medicare Prescription Drug Reform Act signed by President George W. Bush in December 2003, which claims to cover most prescription medicines used by its forty million elderly and disabled beneficiaries.[6]

The third issue expressed in PhRMA's message is cost-effectiveness reasoning. It is no wonder that the United States has the highest per capita spending on healthcare, as well as the highest percentage of gross national product dedicated to this sector. Between the years 1970 and 1994, the percentage of GNP devoted to healthcare jumped from 7 to 15 percent. The systems of healthcare financing in the United States, from the early forms of private insurance in the 1930s to the Medicare and Medicaid systems established in the 1960s, inevitably resulted in escalating healthcare costs. Although the private sector's various schemes, such as health maintenance organizations, preferred provider organizations, and fee-for-service plans, were developed in the emerging industry of managed care, the problem still remains that the basic level of reimbursement is directly related to services provided. The incentives are very clear: the more services that a practitioner or institution provides, the greater the reimbursement.

Thus it is clear that the pharmaceutical industry has to face scrutiny from critics claiming that it reaps excessive profits at the expense of the health of the general public. It also faces constant threats from government price controls and measures that diminish patent rights. Since the Kefauver Congressional hearings of the 1950s, the industry has defended itself with the argument that high profit margins are necessary to support the massive capital outlay required to develop new treatments. Not only do people deserve better quality treatment—advanced drugs are also alternatives to other courses of treatment and therefore save money by avoiding unnecessary hospitalization and medication while achieving better outcomes. In other words, spending on medicines goes up, but total treatment costs go down. A recent *Health Affairs* study supports this persuasive argument (Thorpe et al. 2004). According to this paper, 56 percent of the increase in health care spending between 1987 and 2000 was due to fifteen diseases. Although many of these conditions have new treatments that are more costly, they are also more effective. Therefore, the authors contend that "some of the concern about the growth in spending may be misplaced," and that for many diseases, the increased use of new treatments is "likely to represent an appropriate if costly

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[6] For a critical comment on health care reform in the United States, see Rothman 1997.

expenditure by society" (W4-443).

The fourth and last issue that PhRMA reminds us of is the increasingly important role the pharmaceutical industry plays in the research and development of health care. Although we observe that the role of government in health research has increased in past decades,[7] it is said that industry takes a crucial role in the cutting-edge fields. For instance, from fiscal year 1989 to 1993, NIH expenditures on human use clinical trials grew from $495.5 million to $869 million, an increase of 70 percent. However, by comparison, the members of the PhRMA reported spending $1.55 billion on clinical trials in 1989. Moreover, in contrast to the government's role in basic and public interest research, PhRMA focuses more on the drugs used by the majority of the population, whose health behavior is guided by the customer-pays system. As a result, the government is left to fund all drugs that cannot be sold to huge number of people. As PhRMA noted in *Rx Minute* (Issue 5, October 5 2004), the NIH has rights in only four of forty-seven top selling drugs. In the same issue of *Rx Minute*, PhRMA cited the NIH's recent report to Congress (NIH 2004), which says that the industry is the dominant, if not the only, research resource that people can rely on. According to that report, the NIH typically contributes to the understanding of basic and clinical biology that help guide translational research toward producing a cure or therapy. However this does not mean that the NIH is responsible for developing new medicines, because the technologies it invents are rarely part of a final product, and when they are, they are only one of many components. Thus the responsibility for protecting "normal" citizens' health has shifted from the government to industry. Citing a study conducted by the Center for the Study of Drug Development and the Department of Pharmacology and Experimental Therapeutics at Tufts University in 1993, PhRMA claims that during 1981-1990, the pharmaceutical industry was the source for 181 of the 196 new drugs approved by the FDA, academia was the source of seven, and the government was the source of two.

The above four routes of persuasion provide reason to appreciate the value of prescriptive medicines, as can be read in the quotes at the beginning of this chapter. As health economist J.D. Kleinke claimed at the release of the PhRMA report, "People often forget how different medical care was just ten or fifteen years ago because we did not have the medicines that are available to us today" (PhRMA 2002: 12). In turn,

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[7] Health care research and development (R&D) is the second largest element of federally funded R&D—only defense ranks higher. In 1993, the federal budget included more than $12 billion for health care R&D. About 70 percent of all federal health care R&D expenditure is funded through the National Institutes of Health. The remaining expenditure is funded through other agencies in the Department of Health and Human Services, as well as other federal agencies.

PhRMA would like to take responsibility for the future health care and the vast investment in research and development that is its promise. The report concludes that PhRMA will "continue to work intensely to discover and develop new treatments for these debilitating conditions, investing an estimated $32 billion in 2002 alone and more than $200 billion in the past decade in researching and developing new medicines." Yet, on the other side of the "New Medicines, New Hope," R&D is also a "scare card" against criticism. Any attempt to threaten the profits of PhRMA will be blamed for any reduction in its R&D productivity.

A Look at the R&D-Based Pharmaceutical Club

Following the preceding examination of global pharmaceutical companies' claims, this section will step back and give an overview on the world of proprietary drugs and the "club" that dominates it. Despite its early origins, the modern pharmaceutical industry only began to assume importance after World War II. Its growth over the past few decades has been remarkable. World production has increased more than twofold since 1975 and in 1990 stood at $150 billion. Roughly sixty countries each produce at least $100 million worth of pharmaceuticals each year. The markets for drugs have generally grown almost as rapidly.

Even so, looking into this business, we find it has four distinct realms, or "sectors" in industrial terms: proprietary, generic, over-the-counter (OTC), and biopharmaceutical. Each is run by different logics and requires a different range of technologies. The proprietary pharmaceuticals are the most advanced, and include those drugs in which the effective substances are protected by patent and trademark. Proprietary drugs are named by the companies that invent them. When the patent on one expires, other producers are able to make copies of this product that claim to be identical or bioequivalent to the brand name drug in dosage form, safety, efficacy, route of administration, quality, performance characteristics, and intended use. Because they are copies utilizing the same effective substance, these products are labeled with the generic name of that substance rather than the brand name, which is why such drugs are called generic. In contrast to these first two realms, which are usually described together as prescriptive drugs, meaning medicines that are regulated by legislation to require a prescription before they can be obtained, OTC drugs may be sold without a prescription and without a visit to a medical professional. The oldest and most well known OTC drug is perhaps aspirin, which used to be a Bayer product exclusively and first appeared in the world in 1899. Unlike the above chemically synthesized

small-molecule drugs, biopharmaceuticals are complex macromolecules created through the genetic manipulation of living organisms, so they merit a category distinct from the above three.[8]

The importance of these realms is reflected in the size of their territories in the drug industry. According to a study by the IMS Health Inc. shown in table 2.1, the pharmaceutical industry is the pharmaceutical industry is continuously expanding, and is currently doing so at a rate of 8.7 percent annually. Among this industry's four sectors the proprietary sector is the biggest, accounting for 74% of the total world pharmaceutical market. This sector is growing at double-digit rates but is under increasing pressure owing to strong competition from the generic realm, which is currently valued at $30.5 billion and holds 6 percent of the total market. Owing to their efficacy and ability to act on hard-to-treat conditions, biopharmaceuticals constitute a small but increasingly popular mode of treatment. Overall, however, it is safe to say that this industry is dominated by the production of proprietary drugs.

Table 2.1 Worldwide Pharmaceutical Market Watch by Realms, 2000-2003, and the Estimation Through 2008 (in billions)

	2000	2001	2002	2003	2008	Average growth rate, 2003-2008
Proprietary	317.1 (73.1)	363.4 (74.1)	401.0 (74.1)	437.6 (73.8)	677.8 (75.2)	9.1
Generics	24.0 (5.5)	27.0 (5.5)	30.5 (5.6)	37.0 (6.2)	64.0 (7.1)	11.6
Over the Counter	70.5 (16.3)	73.8 (15.0)	78.5 (14.5)	82.0 (13.8)	101.0 (11.2)	4.3
Biopharmaceuticals	22.1 (5.1)	26.3 (5.4)	31.0 (5.7)	36.5 (6.2)	58.6 (6.5)	9.9
Total world market	433.7	490.5	541.0	593.1	901.4	8.7

* In parentheses are percentages of total world market

Source: Adopted from BCC, Inc. Data based on IMS Health Inc. 2003.

[8] Some biopharmaceutical milestones include the first recombinant protein (human insulin), launched in 1982, the first recombinant vaccine (against hepatitis B) in 1986, the first therapeutic monoclonal antibody (against kidney transplant rejection) also in 1986, and the first and only oligonucleotide to date in 1998 (against cytomegalovirus retinitis in AIDS patients). And although it is a hot topic for the future, no gene therapy product has yet been approved.

Even so, only few companies have the qualifications to enjoy this market. In global terms, a small number of about fifty pharmaceutical multinationals accounts for two thirds of the world's production and exports each year. It is documented that a high degree of concentration prevails in international markets. The top 25 companies reported sales of $67.7 billion in 1988, or 44 percent of the world market (Ballance et al. 1992: 108-109). This concentration is emphasized in a 1995 report that indicates that the ten largest companies hold 34.3 percent of total market share (Schweitzer 1997:116). These companies, according to Liebenau (1987), have existed in one form or another since the nineteenth century. In addition, among the largest ten firms, six have chosen to locate their headquarters in the United States, two in United Kingdom, one in Germany, and one in Switzerland (Schweitzer 1997, Table 5.2.).

Table 2.2 Typology of the World's Pharmaceutical Industries

Stage of Development	Number of countries		
	Industrial	Developing	Total
A. Sophisticated pharmaceutical industry with a significant research base	10	Nil	10
B. Innovative capabilities*	12	5	17
C. Reproductive capabilities			
i) those producing both therapeutic ingredients and finished products	6	8	14
ii) those producing finished products only	2	87	89
D. No pharmaceutical industry	1	59	60
Total	31	159	190

* Each country in this group discovered and marketed at least one NCE between 1961 and 1990.

Source: Adopted from Ballance et al. 1992:8-9, Table 1.1.

A more detailed typology made by a study sponsored by the United Nations Industrial Development Organization (UNIDO; Ballance et al. 1992) is outlined in table

2.2. In order to give a picture of this industry's configuration, states are classified according to the development of their pharmaceutical production capacities. Putting aside the countries in the C and D categories, which include most countries in the world, only ten countries are recognized in category A: Belgium, France, Germany, Italy, Japan, the Netherlands, Sweden, Switzerland, the United Kingdom, and the United States. This category is a club in which membership is restricted and limited. The states in this category are not only responsible for 60 percent of world pharmaceutical production in 1975 and 69 percent in 1990, 78 percent of world exports in 1975 and 68 percent in 1990; they also consume over three quarters of all medicines produced. Therefore, unlike textiles, food processing, or clothing, the pharmaceutical industry has an international character but is a closed system. Only in a handful of countries have companies benefited from drug production and people from the latest medicines. Of course, the United States is the leading figure in this club. Among the top 25 companies reported in 1988, 14 are based in the United States and have combined sales of more than $30 billion, equal to one fifth of the world sales in that year. All this is what PhRMA's claim in the previous section is based on.

According to Ballance et al., the prominence of the countries in Category A rests on two cornerstones (Chapter 1). First, although all types of firms exist in each of these countries, it is the large, vertically integrated, sophisticated corporations which have taken absolute domination in this sector. Their abundant market power provides the necessary impetus to lead, and this leadership is the main reason for their overwhelming contributions to world production. Most of the integrated producers are multinationals with large foreign sales and investments in other countries which are also club members. Through these connections these companies have formed a transnational class in which the flow of capital is vast yet hard to trace. The recent trend of mergers between these companies strengthens their power. As the *Guardian* observed about these "pharmaceutical giants," "There were times not long ago that drug companies were merely the size of nations. Now, after a frenzied two-year period of pharmaceutical mega-mergers, they are behemoths which outweigh entire continents. The combined worth of the world's top five drug companies is twice the combined GNP of all sub-Saharan Africa and their influence on the rules of world trade is many times stronger because they can bring their wealth to bear directly on the levers of Western power" (June 6, 2001).

The second factor, related to the first, explains the industry's heavy concentration in these countries. Their own drug markets have grown exceptionally fast. Levels of per capita consumption increased dramatically between 1975 and 1990, from $65.80 to

$150.50 (in 1980 dollars), many times greater than those in other parts of the world. Two obvious facts about this growth, as pointed out in the PhRMA report discussed in the previous section, are worthwhile noting. One is that the populations of these countries are aging rapidly and their disease patterns have changed to chronic ailments. Medical demand has shifted toward more expensive types of medicines and the frequency of drug consumption has risen. The second is that the governments of these countries have established very generous systems of public health care at times when national incomes were rising and the proportion of elderly was comparatively small. The public sector now accounts for more than half of all drug expenditure in all the countries in category A (the United States was the last country to make this promise).

Table 2.3 Distribution of consensus New Chemical Entities (NCEs)* by nationality of originating firms, 1970-1983

Country	Number	Percentage
United States	71	41.7
Switzerland	22	12.9
Germany	17	10.0
United Kingdom	17	10.0
Sweden	12	7.1
Italy	8	4.7
Japan	7	4.1
France	4	2.4
Others	12	7.4
Total	170	100

* Consensus NCEs are defined as new drugs introduced in at least 6 of 11 major markets over the period.

Source: Grabowski (1989), cited from Ballance et al. 1992:88, Table 4.3.

The above observation goes to the center of the logic that operates the realm of proprietary drugs. Since health is invaluable and the last thing to the sacrificed, the main battlefield for these companies, as Joseph Schumpeter's insights on the role of new technology in industrial competition suggest, is the ability to keep innovating. If

there is an "innovation system" in this industry, it is the search for new chemical entities (NCEs) that must be the most essential element of it. Only through continuous R&D and the creation of new markets can capital be accumulated. From 1961 to 1990, about two thousand NCEs were produced by the United States, Japan, and Europe, at a rate of hundreds per decade. If we take into the consideration the fact that some NCEs are much more significant than others, we find that the United States was the most productive. From 1970 to 1983, about 41.7 percent of the "consensus NCEs" were produced in that country (table 2.3).

Moreover, these innovations were secured by patents. This was an issue when the therapeutic revolution began in the mid-1940s: some countries in Western Europe and Japan had not introduced the concept of a product patent. Until amendment of their patent laws, only manufacturing processes could be subjected to a patent, and thus it was argued that these countries provide the most convincing argument that a patent-free environment is essential for the technological development of the pharmaceutical industry. This environment started changing when France introduced product patents in 1960. It was followed by Germany in 1968, Japan in 1976, Switzerland in 1977, and Italy and Sweden in 1978. Under this scheme, governments can regulate local copyists in the countries these drugs are aimed to be marketed in.

As a result, big pharmaceutical companies' profits can be even higher due to the limited competition resulting from strict patent laws. When a company owns a patent for a key drug, profits can mount up since the company faces no competition. Furthermore, high barriers are set for small firms to enter the industry. This logic also drives production for the future. As PhRMA notes, at the end of 2002, 28 percent more medicines were being investigated by pharmaceutical companies for approval by the FDA than a decade ago, with more than one thousand medicines now in the development pipeline. As Alan Holmer adds, "The story of pharmaceutical discovery and its importance to people living healthier and longer lives is also a story of renewed hope and restored futures." The drug giants cannot track all new developments themselves, but they keep their pipelines full.

"Why Do Prescription Drugs Cost So Much?" The Construction of High-Risk, High-Profit Discourse

The pharmaceutical industry is tremendously successful by almost any measure. Industry operating margins typically exceed 30 percent, net margins averaged above 17 percent from 1995 to 2000, and return on equity averages over 25 percent. In this

section, let us return to the starting point of this chapter and ask a simple yet important question: why do prescription drugs cost so much? In the following section, I will discuss this from the viewpoint of industrial innovation; in part II of this chapter, I will deal with the same question, but from the perspective of regulatory science.

Unlike other commodities, prices of proprietary drugs are not determined through a free-market mechanism. If a drug is affordable, a patient will not adjust the demand for a product in response to a small change in price, particularly when there are no close or available substitutes. Thus, the domination of handful "behemoths" enables large companies to dictate drug prices. In past two decades, pharmaceutical prices have risen faster than the rate of inflation. Since the actual manufacturing costs of medicines are relatively low, the fact that there is very little price elasticity associated with price increases is a major factor contributing to the high profitability of the pharmaceutical industry. Gross profit margins of some of the leading pharmaceutical companies in recent years have been around 70 to 80 percent.

However, as discussed above, PhRMA knows how to persuade customers that they deserve the most advanced medicines. Industry presents a scientific discourse on the high-risk nature of innovation by which its high-profit agenda is justified. In *Why Do Prescription Drugs Cost So Much? ... and Other Questions About Your Medicines*, for example, a PhRMA report explaining the cost of research and development, three contributing factors are listed: first, of every five thousand chemicals tested, on average only five are tested in clinical trials and only one of those is approved for patient use. Second, it is expensive to develop an innovative drug—the average cost of bringing one new medicine to market is hundreds of millions of dollars. Third, it takes an average of twelve to fifteen years to discover and develop a new medicine. Most of that time is spent testing the drug to make sure it is safe. These carefully chosen facts illustrate the core of drug company R&D activities: they must be scientific and tough enough to reconcile all doubts about the high price that is charged. As illustrated in the PhRMA medicine bottle graphic below, a single medicine contains "years of scientific education, state-of-the-art research tools, and 12-15 years worth of research and development."

Let me briefly review the origin and early development of this process. According to Weatherall (1990, Chapter 6), one of the most important industrial roots of modern pharmacology back in the nineteen century was the German chemical industry, which at the time was far ahead of any others. Germany's academic environment of universities, research institutes, and clinics was also significant. However, theories on how drugs interacted with the body were primitive. Throughout the nineteenth century there was a slowly developed understanding that drugs react with specific bodily

components. In the twentieth century progress was made towards understanding the properties of these components and differentiating the effective outcomes resulting from chemicals with slightly different structures. Even so, most pharmacologists in early twentieth century were investigating familiar medicines and sometime seeking to improve on them. On the other hand, there was lack of understanding between scientists and clinical doctors. Sometimes the former happened to find substances that were effective in some cases, yet such knowledge played little part in physiological discoveries.

Since this was the case, the inefficient "synthesize and screen" approach to drug discovery—that is, searching through variations of a substance for some useful medicinal property—was created and has been widely followed ever since. Without much knowledge on how a drug acts on the body, this process does require an extensive knowledge of the chemical makeup of compounds. The makers know well that the responses of living tissues are very selective; some changes that seem to be of no significance can radically alter the properties of drugs. Thus scientists had to master this field before they could begin to perfect systematic methods of synthesizing drugs. In the process of drug discovery, much work, particularly in industrial laboratories, consists of operating suitable test systems, or screens, which are used to select the most active of a range of novel compounds created by chemical scientists. The painstaking nature of this process is illustrated by the search for a drug to guard against malaria. It is reported that more than 230,000 chemicals were screened for anti-malarial activity between 1964 and 1974, whereas only about thirty were selected for clinical study in human subjects (Ballance et al. 1992:92). It is indeed a tedious, inefficient and wasteful method, some might say, yet it has led to many modest and some very remarkably beneficial new agents. A multitude of new and miraculous drugs began to flood the market soon after the end of World War II, including antibiotics, medicines to treat asthma, arthritis, cancer and heart diseases, along with contraceptives and vaccines.

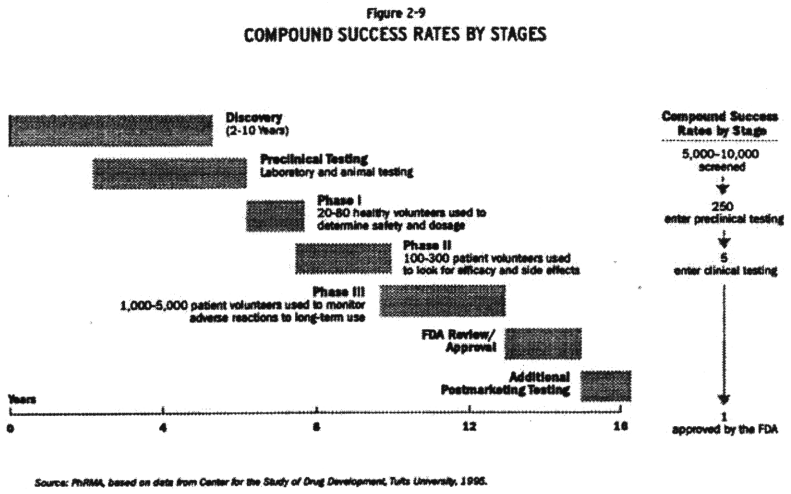
Parallel to the progress of drug discovery is the process of manufacturing, which supports and refines the discovered chemicals. In *The Economics of Industrial Innovation* (1982), Christopher Freeman points out how process innovation, rather than product innovation, played a decisive role in the high rate of productivity that the chemistry industry has enjoyed for over a century (Chapter 2 and 3). As he noted, the most important general change in the techniques of the industry has been the move from batch to flow processes of production; several improvements were made to save cost, increase efficiency, and even create new procedures that may lead to new discoveries. Freeman's observation can be applied to the pharmaceutical industry. For

instance, based on the 1905 revision of the *United States Pharmacopoeia*, German companies took out U.S. patents on any new final or intermediary product developed in their laboratories. It was a strategy that discouraged competition because there was little incentive to work through a development phase when patents are already held on every conceivable related product.

Furthermore, it must be remembered that after the introduction of a new process or the construction of a new plant, many minor technical improvements would be made. These changes were equally important, but they were not recorded in patent statistics for reasons of secrecy and of patentability. Major U.S. drug makers, such as Merck, Squibb, Abbott, and Parke-Davis, made daring reforms during the first two decades of the twentieth century, and Eli Lilly and Company is also exemplary in this regard (Madison 1989). Eli Lilly, the grandson of the company's founder, brought revolutionary changes to this Indiana-based firm, and improvements in manufacturing resulted. For instance, Lilly initiated a plan determining which drugs were low in material costs and less burdensome to the inventory. Meanwhile, he attacked the problem of determining the most economical lot sizes for each product. High inventory costs necessitated small lot sizes, while lower unit costs resulted from the manufacture of large lots. Based on the substantial investment spent, by 1930, Eli Lilly had become a modern industrial corporation through these improved methods of production and was encouraging the development of new products.

However, starting around the same time, more "stockades" were set up between the discovery of potentially effective chemicals and their production that made it much more difficult to bring an NCE into the market. Among such regulations, the ones in force in the United States are the most difficult. As shown in fig. 2.1, it is said that the involved sequence of steps is the main reason for the high costs and risks of drug development. The sequence includes pre-clinical testing and clinical trials, each of which consists of several steps, which I will introduce one by one. The pre-clinical stage of drug development consists of several complex empirical analyses of the biological activity of candidates for products. They are conducted to identify potential uses for the chemical tested and to assess toxicity. It is a long process that usually takes and average of six-and-a-half years, and during which most of the possible candidates are tested and dropped before going to human trials. A rejection rate of 999 out of 1000 test compounds is not unusual. Even so, there is regrettably no way to predict the potential applications that each new compound may have.

Fig. 2.1. Process of Drug Development



Source: PhRMA 2002, based on data from center for drug development, Tufts University (1995)

Promising products go on to the clinical stage, where the first step is to conduct tests on healthy humans. The profile of each candidate's activity in humans is built up based on the pharmacokinetics and pharmacodynamic data obtained from twenty to eighty healthy volunteers. Potential side effects are identified, and a dosage range is determined. If the drug is tolerated and produces the desired effects, it enters phase II of clinical trials, in which approximately 100 to 300 volunteers with the targeted disease are tested with several dosages suggested in the range determined in the previous phase to determine the drug's effectiveness. Again, it is time-consuming work with a high failure rate. Four years on average is spent here and only five out of 250 tested drugs get a chance at large-scale trials after tough evaluation. The phase III clinical trial is the most expensive and time-consuming step in the process of drug development. It is so expensive that only handful successful drugs can be selected. Usually one thousand to five thousand patients are involved at this stage. The aim of this trial is to determine the ideal dosage that will produce the best performance from the drug. At the same time, studies on the use of the compound as a drug are performed. All these concerns make this phase difficult to pass. During the four years spent on average at this phase, about eight out of ten drugs fail for various reasons, such as the compound's instability, lack of efficacy, undesirable side effects or toxicity problems.

Only when the compound tested overcomes these barriers does it have scientifically guaranteed access to the market. However, aside from regulatory

requirements for approval, there are two additional obstacles that may make the previous efforts all in vain. The first is post-marketing surveillance. After a medicine is approved, the manufacturer and health care professionals monitor the safety and efficacy of the product when it is used by a larger number of patients than participated in the clinical trials. This is done to detect adverse reactions that occur infrequently in patient populations or cannot be found in the relatively short trial period. The second obstacle is the clinical trials requested by the markets where a product is intended to be sold. For most of the cases these are just a repeat of the initial trials, yet they still take times and money, and the drug maker has to risk the possibility that the product may fail to show the same efficacy as in original studies.

According to this explanation, we can understand why the PhRMA apologists describe drug development as a long, massively expensive, high-risk activity. The time and money spent during this process are estimated is table 2.4. In total, development times have been increasing steadily over the past twenty years, from eight years to an average of ten years, at an average cost of $230.8 million each. As an illustrative measure of investment commitment, in 2003 alone U.S. industry researchers, together with some of their European and Japanese allies, will have invested well over $33 billion in the name of research and development.

Table 2.4 Stages of Pharmaceutical Research and Development

Stages	Mean time (months)	Cost per successfully marketed drug (in millions of 1987 dollars)	
		Direct cost	Capitalized cost
Preclinical studies	42.6	65.5	155.6
Clinical phase I	15.5	9.3	17.8
Clinical phase II	24.3	12.9	12.4
Long-term and other animal studies		5.7	8.9
Clinical phase III	36.0	20.2	27.1
Total	119.4	113.6	230.8

Source: Adopted from Schweitzer 1997:29, Fig. 1.3, from DiMasi et al. 1991.

For this reason the high profits of the pharmaceutical industry are said to be justified. The logic was clearly reasoned in an oft-cited study led by health economist Joseph DiMasi (DiMasi et al. 1991). According to this study, high cost does not necessarily represent a problem for pharmaceutical innovative activity. The article states,

> [I]f the higher costs are reflective of higher probabilities of commercial success and/or higher average sales per new drug introduction, then strong incentives to undertake pharmaceutical R&D can be maintained even in the face of rising R&D cost. (134)

This is exactly what these giant companies claim to do. Currently, they have in excess of one thousand new drugs, biologics and vaccines in active development. To take PhRMA as an example, annual investment represents over 17 percent of its domestic pharmaceutical sales, a higher R&D-to-sales ratio than any other U.S. industry. It is what they have done in order to survive in a high-risk and high-profit business.

However, while reading the above discourse, we should not take for granted that it truly reflects the reality of this business. The "high-risk" persuasion gives the necessary justification for the pursuit of extravagant profits. It is the discourse drug companies construct for the public; but they construct it for themselves, too. In fact, in addition to fitting the public's image about medical care, this "formal" discourse has also set the terms by which these companies create new rules. In the next section, I will argue that it may not be necessary to follow this discourse by questioning whether research and development is really that risky, and instead the low product success rate implied in this discourse has driven these companies into an endless race of toughening standards. Again, they may not reflect the reality of their practice; however, they set up the route whereby their development depends.

PART II
SURVIVAL LOGIC: THE CONSTITUTION OF REGULATIONS

Behind the "$500 million" Myth

The preceding section discussed the unusual nature of the innovation of proprietary drugs; this section tries to make sense of it from the perspective of regulation. Let us begin again with the cost of developing a drug. Although it is substantial, according to the study by DiMasi et al., the cost PhRMA tells the public is much higher based on its own calculations. This "$500 million" claim was ubiquitous

in the 1990s and widely accepted as the base for the debate over the price of innovative drugs. Along with the increasing costs estimated by academic studies, such as $259 million in 1990 and $302 million in 1995, the estimated costs that PhRMA released rose as well. In the latest update in 2001, based on a study done by the Tufts Center for the Study of Drug Development, the figure had reached $802 million.

Of course, there are criticisms of the bases of these numbers, such as the report released by Public Citizen in 2001. This report calls the $500 million figure misleading because it includes tax-deductible expenses. It also points out that costs are often significantly reduced by public funding, which has helped to launch most medically important drugs in recent years. Furthermore, many so-called NCEs are not that innovative and therefore do not cost that much.[9] No matter what the details of its reasoning are, the question is straightforward: since the drug business is so profitable, it should not be considered high-risk. As the report asserts in its conclusion:

> It [the drug industry] claims to be a high-risk industry, yet for almost two decades it has topped the profit charts by factor of two and more recently three.... In 2000, the 11 largest drug companies netted $28 billion in profits, a 15 percent increase in their return on revenue over 1999....
> Public Citizen believes that it is essential that America maintain a strong and vibrant prescription drug industry.... However ... the industry has massively overstated the amount it spends inventing new drugs. (21-22)

Thus, the report suggests more action from government, such as drug price cost containment, transparency on the costs of R&D, and restriction on patent extensions, to put these "over-grown dinosaurs" back in their original position on the path of "evolutional equilibrium" of thirty years ago.

Although Public Citizen's criticism is insightful, one thing that always troubles me when reading this document is the notion of "risk." What do they mean by that? In order to achieve a better understanding, we have to see how risk is considered in a modern society, for which sociologist Ulrich Beck's innovative analysis of risk is useful (Beck 1992). Beck successfully calls attention to the way the changing idea of risk demarcates industrial society from the society in which we live. Unlike the naturally occurring hazards considered as risks in pre-industrial society, or the socially accountable hazards of industrial society, in "risk society" risks are not limited in time or space; for some, the global is the proper scale for estimating the effect, and even

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[9] They are also the criticisms mentioned in Marcia Angell's recent book (2004, Chapter 3 and 4). Angell points out that in fact, big companies hide the real cost of R&D in several ways while exaggerating the innovativeness of their activities.

future generations can be affected (e.g., by global warming). The rules of accountability become diffused, since everyone in the group can be held responsible (183). In this sense, the pursuit of healthy bodies is the original route of risk management, and medicine is the means called to this effort. As a rational pursuit, modern medicine is expected to deal with the risks to vulnerable bodies that may be individually encountered; however, its practices generate additional risks because it is so privileged, with the help of scientism, as to "monopolize" the way the problems of risks and possible answers to them are interpreted. The public perception is of the "risk-free" drug, designed as an absolutely safe, technologically neutral instrument that will target only the problems our bodies have encountered in the past, are experiencing in the present, and will meet in the future.

From this perspective we see more clearly the problem in the debate over the risk in the process of drug development. As written previously, drug companies favor the "high-risk" discourse because it justifies the high price they demand. On the other hand, admitting that health is the last thing to be sacrificed, health activists in fact accept this discourse by only debating the way it is calculated. I do not mean that Public Citizen's attempt is wrong, but it is an extremely difficult argument for the very simple reason that, as I have written, the information by which "risk" can be assessed is held by drug companies; from my perspective, this may not be the best way to confront this giant if the information is terribly unbalanced. Thus instead of directly questioning the "unrealistic scenarios of risks" in drug development, my strategy is a two-step analysis of the practice of risk analysis in drug development. First, I will try to differentiate the claim of "risk" from that of "low success rate" (or high failure rate). In my opinion, what both PhRMA and Public Citizen mean by "high-risk" is the fact that very few candidates can go through the process and become profitable products; even so, this does not necessarily equate to calculations of risk. Second, if extremely high standards are the basic rule set for drug development, then how have these regulations or "risk management process" evolved and become the way drug companies set the course of future development? Instead of making a direct judgment on whether these practices are right or wrong, this strategy is an effort to see how drug companies reached the place they are now and what problems this course has entailed.

From a technical point of view, it is not difficult to separate "low success rate" from "risk." In fact, when DiMasi et al. calculated the cost of developing an approved NCE, they used "success rate" instead of "risk." They set preferred parameters: a five-year lag, a discount rate of 9 percent, and a clinical success rate of 23 percent. According to them, given plausible ranges for these parameters, the corresponding

range in R&D cost is as wide as between $105million and $425 million. And PhRMA has turned this uncertainty into parameters that they incorporated into their own calculations. It is not "risk," we can see, because "the revenues from successful medicines must cover the costs of the 'dry holes.'"

Even so, we should recognize that the drug success rate is extremely low, and that this is the immediate result of the extremely strict reviewing and approval process carried out in the name of safety. According to PhRMA, producer commitment to high safety standards is required by the regulatory agencies. As seen in its 2002 profile, PhRMA interprets the research and development of drugs as a "careful scientific procedure" in order to ensure patient safety (PhRMA 2002:24-26). This includes four distinct stages of pre-clinical safety assessment, pre-approval safety assessment in humans, safety assessment during the FDA regulatory review, and post-marketing safety surveillance. According to this interpretation, the vast investment in drug R&D is spent to fulfill these rigorous regulations, which are all necessary in order to ensure the absolute safety of the products. This process starts back at the very beginning when a company determine whether a new chemical is worth developing. "The development of a drug is terminated when tests suggest that it poses a significant risk for humans—especially organ damage, genetic defects, birth defects, or cancer" (24).

Even after passing animal tests on toxicity, these candidates must also pass evaluations for safety in each clinical trial conducted on human beings. All subjects involved (healthy volunteers and patients) are observed for adverse effects and all detectable harmful reactions are reported to the regulatory agency. In a phase I study, an initial dose is tested, followed by "real testing," which consists of various dosage levels used in the target population. Doses that fail when applied are dropped. The true challenge comes in the large-scale phase III trial, in which the elderly, patients with multiple diseases, patients who take other drugs, and patients whose organs are impaired are all included.

These studies are overseen at the sites where the trials are conducted, and the data collected is carefully reviewed by the regulatory agency.[10] The central regulatory agency for clinical trials in the United States is the FDA. In the four-stage process of safety assessment, the FDA first controls the possible safety problems by a review of the Investigational New Drug (IND) application set up prior to any human testing. If the FDA does not approve the IND within a thirty-day period, no clinical trial can be conducted. The FDA continues to be updated during the trials. According to federal

[10] In addition, the Institutional Review Board (IRB), the on-site regulatory body for the participating physicians and scientists, is also involved.

requirements, a sponsor must report an adverse event that is unexpected, serious, and perhaps drug-related to the FDA within fifteen days (and adverse events that are fatal or life-threatening within seven days).

Even so, the most important measure the FDA exercises on drug safety is in the review of the new drug application (NDA), which contains an integrated summary of all available information received from any source concerning the safety of the drug. The main sub-agency that deals with this task is the Center for Drug Evaluation and Research (CDER).[11] The CDER has sixty days from the date of an NDA submission to decide if it contains sufficient information for review. The Review Division carries out the process of review. Once the decision is made, it sends a letter to the company explaining the decision. The company has ten days to respond to the FDA decision before the agency automatically withdraws the NDA. As for the review results, a recent analysis by CDER revealed that for the sixty-eight NDAs in 1984 and 1985, the sponsoring companies filed a total of 1,141 amendments (Schweitzer 1997:158). As a condition of approval, the FDA may require a company to conduct post-approval research (a "phase IV" study) to gather more safety data.[12] Further, federal regulations require manufacturers selling drugs in the United States to notify the FDA periodically about the performance of their products, and safety monitoring continues throughout the life of a medicine.[13]

The above description reveals how risks to the body are addressed by the supposedly "risk-free" instrument of medicine, the drugs. It is not a "risk scenario" as Public Citizen portrays, nor does the industry reject this same idea; but these high standards do facilitate the image the industry desires to present to the public, as concluded in its literature:

> Pharmaceutical companies and the FDA take as a primary responsibility the duty to ensure the safe use of all approved medicines in the United States. Throughout the long and careful process...the principal concern of both the agency and the industry is that patients receive medicines that have been

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[11] The other agency that deals specifically with biological products is the Center for Biologics Evaluation and Research (CBER).

[12] These studies may consist of new clinical trials or may be evaluations of existing databases and are designed to detect uncommon but serious adverse reactions typically not revealed during pre-marketing testing (i.e., long-term effects).

[13] While reading these regulations it is important to keep in mind that they do not faithfully reflect the real practice of these companies after their drugs are marketed. The strict regulations, as I will explore later in this section, can be understood as a political strategy of "structuring the world so you can win." For a complete criticism on the devices the drug industry applies to squeeze more profit from their products, see Angell 2004.

> demonstrated in every reasonable medical, scientific, and practicable way to provide more benefits than risks when used appropriately in accordance with label instruction. (PhRMA 2002:25)

In order to benefit the bodily condition with almost no risk under the guidance of modern medicine, only a very few drugs are chosen, and the cost of finding them covers all the others that failed to complete the process.

However, safety concerns offer only a partial answer to the logic behind the "$500 million" myth. They do not exhaust the reasons for the extremely low rate of success. Beck's notion of modernity tells us that while engaging in the management of risk, it is equally important to assess how much benefit an action would bring. Thus the role regulation plays in drug approval is to make every new body-changing drug visible and quantifiable, and to put all these factors in an assessment equation in which one factor can be exchanged for another.

Let us take a closer look at the benefit side in the consideration of the development of a new drug, which is emphasized in the United States. Under the 1962 FDA amendments, substantial evidence of efficacy in the intended use of the drug is required before marketing approval can be granted. Thus the logic of a drug's benefit, simply stated, is maximum efficacy. In practice, the efficacy of a drug is measured in phase II and III trials (in the case of cancer drugs, phase I is also involved), but the consideration of efficacy can come as early as at the beginning of chemical screening. Another goal of the phase I study is to estimate the maximum recommended starting dose (MRSD). MRSD, defined as the largest dosage possible with no observed adverse effect, is then recommended for use in the first human clinical trial. The way this dose is found can be as simple as administering different doses and seeing how much the body can tolerate, or it can be a complicate decision tree determining the dose and the way to administer it. Nonetheless, both approaches share the same logic: the larger the dose, the greater the efficacy that can be expected.

The major work of testing a drug's efficacy starts in the phase II study, in which patients whom the drug is intended to benefit are used as test subjects. Although the FDA does not specify trial design, efficacy is most likely to be shown by an absolute measure instead of a comparison with existing drugs on the market.[14] The absolute value of a drug's efficacy is calculated by comparing it to an artificial, inert substance—a placebo. Therefore, every drug can be considered independent and self-contained in the equation of adverse effects (risks) and efficacy (benefit). It is

[14] In some cases, such as psychiatric, anti-cancer, AIDS drugs, the comparative study is allowed.

compared to itself in the phase II study by using several dosages. The way their medical values are judged is by comparing their efficacy with the "baseline" established by placebos. The phase III study, following the same concept, tries to identify as much as possible the effectiveness of the chosen dose by using large sample sizes. The goal of the trial, therefore, is to maximize the efficacy of this "ideal" dose while limiting possible adverse effects.

As expected, tough mechanisms of selection exist at every step on the way to finding the most effective agent and dosage. From pre-clinical study to trials on human beings, from dose-finding studies to large-scale trials on targeted patients, thousands of chemicals and doses are abandoned because they do not show enough effectiveness. Because of the way "absolute" effectiveness is calculated, each product presents a closed-system in which body and drug interact with each other. The purpose of this system is simply to claim a new chemical entity that can address the following requirements: a bodily condition that needs to be changed or cured, an indication that it could treat, a particular usage of the agent, proof of no or tolerable side effects with use, and evidence of its absolute therapeutic effectiveness in treating a condition. The high standards of regulation result in a very low success rate in the development of new products, and in what I call the logic behind the "$500 million" myth. To reiterate: the process should not be portrayed "risky," but as tough, expensive and time-consuming. More importantly, regulation plays a crucial role in establishing this system. Innovations in regulatory science, as discussed in the next section, may facilitate and/or hamper prospects for product innovation.

"Faster! Faster!" The Red Queen Race between Regulator and Regulated

The above discussion of the current regulations for drug approval helps us to understand the low success rate in making marketable drugs. Again, readers should notice that I am not talking about the reality of this business, but the regulatory system by which the world of proprietary drug operates.[15] In this section I will further explain how this system has evolved. Despite of its complexity—as briefly introduced in previous sections—it is interesting to know how it developed, as it is only a few decades old. Or, one could say, the environment of drug use and its conception now is

[15] Similarly, we cannot assume that the analysis of laws corresponds either to the ways they are used or to the ways drug companies respond to them in practice. However, it is still important to do such analysis in this thesis, because these formalities set the framework within which drug companies survive. Along this line of argument, the achievement of a universal standard, as I will reveal in the third part of this chapter, is what most concerns pharmaceutical companies

very different from what it was one hundred years or even fifty years ago.

Let me briefly review three milestones in the history of drug regulation in the United States.[16] The first is the Pure Food and Drug Act of 1906. It has been said to be the foundation of modern food and drug law, and it made it illegal to distribute misbranded or adulterated foods, drinks and drugs across state lines. Under the directorship of Harvey Washington Wiley, its founding father, the FDA began to actively pursue this newly assigned task. The second milestone is the 1938 Federal Food, Drug and Cosmetic Act, which began the regulation and approval of NDAs, requiring that new drugs be shown to be safe before they were marketed and that adequate instructions for safe use were provided. At the same time, the FDA extended its control over cosmetics and therapeutic devices. The third and most important milestone was the Kefauver-Harris Drug Control Act, which took effect in 1962. It regulated the efficacy of drugs, requiring drug manufacturers to demonstrate the efficacy of their products with "substantial evidence." It also attempted to unify standards for drug approval, authorizing the FDA to review all drugs marketed between 1938 and 1962. As a result, the FDA grew into a huge, complex organization with over 9,000 staff members and 167 field offices working to regulate over $1 trillion worth of products.

From a progressive perspective, drug regulations seem to demonstrate that the more regulations were made to protect consumers' safety, the better public health was—like the motto of the FDA states, "Protecting consumers, promoting public health." However, as addressed in this section, the process marked by these milestones should rather be considered a dynamic evolution of the drug environment, in which conceptions of drugs and the government's role in dealing with them kept changing. Briefly, in the first half of the twentieth century, drugs were regarded a commodity, like food. They were mainly sold directly to customers, in drugstores, without prescriptions. Therefore, the predominant aim of government intervention was to ensure fair value for money spent. In the 1950s—the period of the "therapeutic revolution," as it has been called by policy analyst Peter Temin—the perception of drugs changed. They became an area that required a high standard of regulation. More and more drugs were removed from consumers' reach and sold through doctors by prescription. The government began to take a more authoritative role than before in dealing with the control of the innovation, manufacture and distribution of drugs. Regulatory science was soon developed to serve this need, and it formed the highly regulated world of proprietary

[16] For a journalistic review on the history of the FDA and its relationship with the pharmaceutical industry in the United States, see Hilts 2003.

drugs in which the industry, rather than any professional group from the field of medicine, was the party with which the FDA communicated directly. In the rest of this section will summarize first the changes in the drug environment and then the "scientific language" or rules of the game that have developed for the increasingly sharp dialogue on clinical trials between the FDA—the regulator—and the drug sponsors—the regulated.

Although the Drug Importation Act was enacted in 1848 to authorize the Customs Service to stop the entry of adulterated drugs from overseas, the origin of the federal efforts at drug regulation can really be traced back to the Biologics Control Act of 1902, which resulted from concerns about public health after the St. Louis tetanus outbreak. The act mandated that the Hygienic Laboratory of the Public Health Service (later the National Institutes of Health) regulate interstate commerce in biological products such as viruses, serums and toxins. The Hygienic Laboratory, under the act's authorization, was able to annually license manufacturers, set standards and test the potency of approved items, inspect manufacturers' facilities before and after licensing, and to a limited extent evaluate manufacturers' claims about the therapeutic value of their products (Marks 1997:73-74).

However, under the competition between groups of health care producers and manufacturers, the 1906 Food and Drug Act in fact granted fewer powers to the government while covering a greater range of products. The act gave the Bureau of Chemistry, which became the FDA, no right to screen drugs before their commercial introduction; its function was restricted to informing consumers about the composition of drugs. The act stated that some ingredients, such as alcohol and opium, must be listed on the label or package. Any design or device regarding the medicine or its ingredients that was false or misleading in any particular was illegal. There were no requirements for the manufacturer to prove the truth of statements or the efficacy of ingredients. In essence, the burden was on the government to prove that a claim was false or misleading after a product was already on the market and being sold.

At that time there was no clear distinction between what we call prescriptive drugs and the over-the-counter drugs, but rather, as Temin reminds us, a distinction between "ethical" drugs and "proprietary" drugs (Temin 1980:3-4). Consider as a kind of commodity, ethical drugs were those advertised only to doctors, and proprietary medicines were those advertised directly to the public, including so-called patent drugs.[17] During the Progressive period, because there were few effective drugs and

[17] Temin writes that the term "ethical" here refers to the original 1847 code of ethics of the American

because most regulatory activity occurred in the context of food production rather than of medical care, consumers got less than 5 percent of their drugs directly from doctors. What is more, consumers could simply buy any non-narcotic drug (and some narcotic drugs such as laudanum) they desired without a prescription.

Further reforms were not made until the Elixir Sulfanilamide, a sulfa drug that contained the poisonous solvent diethylene glycol, was released in 1937 and killed 107 Americans, mostly children. In a response, a new law was drafted enacting the reforms originally undertaken within the FDA. The resulting 1938 Federal Food, Drug and Cosmetic Act differed from the 1906 law in being far longer and in organizing regulations by commodity rather than by type of violation. A new drug could not be delivered for interstate shipment unless an effective application had been filed with the Secretary of Agriculture. The application had to describe the content, manufacture and uses of the drug and demonstrate that it was safe for use under the recommended conditions. It became effective sixty days after filing unless the Secretary objected.

Meanwhile, the government policy toward medical drugs has progressively removed control over drug choices from the customers. In section 502 (f), the 1938 Act states that drugs with certain kinds of labels, such as "Caution...," can only be sold by prescription, thus allowing drug companies to create a class of drugs that cannot legally be sold without prescriptions by putting appropriate labels on them. The change of policy has been described by one of the authors of the act, Davis Cavers, using a baseball analogy: "Lives are at stake and ...we are entitled to ask for something pretty close to errorless ball" (as quoted in Temin 1980:1). The consequences of this regulation can be seen in the change in the way that drugs were sold. As seen in table 2.5, more and more drugs came to be sold through physicians with prescriptions.

As a primary attempt to separate drug regulation from food regulation, the 1938 Act also shaped the way entirely new drug technology was introduced after World War II. The number of drugs available, the range of diseases and conditions amenable to drug therapy, and the power of drugs increased dramatically. The 1950s is the decade of the "wonder drug," when antibiotics, steroids and other therapeutic novelties flowed from manufacturers' laboratories and plants in a seemingly endless stream (Hilts 2003, Chapter 6). A new drug industry thus emerged in the context of the FDA's prescription-only regulation. Characterized by large firms selling new, patented drugs,

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Medical Association, which excluded advertising to the public as part of ethical medical practice. The term "proprietary" in proprietary medicines signified that the ingredients of the medicines were secret, not that they were patented.

the industry earned high profits and got extensive legislative attention.[18]

Table 2.5 Consumer Expenditures for Prescription Drugs and All Medicines, 1929, 1949, and 1969 ($ million)

Year	Prescription drugs	Drugs and other medicines	Prescription drugs as a percentage of all medicines
1929	190	600	32
1949	940	1640	57
1969	5395	6480	83

Source: Temin 1980:4, Table 1.

Although, as mentioned above, the famous Kefauver hearings gave birth to the 1962 Kefauver-Harris Drug Control Act, the initial goal of this hearing was in fact a limited one: to examine the high prices of proprietary drugs. Nonetheless, when passed in the Congress, the act was given a new face by public perceptions of threats to health, and came to include stricter regulations on safety and efficacy. The thalidomide tragedy was the trigger. In 1960, William Merrell Company applied to the FDA for approval of Kevadon, a brand of thalidomide. Although Kevadon was not granted approval before it was identified as a source of deformities in newborn children of women who took it, over 2.5 million tablets had been distributed for the purpose of clinical testing. However, the FDA did not have authority to supervise the clinical testing of drugs under the 1938 law, and this resulted in a small yet highly visible group of deformed children in the United States.

Like the regulatory acts of 1906 and 1938, the Kefauver-Harris Amendment was an immediate response to tragedy (Hilts 2003, Chapters 9, 10, and 11). Instead of letting a firm's NDA take effect automatically if the FDA did not object, the new law required affirmative FDA approval before marketing could begin. In addition, the amendments gave the FDA jurisdiction over the testing of all new drugs before they were approved for marketing. A drug firm had to apply to the FDA for approval of its procedures for testing an investigational new drug before it could undertake the tests needed to file an NDA. The testing of drug like thalidomide could no longer be undertaken without prior notification of the FDA.

[18] See also the case of Eli Lily in section 3, Part I of this chapter.

However, the most important impact of this amendment on drug regulation practices was regarding drug effectiveness. The FDA was empowered to withdraw approval based on a "lack of substantial evidence" of effectiveness. Although the discussion of drug effectiveness can be traced back to the Supreme Court in *U.S. vs. Johnson* (1910) on the basis that therapeutic effectiveness was a matter of "opinion," this vague term was added into the Act that the claims of effectiveness in the NDA or thereafter had to be supported by "substantial evidence."[19] It defined "substantial evidence" as follows:

> [T]he term "substantial evidence" means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof. (Chapter 5, subchapter A)

Apparently, drug makers needed to provide the FDA with full details of clinical investigations, including drug distribution, and the clinical studies had to be based on previous animal investigations to assure safety. For this purpose the drug industry formed the first advisory committee, the Advisory Committee on Investigational New Drugs, for assistance in complying with the new law. Nonetheless, what was at stake here, and how could this evidence be generated?

This need was served by newly established medical research methodology that relied heavily on statistics. According to Harry Marks's research (Marks 1997), before the 1950s, clinical investigators sought to master uncertainties by accumulating experience. Experience alone brought detailed knowledge of the vagaries of specific diseases, knowledge that might then be applied in devising proper experimental controls. The value of a study depended on the prior state of knowledge about diseases and treatments. The more that was known, the better the experiment that could be designed. However, the methodological breakthrough of statistics entered the scene of therapeutic research, as it did in other fields, after World War II. Of course, the notion of using statistical analysis in medicine is an old one, dating back virtually to the

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[19] Judiciary Committee members considered two options: preponderant evidence and substantial evidence. In fact, the latter was weaker, according to the committee, as it did not require agreement among the majority of experts for the approval of a new drug. This agreement was not considered necessary as long as there was "substantial evidence" of effectiveness.

origins of modern probability theory. Even so, it was not until the early twentieth century that some medical researchers introduced statistical methods and concepts into physiological, biochemical and clinical research. It was the introduction of statistician R.A. Fisher's ideas about experimental design with the U.S. Public Health Service and British Medical Research Council's trials of streptomycin for tuberculosis in 1948 that opened up a new approach to establishing therapeutic effect.

Statistics had an impact on how clinical trials—especially later, large-scale phase III trials—are done and how the results are interpreted. For the former, randomized sampling and blinding were the two most important, though controversial, concepts. Assuming the similarity of the trial subjects involved, randomization is a method used to prevent bias in research. Participants are assigned by chance to groups that are comparable in terms of factors affecting prognosis and other participant characteristics.

This sounds as if it should be perfect. However, this methodology has a possible clinical effect on professionals, who in practice might unconsciously assign participants with a more hopeful prognosis to the experimental group, thus making the new therapy seem more effective than it really is. Double-blinded trials, in which neither researchers nor participants know who is in the investigational or control group, were introduced to avoid such bias by detaching physicians from the assignment making. This ensures that people assessing the outcome will not be influenced by knowing which intervention a participant is receiving. Thus while information from clinical observations and investigations is collected, the physicians in charge no longer control the study—the scientific method does. It does this by creating a self-constructed system according to which the investigation starts and finishes, data are generated and analyzed, and results are interpreted.

Thus an "adequate and well-controlled investigation" is defined as follows: participants should be selected by eligibility criteria, such as age, sex or prior treatment. The change a new drug brings to the participants is quantified by comparing it to a placebo.[20] The study is stopped when it reaches the endpoint, which is defined as a measurable outcome that indicates an intervention's effectiveness. The results achieved should be interpreted in terms of probability. Effectiveness is basically judged by whether the difference a new agent brings has any statistical significance, defined as when the data comparison results in a p-value of 0.05 or smaller. The smaller the value

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[20] In order to high the main factors incorporated into a modern clinical trial, such as placebos, this section does not intend to exhaust all considerations when they are considered in different situations. For more discussions about the meaning of placebo and its use in the proposal of clinical trails, see Harrington (ed.) 1999 and Moerman 2002.

of p is, the greater the likelihood that the results are not due to chance. The effectiveness of a clinical study is also defined this way. Confidence intervals indicate whether the results of small-sized trials that are not statistically significant are nevertheless medically significant. On the other hand, in order to avoid testing more people than are needed to obtain statistically significant results, the concept of statistical power is used to distinguish statistically significant results from insignificant ones. The combined use of all these techniques creates a proper clinical trial. If in 1910 the Supreme Court argued that therapeutic claims were opinions, now they are "facts" justified by statistical equations. Statistics are the rule of the game agreed upon by the regulator and the regulated. Accepting it means accepting it all.

Since the FDA's acceptance of "appropriate statistical methods" as the standard for "well controlled" studies in 1970, the phenomenon of the clinical trial has become so large and complex that nobody can really see it as a whole. At almost the precise moment when the Kafauver-Harrison amendment was passed, the postwar rate of new drug introductions fell off sharply, from an average of fifty per year in the 1950s to an average of twenty per year in the 1960s. As a consequence, a number of economists investigated the effect of the 1962 amendment on the availability of drugs. Among these studies, economist Sam Peltzman's is perhaps the most famous. Peltzman concluded that although the amendment attained its goal of reducing consumer waste spending on ineffective drugs, "the costs in the process seem clearly to have outweighed the benefits" because of the decline in drug innovation (1988[1973]:346). It seems like the tough standard, as the new rule of the game, was not made for the sake of the availability of drugs.

This also sparked what I call the "Red Queen's race" between regulators and regulated. This term refers to a race in *Alice in Wonderland* in which Alice and the Red Queen, running hand in hand, never actually go anywhere. Although Alice does not see any change of place, the Queen keeps crying, "Faster! Faster!" and says to the puzzled Alice, "If you want to get somewhere else, you must run at least twice as fast as that!" This is exactly what happened for regulatory authorities and pharmaceutical companies after these rules were implemented. The fear of putting health at risk is so real that nobody would dare to lower the standard once it came into existence.

During this new round of the Red Queen's race, both the FDA and the industry, both rapidly grew in size. In early 1970s the FDA increased its statistical staff and gave them a significant role in the review of NDAs. An expansion of the Division of Biometrics in 1979 led to the formation of three branches: the Statistical Evaluation Branch, the Statistical Application Branch, and the Computation Branch. The Statistical

Evaluation Branch was responsible for the statistical reviews of all the clinical trials submitted as NDAs. There were fewer than twenty people in the division, and the Statistical Evaluation Branch accounted for about half of them. This change led to a similar increase in the hiring by industry of statisticians. Furthermore, the development of statistical program facilitated sophisticated analyses and also created a barrier to entry into this profession. By 1985, the pharmaceutical industry and its regulators were probably the largest employers of statisticians in the United States (Segreti et al. 2001, Section 3).[21]

Table 2.6 Illustrative Breakdown by Activities and Purpose of R&D Costs of a Typical NCE (in percent)

Activities	Estimated share in total research cost (%)	Purpose
Synthesis and extraction from natural substances	11-19	Search for lead compounds
Biological screening	8-12	
Animal pharmacology	8-12	Verification of their basic uses
Toxicology and safety	9-10	Effects; determination of specific pharmacological properties
Metabolism and pharmacokinetics	6-7	
Analysis research	5-6	
Clinical trials	16-28	Efficacy; safety
Chemical process	10-12	Standard quality
Pharmaceutical technology	7-10	Optimum dosage form
Documentation for regulatory authorities	3-4	Registration

Source: Ballance et al.: 97, Table 4.6, cited from UNIDO.

[21] Another aspect of this increase can be seen in the number of the biopharmaceutical subsection members in the American Statistical Association. According to the ASA Biopharmaceutical History Committee (2005), from 1966 to 1979, the number grew from 100 to approximately 1,500 (11).

The complex procedures of clinical trials today represent what these two giants achieved over the past three decades. They comprise the basic framework of the world of proprietary drugs and exclude unqualified players. Many researchers have found that the clinical trial has become the most costly step in drug development (table 2.6). In the drug risk-benefit equation, the industry is trying to find an optimized dose with the lowest possible incidence of side effects. The FDA, on the other side, adds more considerations for review. The total development time was prolonged from 8.1 years in the 1960s to 15.3 years in the early 1990s; most of the increase is due to the new requirements for clinical trials. Furthermore, since the 1960s, the FDA has added 2.3 years on average for the review of each application.

A number of things contribute to this new "drug lag" (Schweitzer 1997: 160-165). Unlike in developing countries, where advanced drugs are often delayed for economic reasons, in developed countries this lag happens as a result of the long and complicated regulatory process for drug approvals. However, I do not think it is the basis of the problem. In fact, before the recent proposal of reforms restricting safety regulations in response to the adverse effects in the Vioxx case, many legislative efforts had been undertaken in the attempt to speed up drug approval, such as the 1993 Prescription Drug User Fee Act and the 1997 FDA Modernization Act. The fundamental problem, as I explained in this section, is the construction of rules that are supposed to generate "risk-free" drugs. Here is the *real risk*. For the drug industry, it is whether it can keep its promises to provide "risk free" cure as the legal bar continues rising. For the regulators, it resides in the promise of safe drugs: how long can people stand the lag in the introduction of advanced drugs due to this high bar?[22] It is a Red Queen's race that there is no way to end. No one actually wants to run but they continue to do so.

All in the Name of Health: The R&D-Based Pharmaceutical Industry Inside and Outside of the United States

From last section we have an understanding of the evolution of the world of proprietary drugs. I have discussed how the regulator and regulated pursue and keep up

[22] As Philip Hilts (2003) concludes about this dilemma for the FDA in the last two decades of the twentieth century, "Regulation has become one of the most contentious and even inflammatory issues in politics and society. It was asserted that regulation, regardless of its type or apparent usefulness, cost society money and freedom. But now after the fever has passed, in looking back over the whole history of the agency, it is clear that regulation has become a vital part of society for both citizens and business" (337). Although the current work does not pursue a philosophical study on the ethics of promise, it calls attention to this problem and tries to elaborate how experts and regulators figure a way to solve it by means of the global forum of the ICH.

with each other. In this section, however, I would like to call attention to their companionship within the rules that they have created. As I have pointed out, the rules are both beneficial and risky. Through the Red Queen's race mechanism of statistical methodology, the regulator and regulated excluded other players by controlling the field; those excluded include individual physicians, life science-researchers, policy makers, health care planners, and, most importantly, consumers. These others can play minor roles and establish some relationships with each team; however, it is very clear that the FDA and PhRMA are the main players and the ones capable of adjusting the rules of the game.[23] On the other hand, the rules have changed the behavior of regulators and drug sponsors by posing moral questions—in the form of marketing scandals and clinical trial malpractice—about how strictly they should be followed.

Let me make a brief sketch here. Peter Temin (1980) has pointed out the changes on the regulatory side that followed the 1962 amendments. He argues that the medical behavior of drug use was changing from customary behavior, with consumers' free choices driving the market, to behavior based on command and institution (Chapter 8). A hierarchical structure is presented in the name of health. Considering drugs not as pure commodities but as instruments of health maintenance, the regulator chose to control not only whether there should be risk to users' lives, but also whether drugs provide any benefit to their health. On the other hand, the ecology of the pharmaceutical industry changed. Although risks took time and effort to deal at the beginning when the new rules were introduced, once they could be estimated and turned into factors in the calculation of cost, risks were no longer "risks" at all. They just required a high investment that only a few could afford. However, everything that was spent had to be recovered by the sale prices set by the industry itself.

This change of landscape can be described as a double "Matthew effect," as described by sociologist Robert K. Merton in his observations of the activity of scientific research (Merton 1968). The Matthew effect refers to the words of the master in Jesus' parable of talents in the Gospel according to Matthew: "for everyone who has will be given more ...and everyone who has nothing will forfeit even what he has" (25:28). The reward system in science favors scientists who are more senior and more powerful over those who are more junior and less powerful. It is the same in the pharmaceutical industry: the established companies are able to invest more in drug discovery and thus can gain more market share than smaller companies. The other

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[23] The history of the biopharmaceutical section of the American Statistical Association (ASA Biopharmaceutical History Committee 2005) in fact reveals how the regulator and the regulated had to work together to make the standards for clinical trials.

"Matthew effect" aspect of drug industry is the role of the institutional consensus of scientific novelty, something that Merton does not mention in his paper. The big companies define which products constitute unique or useful contributions and should therefore be given rewards. Tough regulations, in this sense, create the monopolistic character of drug production.[24]

The 1962 amendment applied not only to drugs to come—it was an effort to regulate all existing products. The FDA instituted the Drug Efficacy Study Implementation Program in which the National Academy of Sciences-National Research Council was commissioned to review over four thousand drugs from 1966 to 1973. Although products innovated before 1938 were not included, these soon disappeared from the prescriptive drug market anyway. The consequence, as table 2.7 shows, is that the pharmaceutical giants grew larger in the 1960s and the gap between big and small companies became wider, as only the former had a large volume of capital that they could use to leverage the creation of profits through investment.

Table 2.7 Market Share and Number of Drug Firms by Size of Assets, 1948-1973

Year	Share of total market receipts by size of assets (in percentage)			Number of firms by size of assets		
	$1-10 million	$10-100 Million	Over $100 million	$1-10 million	$10-100 million	Over $100 million
1948	22	56	7	82	22	1
1953	19	48	23	92	25	3
1958	17	45	28	101	29	5
1963	11	20	61	138	31	14
1968	6	9	83	147	26	21
1973	3	4	92	119	21	30

Source: *Sourcebook of Statistics of Income*, cited in Temin 1980:76, Table 5.

Meanwhile, the behavior of big pharmaceutical companies changed. They now

[24] Though it works in a different direction with a different framework, I would like to acknowledge psychiatrist and author David Healy's notion of the "Luke effect" (Healy 1997, Chapter 6), which nicely draws the ambiguous social ground on which science and commerce trade with one another in ideas about drugs and views of disease to which these ideas are applied.

know that in the name of health improvement only two items are worth more investment: marketing and R&D. The former serves to let consumers and physicians know how many new choices they have; the latter overcomes the difficult standards required to send a product to the market. The trend can be clearly seen in the changing structure of company costs as shown in Ballance et al.'s study (1992:123, fig5.2). Although manufacturing is still the largest component in the total cost, the percentage has dropped significantly from 40 percent in 1973 to 25 percent in 1989. Meanwhile, expenditures on both R&D and marketing have increased—especially marketing, which accounted for 24 percent of total spending in 1989. This change coincides with the steadily growing percentage of operating profits.

Let us put aside the regulatory strategies industry has used to reduce its R&D cost, which deserve their own study, and focus on the immediate changes to big pharmaceutical companies' marketing strategies. The first change is the "return" of direct to consumer (DTC) advertising. According to Temin (1980, Chapter 5), doctors were appointed the consumer's agent, responsible for choosing "dangerous" drugs, shortly before World War II. The description "dangerous" in this context does not mean toxic, but rather potent; doctors were to prevent the misuse of powerful drugs by patients. A new relationship between doctors and drug manufacturers began to take shape in the mid-1950s and lasted until the mid-1970s, when the increasing availability of generic products began to threaten it. With new drugs came competition within the drug industry wherein the more integrated, innovative drug producers, those who advertised heavily to doctors, started to overcome the limitations of their market to establish personal relations with potential customers.

The most notable example is perhaps that of Tagamet (cimetidine), the first H2-antagonist. Introduced in 1977 by SmithKline Beecham, Tagamet was the pioneer acid-blocker. However, it is seldom noted, according to Cynthia Crossen, as the first product that drug companies advertised on television news.[25] This was done even before the drug became commercially available. Patients came to their doctors demanding this revolutionary new drug. This response hinted to pharmaceutical giants that they did not really need doctors or medical journals to filter their products. They could get the same effect by using the mass media (Crossen 1994:173-175). And Tagamet's marketing performance was amazing: worldwide it has earned the company

[25] Some may not agree with this understanding. Wayne Pines, for example, points out that there is not identifiable point where the information about prescriptive drugs began to open to the public (1999: 489). According to Wayne, one of its legal origins can be found in FDA's patient package insert developed in 1968, and the first direct-to-consumer advertisement was a price advertising for a ibuprofen product called Rufen in the late 1970s (491).

a total of $14 billion. Meanwhile, other companies joined this battle. Three other H2-antagonists, Zantac, Pepcid and Axid were launched between 1983 and 1988.

The anti-acid battlefield moved to the OTC drug market when the patent for Tagamet was about to expire in 1994. As Leon Jarnoff portrays (1995), in 1993 SmithKline began conducting clinical trials and seeking FDA approval of an OTC version of the drug, Tagamet HB. However, Johnson and Johnson/Merck, the producers of Pepcid, beat out SmithKline by winning FDA approval of their OTC acid-blocker, Pepcid AC, and began marketing it two months before Tagamet HB first appeared in pharmacies. The companies stoked the fires of mass media attention by fighting with each other.

The story of Tagamet does not stop here. In addition to DTC advertising, "abusing" the indications of an existing drug is another way to prolong the life of its patent. This is a short cut in which pharmaceutical companies create a convenient "health need" in the population. Soon after the marketing of cimetidine in the late 1970s, industrial scientists started to search for new indications for this drug, first for gastric cancer and then for colon cancer (Morrow 2002). Like the (eventually withdrawn) attempt to indicate the use of Vioxx for patients at risk of developing recurrent colon polyps, in 1988 scientists tried to validate cimetidine's utility as an inhibitor of tumor cell propagation and metastasis, and a clinical study found that it significantly increased the survival rate in patients with stage II and stage IV disease. More indications were added. The latest indication for the drug, published in the *British Journal of Cancer* in 2002, showed a three-fold improvement in the ten-year survival of Dukes C colon cancer patients who were given cimetidine after surgery.

It seems as if the indications for a drug can be unlimited: new indications are derived from old ones; an indication as a cure for one disease can be transferred to the prevention of another disease. Echoing Dumit's observation on the cooperation of science and markets in the drug business (Dumit forthcoming), the increase in indications seems to show how an additional market can be created by either defining more people as at risk (modifying risk factors or lowering the thresholds of having a diseases) or turning invisible pathogens into the subjects of treatment (creating markers and tests to detect invisible pathogenic changes within the body). This market comes from the most fundamental part of the world of proprietary drugs and expands by the power of its own logic.

Indeed, all of these manipulations in the name of health seem to be unquestionable. Dumit nicely analyzes the motivations of the drug industry in terms of a twenty-first century version of *Capital* for life science (Dumit 2004). From this

perspective Dumit calls attention to a paradigm shift in the perception of the body when encountering disease. The notion of the body has shifted from one considered "inherently healthy" to one considered "inherently ill." The older notion of diseases of the body has not totally gone, but the new notion of illness is one that "is now promoted to us in advertisements and in awareness campaigns throughout our daily life" (17). As this mechanism continuously acts, it can drive the medical care system to absurdity. As Dumit points out, health is not evaluated on the basis of how many people are already going to see their doctors, but by imagining "a threshold diagnosis and then [calculating] how many people *would* be part of that threshold and therefore *should* be consumers of that drug" (25). The key consideration—to what extend can this market grow—is not a purely scientific concern, but one of political economy. To take screening as an example, Dumit argues that the number of people diagnosed as sick will theoretically reach its maximum when all possible cases found can obtain the required treatment (22-24).

The political economy of the drug market is far more complicated than what Dumit suggests. Although the United States is an enormous market in which there seems to be no limit to people's pursuit of health, drug sales are limited by the duration of patent protection. In the case of Tagamet, sales plummeted from $600 million in 1993 to only $400 million next year, mainly due to the sudden fall in price after the drug lost its patent protection in May 1993. Drug makers often resort to legal tactics, such as Hatch-Waxman Act of 1984, to protect and extend their patent rights, yet the marketing time for each patent drug is short because a large portion of the patent period is taken up by research and development activities and FDA review. Effective marketing time was shortened to less than ten years in the 1980s (Schweitzer 1997, table 9.1). For marketing, the key consideration is not how many patients a patent drug can catch, but how many can be caught in *a given period of time*. The tactics used in the American scene are of limited use for this, and additional markets appear to be an immediate solution to this problem. This logic in capitalism, as Michael Hardt and Antonio Negri call, is the "need for an outside" (222-225).[26]

This can be seen in the shift of exports and pharmaceutical sales abroad by U.S. firms. According to Temin (1980:145, table 21), along with the expansion of the domestic market, the foreign sale of pharmaceuticals rapidly increased in the 1960s and 1970s, and the trend continued. Among these sales, total exports accounted for no more than 17 percent, and the share of intra-firm trades (from the home company to oversea

[26] In his politico-economic analysis of U.S. research pharmaceutical firms, Christopher Harrison also suggests that patents and intellectual property rights issues are the reasons that drive U.S. firms to overseas markets. See Harrison 2004, Chapter 3.

subsidiaries) in exports has increased in the 1980s and makes up the bulk of exports. The extent to which companies trade within their own organization is clear evidence that strong links exist between the parent company and its foreign subsidiaries. Meanwhile, these subsidiaries are the entities that deal with local governments. Overseas markets are not just marginal. There has been a widespread increase in the amount firms allocate to distribution and promotion overseas. Traditionally, R&D-based firms concentrated their marketing resources on a few national markets when they launched a new product. In the 1990s, however, they launched new products in all major markets ("first wave" countries), and sometimes even some developing countries ("second wave" countries), to maximize revenue. This adjustment requires larger marketing forces and heavy sales promotion. The sales staffs of the world's top pharmaceutical firms grew by 50 percent in the period from 1983 to 1988. With such resources at their disposal, large firms are able to accomplish a worldwide launch in only three years where they once required eight to ten years.

Of course, companies claim that this change in marketing tactics holds some benefit for consumers across the world. Consumers now have access to the latest drugs with a minimum delay. Again, this claim is made in the name of health. However, from the viewpoint of political economy, it can be interpreted in terms of the drug companies' urgent need for drugs that can clear regulatory hurdles and earn back development costs as soon as possible.[27] In the process, global marketing places these capitalists in a situation that they are not familiar with. In the markets of developing countries, patent piracy is a major problem. The business rhetoric of intellectual property protection, as we often hear, is that it gives R&D-based pharmaceutical companies a period of market exclusivity that they require in order to recoup their huge investments and take in capital necessary for developing the next generation of medicines and vaccines.

For developed counties, the problem is different and more difficult. Those who can afford to may simply not accept drugs the United States has approved. In fact, some major national markets, such as Germany and France, have improved their own drug approval and manufacturing regulatory systems since the 1950s. It may be hard to judge whether their standards are higher or lower than the FDA's, but one thing is for

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[27] Marcia Angell points out the crisis the American pharmaceutical industry faced at the dawn of the new millennium (2003, Chapter12). First, the public pay more attention to the prices of the drugs they use. Second, more and more Americans buy their drugs abroad, where they are much cheaper. Third and last, the R&D "pipeline" is running dry—only handful of candidates meet the tough standards for approval. All these factors contribute to the industry's increasing attention to markets outside of the United States.

sure: they cannot simply be replaced, because they have their own special requirements and concerns. For industry, this poses the biggest problem: there is no point in fulfilling the increasingly complicated standards one by one. Thus the standardization of standards became important and urgent. It would both ease the movement of drugs from one country to another and create a larger single market that will reduce costs.

PART III
THE NEED TO STANDARDAIZE STANDARDS

The Need for a Universal Standard

When they step outside the United States, the global companies have to face the problem of fitting other local standards. Of course, we need not review here the history of standardization, which is long and complex. As Hashimoto Takehiko writes (2000), the modern origin of technology standardization can be found in Thomas Jefferson's visit to France in 1785, during which he learned of the standardization of parts for building muskets. The shop of Honoré Blanc, a French mechanic, made these handcrafted parts to such precision that they could be interchanged (Chapter 1). The idea of "interchangeability" was soon introduced in the United States and became the central theme of its industrial production.

This concept also triggered the second stage of standardization, the standardization of process. As one of the keys to mass production, process standardization was combined with the introduction of machines and later the creation of assembly lines. The standardized machine tools constructed a world of their own logic that economist Winfred Rothenberg called "American production," and human beings became subordinated to it. They had to be trained to be compatible with the machines they worked with. In this situation we cannot forget the conclusions Karl Marx draws in the first volume of *Capital* (1976[1867]):

> In handicrafts and manufacture, the worker makes use of a tool; in the factory, the machine makes use of him. ... we have a lifeless mechanism which is independent of the workers, who are incorporated into it as its living appendages. (548)

It is not surprising that the first standardized mass production and the standardization of process were both originated in the United States. Their origin can be traced to the control of production in Harpers Ferry Armory in the nineteenth century (Smith 1980); however, it was Henry Ford's Model T car and Frederick W. Taylor's scientific

management of human factors that made standardization a trademark of the United States. These phenomena demonstrated how the most efficient production could be achieved without special requirements in terms of laborers' skills; their goal was clearly to provide consumers with a quality product at a minimum price.[28]

At first glance this is an optimistic "win-win" vision. Quality mass production was the gospel of modernity and those things previously considered to be luxury items were now accessible to the public. Mass production also created an institutionally based trust that quality would never vary with the place or time of production, just like how McDonald's or Kentucky Fried Chicken customers would not expect differences in the burgers they order even in restaurants in remote places. It seems that in the progressive context of the industrial revolution, mass production and standardization were proposed by the producers in order to offer customers better goods at cheaper prices. The above discourse raises at least two questions related to our story: first, by what process can people decide the best standard for all customers, and second, which standard is best for which customer? In the rest of this chapter I will try to answer the first question in the case of pharmaceuticals. The second question, which is more crucial to this anthropological investigation, will be dealt with in later chapters.

Concerning the mechanism by which a "perfect" standard is chosen and widely spread, Paul David's historical study of the emergence and domination of the QWERTY keyboard is worth noting (David 1986). The paradox of the QWERTY keyboard, the widely used layout that appears on nearly all of the world's typewriters, is its relative inefficiency. But using this example, David shows that there are very rational and interrelated causes that explain the embedded dominance of some standards despite apparent discrepancies in efficiency. He offers three socio-economic factors—technical interrelatedness, the "first mover" effect, and quasi-irreversibility of investment in labor[29]—which together form what David calls "path dependency." As he explains it, this is "a sequence of economic changes...in which important influences upon the

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[28] It might be a too short and too "America-centric" review of the development of standardization. I only list key events that present conceptual changes in the United States and are related to the following discussion. In fact, to my knowledge, there is still no good history available concerning this topic.

[29] Technical interrelatedness is described as system compatibility between keyboard "hardware" and the "software" represented of the touch typist's memory of the particular arrangement of keys. It suggests that the present value of a typewriter as a capital good was dependent upon the availability of typists trained on the keyboard arrangement. As the most important consequence of technical interrelatedness, the "first-mover" effect is seen in "the process of intersystem competition to lead toward a de facto standardization through the predominance of a single keyboard design." The first person who creates standard will be likely to lead the whole group. What David calls a "quasi-irreversibility of investment in labor" refers to the situation, in the case of QWERTY keyboard when one typists were taught QWERTY, there was a very high cost to converting to another system.

eventual outcome can be exerted by temporally remote events, including happenings dominated by chance elements rather than systematic forces" (30). The story of the QWERTY keyboard is meant to demonstrate that the role of a technology doesn't necessarily depend on the relative merits of that technology. Rather, technological "innovation" is part of an essentially dynamic historical process and must be understood as such.

Let us draw parallels in terms of standard making between the story of the QWERTY keyboard and that of pharmaceuticals. The first is the high bar for latecomers. In the past thirty years regulatory agencies and industry have constructed extremely high standards that protected all stages of the monopoly, from innovation to production. As described earlier in this chapter, costs have been raised in order to produce high returns in a short time. Thus, in this chain of innovation, companies must allocate what they have earned from their previous products into their quest for future profits. Like typists having the social capital of being familiar with the QWERTY keyboard, once a company overcomes the difficulties of this game and survives in it, the game itself resists new market entrants.

The second parallel is found in the existence of the exclusive club of global pharmaceutical companies. Although they compete with each other, these companies have developed common standards as the rules for competition. These seemingly trivial standards—such as the proper temperature for stability testing, the period when a drug is effective, the standard dosage for each pill—create fundamental principles upon which a tablet or a pill can be produced, tested, sold, and finally consumed. However, this phenomenon is only of consequence because of the existence of the "first-mover" effect, the third parallel. As discussed above, the FDA was the first governmental agency involved in the story of pharmaceuticals. However, in the 1970s and early 1980s, there were in fact no comparable regulations in many countries outside of the United States. In those years, the FDA ran almost alone. Even though the thalidomide accident badly harmed the credibility of the FDA, companies knew that once their products got the marketing approvals from it, they could be registered all over the world without demands for more trials.

However, the situation changed. Based on their own considerations, more and more governments added their own requirements for new drug applications. European counties were the first to follow, and then Japan, along with many others. Regulatory authorities in these countries often requested the replication of all or most of the clinical data. As for the manufacturers of the QWERTY keyboards, it was hard for drug manufacturers to switch from one system to another between different markets. If it was

not possible to waive all standards, the industry was not able to meet them standards one by one either. Thus the call for a universal standard arose in the name of public health. The standard had to be the high in order to protect users from unknown risks; it also had to be unified, by definition. From an economic perspective, the extensive duplication of clinical evaluations in new regions not only required valuable development resources, but also delayed the availability of new pharmaceutical products to local patients in need.

Along with these factors, others, such as regulatory agencies, scientists, and characteristics of drug industry such as dosage choice, complicated the process of standard making. However, the outcome needed to be a universal standard for drugs and a universal body of consumers that interacts with the drugs produced according to this standard. If Marx's *Capital* describes how workers and machines encounter one another in a new mood of production, the attempt to create a universal standard for drugs pushes this situation to another level, one where "bio-availability" is achieved by the free flow and exchange of material and flesh.[30] More importantly, this flow and exchange are made possible under the logic of the circulation of commodities. For ethnographers, it is a moment when a fundamental structural change in the field of global politics occurs, and at this moment we witness the birth of the ICH.

The ICH as a One-Size-Fits-All Panacea

From the perspective of standardization, the ICH presents a global project that has never previously existed. Founded by the United States, the European Union (EU; at the time the European Commission, or EC), and Japan, this conference tried to create a universal standard by standardizing all standards and thus creating a single global market in which new drugs could be traded freely. Its origins, according to the official documents, are as follows: the harmonization of regulatory requirements was pioneered by the EC in the 1980s as it moved toward the development of a single market for pharmaceuticals. Meanwhile, bilateral negotiations between these countries/regions went on. It was at the International Conference of Drug Regulatory Authorities in 1989 that specific plans for action began to materialize. Soon afterwards, the authorities approached the International Federation of Pharmaceutical Manufacturing Association

[30] In fact, there are various forms of exchanges between supply and demand sides over standards in the medical realm, and that in the area of drugs is just one of them. For example, in order to ensure a successful transplantation, organ procurement organizations have set standard procedures and criteria in their search for available organs. See Hogle 1995.

(IFPMA) to discuss a joint regulatory-industry initiative on international harmonization, and the ICH was conceived.

The birth of the ICH took place at a meeting hosted by the European Federation of Pharmaceutical Industries and Associations (EFPIA) in Brussels in April 1990. Representatives of the regulatory agencies and industry associations from Europe, Japan and the United States joined together and planned an international conference. A steering committee was organized that decided to have the first conference, titled "International Conference on Harmonization," in Brussels in November 1991.[31] From its beginning, the ICH was a focus for everybody related to the pharmaceutical sector, including industry, academia and government. Over 1,200 people attended the first conference, and its popularity increased at following meetings (appendix 1). The ICH became a phenomenal global festival in the world of proprietary drugs, but for the field of STS, it has additional meanings that are worth noting.

The uniqueness of the ICH can be understood by situating it in two political economy contexts. First, from the viewpoint of global politics, unlike other conferences on technical standard making that are dominated mainly by governmental representatives, such as the International Electrotechnical Commission (IEC),[32] the ICH allows industry to have a strong presence. Given the fact that over 95 percent of pharmaceutical research and development is conducted in the industrial sector, the ICH clearly knows that it cannot be a space for only diplomatic gestures and performances. It is fully aware of the fact that any standard for new drugs cannot be isolated from its applications to industry; without the industry's support there would be no initiative to create innovative drugs to which standards could be applied.

Second, from the capitalist point of view, the impetus for the ICH and its principal activities is economic, so it must gain sponsorship from industry. Among this type of organization, the International Organization for Standardization (ISO) is well known for its non-governmental membership. Although many of its member institutes are part of the governmental structure of their countries or are mandated by their governments,

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[31] In this thesis, I use the abbreviated name for general meetings of the ICH, the International Conferences on Harmonization, which consist of "ICH" followed by the meeting number. For example, the First International Conference on Harmonisation is called "ICH1," and the second conference "ICH2," etc.

[32] The IEC is a worldwide organization for standardization comprising all national electrotechnical regulatory agencies. Its object is to promote international cooperation concerning standardization in the electrical and electronic fields. To this end and in addition to other activities, the IEC publishes international standards. Their preparation is entrusted to technical committees; any IEC national committee interested in the subject at hand may participate in the preparatory work. International governmental and non-governmental organizations liaising with the IEC also participate in this preparation.

most have their roots in the private sector, having been set up by national partnerships of industry associations. However, the ICH is different from the ISO. Unlike the ISO, which occupies a special position between the public and private sectors, the ICH emphasizes formal participation by government as well as industry. It consists not only of purely commercial negotiations among major players and competitors on the standards over their products; the ICH also asks for the involvement of the regulatory bodies that have ultimate authority over these products. Global companies know well that without the promise of governments, no product can be sold to the places under their authority.

As we will see, the dynamics between regulators and industry and between industry and science guide the direction this conference takes. This is one aspect of the bio-global. As I have discussed in Chapter 1, the global should not be considered as if it is a coherent entity. Echoing John Law's analysis of the global as "small" and "baroque" (2002), the ICH demonstrates how the small world of proprietary drugs operates. It differs from other health organizations: the dynamics of the ICH reflect the complicated nature of the encounter between public health and economic concerns, and more importantly, they provide necessary momentum that other organizations lack. Take the WHO's health project on developing countries as an example: as Fiona Godlee points out (Godlee 1994), the WHO lost it global influence after its ambitious launch of "Health for all by the year of 2000" in the Alma Mata declaration in 1977, and political and economic concerns were the main obstacles that prevented it from accomplishing its promised goal. The United States first opposed the WHO's code on breast milk substitute on the grounds that it interfered in global trade. Then, under pressure from industry, it opposed the WHO's essential drugs program, launched in 1977.

Thus, although the WHO attempted to develop an international standard for pharmaceutical products to "protect public health by ensuring the regular availability of good quality, safe and efficacious pharmaceuticals and by contributing to their rational use" (WHO 2002: 7) back in the late 1960s, it did not achieve much until the ICH was created. As a primary process to "format" the world of proprietary drugs, the ICH does not put public health in the foreground, but rather business. Its mission is clearly one that is both commercial and scientific. The statement of the ICH2 steering committee indicated

> their commitment to increased international harmonisation, aimed at ensuring that good quality, safe and effective medicines are developed and registered in the most efficient and cost-effective manner. These activities are pursued in the interest of the consumer and public health, to prevent unnecessary duplication

> of clinical trials in humans and to minimise the use of animal testing without compromising the regulatory obligations of safety and effectiveness. (D'Arcy and Harron eds. 1992: xxv)

For industry, the ICH is an attempt to "smooth out" non-tariff barriers, but it is also an attempt in the area of public health to eliminate unnecessary administrative regulations so that the most advanced medicine can be delivered to patients in need. Thus it is important to note its exclusive nature. Unlike other scientific meetings, which are open to all, the ICH carefully selected Europe, United States and Japan, who control 80 percent of world pharmaceutical sales; their combined markets comprise over 90 percent of the world total. In other words, the participants of the ICH are both key producers and the main consumers, and the conference thus avoids possible conflicts of interest from outside.

To achieve this purpose and ensure the efficiency of discussions, six players were chosen. The regulators from the three regions—the FDA, the Japanese Ministry of Health and Welfare (MHW), and the European Community—and industry representatives—PhRMA, the Japan Pharmaceuticals Manufacturing Association (JPMA), and the European Federation of Pharmaceutical Industries and Associations (EFPIA)—make up the main body of this conference. Some organizations were chosen as non-voting observers, such as the WHO, Health Canada, and the European Free Trade Association (EFTA); their presence was considered to be helpful and did not create obstacles to the process of harmonization. The design of this conference was "a stage in a developing process, at a high level, between regulators and industry" (Nutley ed. 2000:2). The structure of the ICH represents this idea. It is administered by a steering committee, which is supported by the ICH secretariat. Since the ICH was established, each of the six co-sponsors has held two seats on the steering committee that oversees the harmonization activities. IFPMA, which is also an observer, provides the secretariat and participates as a non-voting member of the Steering Committee.

The major events of the ICH, as introduced previously, are international conferences on harmonization, hence the name given to the initiative. However, between each conference, the ICH Steering Committee meets at least twice a year together with working groups that are assigned by the steering committee. Both these parties construct the routine activities of the ICH together. Although its goal is a clear and simple one—a universal standard for clinical trials to be implemented as soon as possible—the ICH is fully aware of the process necessary to achieve harmonization. As claimed repeatedly in its documents, it carries out its actions such that the conference, its preparations and its follow-up activities are open and transparent to the public.

The steps toward the harmonization of guidelines gradually developed. At the first steering committee meeting of the ICH the Terms of Reference were agreed upon and it was decided that the topics selected for harmonization would be divided into the categories safety, quality and efficacy, to reflect the three criteria that are the basis of approving and authorizing new medicinal products. It was also agreed, in order to make sure the guidelines were made scientifically, that six-party Expert Working Groups (EWGs) be set up to discuss the scientific and technical aspects of each harmonization topic. These EWGs meet at the same time as the steering committee and report their progress to the committee. Along with the establishment of eleven EWGs at ICH1, the so-called the "ICH process" was first drawn up at the steering committee meeting in Washington, D.C., in March 1992 and amended in Tokyo in September 1992 (D'Arcy and Harron eds. 1992: 558).

Table 2.8 Step-wise "ICH Process"

Step 1	Preliminary discussions of the topic are held by the relevant Expert Working Group or group of experts, mandated by the ICH Steering Committee, which is representative of the six co-sponsors of the Conference. Preliminary data are prepared (guidelines, policy statements, recommendations, points to consider). The draft is reviewed and revised by the experts until consensus is reached and the draft is forwarded by the Expert Working Group to the Steering Committee.
Step 2	On the recommendation of the Steering Committee, the draft is transmitted to the three regional regulatory agencies for formal consultation in accordance with their normal internal or external consultation procedures. This regulatory consultation may include organizations and associations outside the ICH process, as well as the IFPMA, EFPIA, JPMA, and PMA, and the observers, EFTA, Canada and the WHO. The comment period should normally be six months, except when there are special circumstances to take into account.
Step 3	Comments are collected by the regulatory agencies and exchanged with the other regulatory bodies. The designed regulatory rapporteur, in consultation with experts in the other regulatory bodies, analyses the comments and amends the draft. The revised draft is referred to the ICH Expert Working Group and "signed off"

	by the experts designated by the regulatory parties before being referred to the ICH Steering Committee for adoption.
Step 4	The final draft is submitted to the Steering Committee and "signed off" by the three regulatory parties to ICH. It is then recommended to the three regulatory bodies for adoption.
Step 5	The recommendations are incorporated into domestic regulations or other appropriate administrative measures, according to national/regional internal procedures.

Source: IFPMA 1994, Annex 6: 13-14.

Considered one of the key factors that determined the success of the ICH, the "ICH process" is a complicated working process to achieve consensus. It makes sure that every guideline it creates is ready to be implemented. This five-step procedure goes as follows (see table 2.12). Formal proposals for new harmonization have to be brought up to the steering committee by one of the six parties in order to initiate an ICH action. When accepted, a proposal is assigned to an EWG, which advises on the technical aspects of harmonization topics (Step 1). When a primary guideline is drafted, it must first be distributed to all the invited experts to form a consensus (Step 2). After the draft is completed, it is brought back to each region for feedback on other related topics (Step 3). Every guideline has to be agreed on by all experts and the domestic industries before submission back to the steering committee, where the guideline is confirmed and released (Step 4). Two "decision points" are set in the defined process, at Step 2 and Step 4, which have enabled the steering committee to monitor the progress of the topics selected for harmonization. When consensus is reached, every party involved has to "sign off" to confirm its commitment.

Even taking into account these steps, what makes the ICH unique is its final step. A follow-up mechanism is applied to see whether the guidelines are adopted by local regulatory agencies. This is the reason why they are invited. It is requested that this be done within six months of release (Step 5). In the case of the European Union, the Committee for Proprietary Medicinal Product (CPMP) should be responsible for the adoption. In Japan, the final draft should be implemented into MHW notifications, and in the U.S., the FDA should publish it in the *Federal Register*. Information on regulatory action taken and implementation dates are reported back to the steering committee and published by the secretariat. Since this procedure is lengthy, a guideline

requires at least twelve to eighteen months to be implemented. Even so, as soon as it reaches the final step, the guideline becomes the actual law by which all ICH regulatory authorities must abide.

Through this process the ICH forms a powerful discourse that combines scientific precision and capitalistic efficiency. Yet to the public it emphasizes the science on which this process is founded, asserting that neither political negotiations nor commercial compromises are involved. As concluded in the ICH5 steering committee statement,

> The ICH process has achieved success because it is based on scientific consensus developed between industry and regulatory experts and because of the commitment of the regulatory parties to implement the ICH tripartite, harmonised guidelines and recommendations.

It seemed that it is scientific, thus worth waiting for—scientific, thus worth trusting. The ICH marches off on its way to conquer the world.

Guidelines: General Analysis and an Example

Although the ICH set a highly technical process for making guidelines, it has achieved much since its foundation (for these guidelines and the dates they reached step 5, see appendix 2). As we can see in table 2.9, until November 2003, when ICH6 was held, fifty-six guidelines had been finalized in the categories of quality (23 guidelines), safety (15 guidelines), and efficacy (14 guidelines), along with four multidisciplinary guidelines. In addition, some others were in the process of harmonization. Except for common technical documents and medical terminology, the guidelines the ICH makes basically cover this field from early development to production. There are many notable among them, such as good clinical practice (GCP), ethnic factors, controlled trials, statistical assessment, special populations in the consideration of clinical trials, stability biotech/biologics, specifications on the quality of pharmaceuticals, and reproductive testing, carcinogenicity, and genotoxicity in pre-clinical studies.

Industry certainly appreciates this achievement. Stuart R. Walker of CMR International praised it. "I believe that the pharmaceutical industry must continue to strongly support the ICH program. As a result of this initiative, the drug regulatory process has become smoother, quicker and less burdensome, with the result that large numbers of patients all over the world are able to receive life-saving and cost effective medicines sooner than was possible prior to this program" (as quoted in Nutley ed. 2000:9). According to Walker, a single market of proprietary drugs, based on the

framework established by these guidelines, is approaching.

However, looking retrospectively, it is interesting to see how these guidelines were formed. If we see the dynamics of the topics brought up and the guidelines made in the ICH conferences, shown in table 2.9, we can find a rough trend singling out the ICH4 as the turning point. At the first two ICH conferences, 38 topics covering almost all the first priorities were proposed, and at ICH3 and ICH4 most of them had been turned into guidelines that were then incorporated into the basic fabric of the regulatory scheme. Few topics were brought into discussion after ICH4, though there was still some work been undertaken, such as revisions of some guidelines, additional concerns about existing guidelines, and questions and answers about their implementation. In other words, the foundation of the ICH guidelines had been built by ICH4.

A more detailed analysis can be made here on these foundational guidelines. The eleven topics raised at ICH1 were not specific. Many of them changed into more specific ones for discussion at ICH2 and became guidelines at ICH3. Thus despite the time-consuming process of harmonization, in general it did not take longer than two years to make a guideline. In fact, at ICH1 many people thought that this project, though huge and bold , would be done by the ICH3, leaving only differences that would be either too travail to deal with on that occasion or too major to overcome in a timely fashion (D'Arcy and Harron eds. 1992:557).

Table 2.9 Guidelines That Had Reached Step Four in the ICH and Proposals for New Guidelines, 1991-2003

ICH conferences	Number of new topics raised for guidelines	Number of Guidelines that had reached consensus				
		quality	safety	efficacy	multi-discipline	total
ICH 1	11	0	1	0	0	1
ICH 2	27	1	1	1	0	3
ICH 3	9	4	6	4	0	14
ICH 4	4	7	4	3	0	14
ICH 5	5	4	3	4	3	14
ICH 6	3	7	0	2	1	10

Source: Compiled by the author from various documents.

Nonetheless, the following meetings provided positive and negative reasons to continue work after ICH3. On the one hand, they revealed that the ICH process itself was a powerful tool for the implementation of guidelines, and this made industry think that the ICH was an effective forum for dealing with any differences that remained. On the other hand, some seemingly simple topics in fact were not that easy to harmonize. For example, the pharmacopoeia was one of the first eleven topics taken into consideration for guidelines, yet so far no guideline has been completed due to different concepts of some products. Sometimes these topics were not critical and left pending; however there were some that did have effects on the reviewing process, such as the consideration of ethnic factors that would decide whether clinical trials should be repeated for populations different than those involved in the original trials. Thus, in order to take full advantage of this precious opportunity to make guidelines, one more ICH conference was added (ICH4), and then additional ones were arranged by other maneuvers.

Finally, let us take a brief look at how these formed guidelines work. Using toxicity testing as the example, John Abraham and Tim Reed's study provides us with a view of how the ICH successfully reduced the difficulty of requirements in the name of technological innovation (Abraham and Reed 2002). Toxicity is a big part of preclinical stage studies and is regulated in various guidelines under the category of safety (mainly S1B, S1C, and S4A). As one of the "obstacles" transnational industry was concerned about, this issue was proposed at the beginning of the ICH and guidelines were gradually formed and implemented by the ICH4. According to the criticism this study makes of the process of negotiation, the rhetoric of regulatory agencies, no matter their orientation, was always "to put patients as the first priority," but in reality they worked to accommodate industry's desire to loosen the necessary requirements.

As Abraham and Reed's study shows, the monitoring duration of chronic toxicity testing was shortened from twelve months to six, and the number of animal species required for carcinogenicity testing was decreased. Some tough standards, such as the maximum tolerated dose method for determining the dosage used in carcinogenicity testing, were replaced by flexible ones. All these changes lacked a scientific base and betrayed the agencies' promises to patients and to public health. The authors conclude,

> [T]he ICH process was an intermingling of technical, social and political judgments, and not a series of scientific calculations. This is significant because the implication is that the ICH process could have been constituted by a broad range of interests, instead of an expert scientific forum for industry and

government. (363)

For the authors of this study the "technical standard" would have a different meaning in this circumstance. It conveniently wraps up the outcomes of complicated negotiations in this conference by formulating a workable consensus via which each drug, as well as capital, flows.

Marching Out: Formation of Global Cooperative Group

In its statement "The Future of the ICH" released at ICH4 (ICH 1997), the ICH Steering Committee wrote that the reason to continue the "second phase" of its work was to ensure three things: a mechanism to harmonize technical requirements based on science, a process for updating and supplementing the current ICH guidelines, and a platform by which future disharmony could be prevented through early collaboration and the exchange of information. Meanwhile, the ICH activities moved out of the regions of harmonization and began to seek the possibility of implementing as many guidelines as possible. The statement reads,

> With the successful completion of the first phase of international harmonisation, it will be increasingly important to ensure that the objectives and outcome of ICH are well understood and widely disseminated.... The important role of WHO, both in actively disseminating the guidelines and encouraging the wide-spread adoption and use of ICH guidelines, is warmly welcomed and is essential if the long-term benefit of international harmonisation, in terms of quicker access to effective new medicines, is to be available to patients throughout the world.

Although the markets outside of the ICH regions, which accounts for over 80 percent of the world's population, were too tiny to be incorporated in the original plan, the ICH decided to extend the marginal effect of their guidelines and included these places in the name of the "globalization of the benefits of harmonization."

The rhetoric the ICH used for this phase was the same: these activities were pursued in the interest of the patient, the consumer and public health in order to prevent unnecessary duplication of clinical trials in humans and minimize the use of animal testing without compromising the regulatory obligations of safety and effectiveness. However, in reality the content was different. Harmonization aimed at ensuring that good quality, safe and effective medicines were developed in the most expeditious and cost-effective manner was not the point, because such guidelines were already in place. For the regions and states outside of the ICH club, the "harmonization" could be done

in a take-it-or-leave-it manner. As its revised Terms of Reference states, the mission of the ICH's globalization of standards was to "facilitate dissemination and communication of information on harmonized guidelines and their use." A PhRMA member even told me that basically the industry would not welcome any extra regulations added on the existing guidelines, because it would not be cost-effective.

Therefore, although the WHO was thought to be the one responsible for the globalization of these guidelines, its function was quite limited. It was too big and too divided to have a focused point for its policy on proprietary drugs (recall its attempt on essential drugs twenty years ago), and its role in the ICH is minor (WHO 2002:25). As presented at ICH4, it would devote itself only to the adverse effects, monitoring and reporting, and guidelines on generic drugs. The job of promoting these guidelines to the non-ICH regions was taken up by the ICH Global Cooperation Group (GCG), an ad hoc organization put together to serve this need.

The GCG was founded in March 1999 as a subcommittee of the ICH Steering Committee. It was organized by the original six parties and serves as a bridge to other countries that are affected by these guidelines. Its objective is "to make available information on the ICH process and guidelines to non-ICH regions and to act as resource for the understanding, and even acceptance, of many of the guidelines" (as quoted in Nutley ed. 2000:10). For this purpose it set principles for controlling the distribution of this information, outlined as follows:

1. ICH will not seek to impose its views on any country, region, or company, but will serve as a resource for information and data.
2. ICH will provide non-ICH member countries or companies with any document related to the GCG initiative without charge.
3. This ICH subcommittee will work as closely as possible with WHO and other international organizations to achieve these goals.
4. This subcommittee will not cause or require any change to the current ICH structure or procedures of operation.
5. While some non-ICH countries are not in a position to utilize ICH guidelines at present, these guidelines will be used as the basis of ICH's response whenever information is requested.
6. The Global Cooperation Group will provide information upon request from non-ICH countries and will make information available about the existence of the ICH web site, the address for communications, and related information.

Obviously, in the attempt to spread the new standards to non-ICH counties, the GCG did not expect to play an active negotiating role; instead, it functioned passively to

ensure that the direction of the information flow from the ICH to non-ICH regions was irreversible. It made several documents about the ICH and the GCG available on ICH website; brochures were distributed at the ICH to non-ICH audiences. But it did only this.

Even so, some regional organizations showed their interests in this group for various concerns. The Pan American Network on Drug Regulatory Harmonization (PANDRH) was the first to express interest. It is a large organization that has a long history back to the interwar years; more importantly, the United States and Canada are active member states of this organization. Thus from beginning it was invited to attend GCG activities. Although the PANDRH contributed a lot to the greater recognition and use of ICH products through ongoing harmonization and capacity-building efforts, the economic diversity among its member states was an obstacle to this effort. According to its presentation at ICH6, it only organizes some committees, and they work on different guidelines; members can join them on a voluntary basis. The same situation can be seen in the Association of South-East Asia Nations (ASEAN). For a long time it was thought of as an EU-like economic body, and thus important to the harmonization of local regulations for products, including pharmaceuticals. Although ASEAN was strongly supported by the governments of member states, differences among these countries' economies is obvious. For example, some advanced states, such as Singapore, did not see much need to be incorporated into the market for generic drugs. But for many ASEAN member states the market in proprietary drugs that Singapore was interested in was too expensive for them.

The Asia-Pacific Economic Cooperation (APEC) represents another interest. Although it is too large to form a single market, the rising economy and consumer power of East Asia enables this organization to be an active participant. Furthermore, because of the subtle political tensions between the United States and the People's Republic of China and tensions within the Western Pacific region, APEC carefully avoids issues that would arouse political implications and focuses only on economic issues. The concept of harmonizing local regulations and forming a single market is in a sense the best topic for the burgeoning industry of biotechnology and pharmaceuticals to work on. Of course, there are other organizations participating in GCG activities, such as the Gulf Cooperation Council (GCC) and the Southern African Development Community (SADC). They showed up off and on with and had little impact for reasons that are pretty simple: they are not able to even think about this issue.

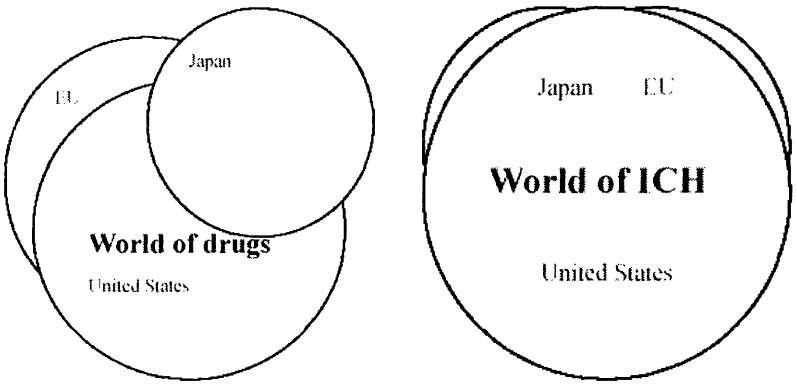
After the formation of the GCG subcommittee, the GCG made its public debut at ICH5, where it organized a half-day symposium one day before the conference. More

than two hundred people attended. In response to requests for more discussion, at ICH6 the GCG extended the symposium to a whole day, and over seven hundred people from around the world attended. This confirmed that the GCG would play an important role in following ICH conferences, and it would come to be more concrete and more attractive to non-ICH regions due to factors such as the promise of permanent representatives to the GCG clearly stated in its Terms of Reference.

CONCLUDING REMARKS: WHEN "HARMONIOUS" WEST AND "NOISY" ASIA MEET

Finally, let me risk simplification by summarizing the ICH as well as this chapter by means of two diagrams. The first illustrates the first phase of the ICH in terms of harmonizing the standards and markets of the United States, the European Union, and Japan (fig.2.2). As we see in the diagram, the isolated markets of these three regions/states started to be brought together by the ICH, and the overlapping area, which indicates the region where drugs can be sold freely, enlarges.

Fig.2.2. World of Proprietary Drugs before (left) and after (right) the ICH

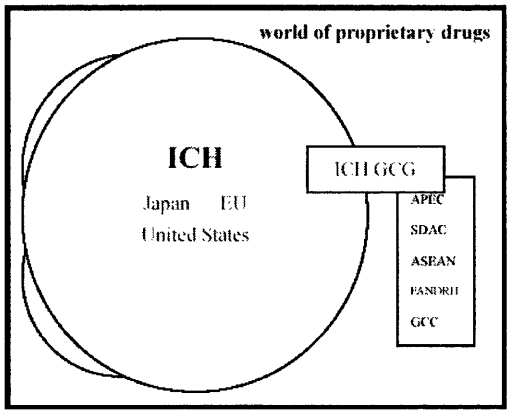


After ICH4, the ICH moved its focus to those countries outside of it. As the second diagram shows (fig. 2.3), through the standardization of all standards, it continues to work to achieve a single global market/health community. Due to different interests, some regional organizations have developed dialogues with the ICH through the help of the GCG. However, the nature of this communication is rather one-directional, from inside to outside.

As the most fundamental and most advanced venture to bring about a single measure in the world of proprietary drugs, the ICH is an ongoing plan for the new

millennium. For global pharmaceutical companies, there will finally be one standard to fit all if the ICH follows this blueprint. The ICH project nicely echoes what Michael Fischer observes about the interconnections of contemporary technologies: there is a confluence of two temporalities on two ethical plateaus, one "operative as legacies of the past in the present" and the other "operative already or potentially operative as the result of a promised technological future" (Fischer 2003:155). The ICH locates its achievements, the guidelines, in the history of standardization, and at the same time persuades the public of possible benefits by projecting these universal guidelines into the present. Both provide necessary motivation for the conference to grow and evolve.

Fig.2.3 World of Proprietary Drugs inside and outside the ICH



Even so, the ICH knew that things would not go as they wished when these rules were introduced to Asia. As the area consisting of the countries that have undergone the most rapid economic growth since the 1970s, East Asia is a new and promising market for advanced commodities. However, the locomotive of East Asia, Japan, is "troublesome" for its infamous protectionism and unique standards for imported goods. Although the Japanese, as Kalman Applebaum shows (2005), have been successfully "educated" about mental diseases and the new anti-depressant SSRIs through the ICH, the interaction is not always that smooth in other cases. This is what I mentioned in Chapter 1 as the second question regarding standardization: what standard is the best for which customers? For the West, Japan's insistence on its own standards is purely a non-tariff barrier. The cultural assumption behind this argument is that only Westerners know the best standards for these West-originated goods. In particular, many say, just twenty years ago Japanese products were not good enough to compete with Western ones. However, is it possible that the Japanese have learned what is best for them?

Take cars as an example. Although Japan reconstructed its manufacturing capacity after World War II, it was still tiny. However, when smaller, less expensive and more fuel-efficient automobiles became popular with the American consumer, sales of Japanese cars improved rapidly. Two oil crises speeded up this trend, notwithstanding the Clean Air Act of 1970. By the end of the 1970s, Japanese automakers were selling 2.5 million cars a year, while U.S. automakers failed to sell their cars in Japan. Some responded to Japanese competition by retooling their factories to build smaller cars; they even introduced Japanese production methods. However, they still to meet the unique standard set by the Japanese. Then the United States started accusing Japan of protectionism. They thought that Japan's unique standards and reviewing system were an excuse that did not allow U.S. makers to fair play in the Japanese market. GM, Ford and Chrysler, the "Big Three" automakers, pressured the U.S. government to negotiate with its Japanese counterpart. Special meetings and programs were arranged in the mid-1980s and further negotiations with European companies were introduced. The goal of these action programs, in the end, was to set a universal standard, a game that was fair to all players.

The Japanese did not consider the problem this way, though. They always felt that they only wanted what they consider fittest for themselves. These unique standards more or less reflect this naïve need in an institutional fashion. Let us examine a fantasized version of this argument by introducing an episode taken from the popular Japanese *manga* (comic) *Sanctuary*. It starts with Ms. Bristol, the special assistant to the President of United States (supposedly Bill Clinton), who flies to Tokyo with the presidents of the Big Three to fix the problem of the American failure to penetrate the Japanese car market. Famous for her tough style of negotiation, Bristol is confident of the quality of U.S. products and believed she would win this negotiation until she meets Congressman Asami Chiaki, an ambitious young elite.

Unlike the Japanese officials Bristol previously encountered, Asami tells her clearly that the problem is not a purely economic one, but cultural as well. He asserts that if Japan and the United States both removed the barriers to each other's products, Japanese cars would beat American ones in both markets. To show her the social and cultural roots of Japanese society, Asami brings Bristol to a public elementary school, showing her how Japanese children are trained to be a part of a group and how they enjoy this. Japanese values, including the pursuit of perfect quality, are one of the things that make the Japanese whole. "It is useless to force Japan to buy your cars and parts," Asami concludes. "If you insist on doing so, I shall say that it is only because of your cultural prejudice [toward] the superiority of Whiteness" (fig.2.4).

Fig. 2.4. The Cultural Dispute between Japan and the United States over Car Imports, Portrayed in *Sanctuary*.

Left: Ms. Bristol smashes a Japanese car in a demonstration before flying to Tokyo. *Right*: Her shocked face when she hears Congressmen Asami say, "It is only because of your cultural prejudice [toward] the superiority of the Whiteness."

Source: *Sanctuary* (Chinese version), vol., episode 6 and 8.

Although this *manga* has pointed out that cultural difference may play a big role in the process of standardization, in the real world it is not easy to articulate and solve.[33] As we will see in Chapter 3 and Chapter 4, Japan has its own logic to running drug businesses and participating in the ICH. At the interface where two systems meet, the eminently cultural issue of racial difference became the last obstacle in achieving a universal standard.

[33] In *Sanctuary*, Asami and Bristol engage in a one-night stand and she leaves Tokyo without achieving anything.

Chapter 3
Local Tones: Medicine as an Instrument of Building Social Trust and State Visibility

> Through ICH, the number of time-consuming, expensive phase III trials required for an international launch will be reduced dramatically. This will not only save time and resources—it will save lives and improve the health of patients all over the world.
>
> Frank Douglas[1]

> A thriving civil society depends on a people's habits, customs, and ethics—attributes that can be shaped only indirectly through conscious political action and must otherwise be nourished through an increased awareness and respect for culture. ... [O]ne of the ironies of the convergence of larger institutions since the end of the cold war is that people around the world are now even more conscious of the cultural differences that separate them.
>
> Francis Fukuyama[2]

PART I
LOCATING MARKETS IN JAPAN AND TAIWAN

Japan and Taiwan as Seen by Global Pharmaceutical Companies

As introduced in Chapter 2, for multinational companies the world of proprietary drugs is expanding. Although it is time-consuming and costly to bring a new product to market, once it is on the market, the reward is enormous. The larger the market, the more benefits will be enjoyed. Thus, pharmaceutical companies' strategy, as the above quote states, is to enlarge markets as much as possible at a minimum cost, all in the name of public health. However, looking at the demand side of drugs, Chapter 2 reminds readers that Japan can be a "troublemaker" and a roadblock on the way to selling drugs to East Asia. It may not be a purely business concern that leads Japan to protect its market. In the era of globalization, as Francis Fukuyama notes, cultural factors should be taken into account. In addition to examining the tactics used in locating the Asian market, this chapter will attempt to show what cultural logic is behind the drug business in this region.

Let us begin by looking at the national markets of Japan and Taiwan and their

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1 In Nutley ed., "Benefit and Value of the ICH," p.11.
2 In *Trust: The Social Virtues and The Creation of Prosperity*, p.5.

structure and size from the viewpoint of the United States. According to the IMS HEALTH report on the worldwide pharmaceutical market, world sales have grown by almost 11 percent between 1999 and 2003 (see table 3.1). Because of demographic shifts (i.e., an increasing elderly population), changing epidemiological patterns, and increasing public awareness about healthcare, as mentioned in Chapter 2, some predict that sales will reach $677 billion in 2008.

Let us take a look at this world map and see where the main markets are. North America is the biggest market for pharmaceuticals, with about a 50 percent share of the total world pharmaceutical market. As expected, the European market is the second largest, accounts for a quarter of the total market, and is dominated by Western European countries. The third largest consumer in the global market is the area of "Africa, Asia, and Australia" (AAA), which includes countries with varying ability to buy brand drugs. If we take a closer look at this market, we find that Japan is the biggest contributor to total consumption. The Japanese market is the second largest national market in the world, and it accounts for about 16 percent of global sales and about two thirds of the AAA market. The above sketch corresponds the parties that are invited to join the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

Table 3.1 Japan and Taiwan in the Africa, Asia, and Australia Market, 1999-2003 (in billions of U.S. dollars)

Year/Country (percentage in the AAA Region)	Japan	Taiwan	Rest of the AAA Region
1999	53.4 (59.9)	1.8 (2)	33.9
2000	51.5 (73.3)	2.3 (3.2)	16.4
2001	47.6 (63)	2.2 (2.9)	25.7
2002	46.9 (59.7)	2.2 (2.8)	29.4
2003	52.4 (58.4)	2.2 (2.4)	35.1

Source: Adapted by the author from various sources.

Recognized as a growing market among the Newly Industrialized Economies (NIEs)—which also include Korea, Singapore and Hong Kong—Taiwan has a noticeable profile in the AAA area on this world map. In the past ten years, the growth of sales of

alimentary tract, metabolism, and especially cardiovascular system drugs, among others, has caught the industry's eye. Although it is much smaller than Japan, Taiwan is the 20th largest national market in the world (fig. 3.1). In the consumption of prescriptive drugs it trails only Japan, Korea ($3.9 billion), Australia ($3.1 billion), India ($3.4 billion), and the PRC ($4.0 billion) in its region (IMS HEALTH 1999). In per capita consumption of pharmaceuticals, it still surpasses many countries, ranking 28th in the world.

Following a brief sketch of Japan and Taiwan's national prescriptive drugs market, I will further analyze the structure of both markets and their implications for global pharmaceutical companies, especially those from the Unite States. Like many developed countries, Japan's pharmaceutical market is characterized by its diversity and dispersion. As shown in table 3.2, Japan has relatively more pharmaceutical companies than other major drug-producing countries. Even so, these companies can be roughly divided into two groups—companies of large size and those of medium or small size, which make up the so called "double structured" market described by Kohara Hisaharu (1996: Chapter 3).[3]

Table 3.2 Numbers of Pharmaceutical Companies in Main Developed Countries, 1987-1991

Country \Year	1987	1988	1989	1990	1991
United States	680	680	790	-	-
*West Germany	1000	1000	1000	1000	-
United Kingdom	369	350	-	387	-
Switzerland	-	-	85	85	85
France	319	358	358	362	353
Italy	320	310	305	303	299
Japan	-	1407	1457	1496	1738

*Since 1989 it has been part of the united Germany

Source: Adopted from the JPMA, *Yearbook 1994*.

The big companies in Japan, which are members of the Japan Pharmaceutical

[3] According to Kohara, the big companies are those whose monthly production exceeds one billion yen. The small companies are those whose production is below ten million yen. In 1993 Japan had 399 big drug companies that accounted for 20.3 percent of the total number of firms and 96.4 percent of total production. The small companies, though they made up over 60 percent of the total number, were responsible for less than 0.5 percent of total production.

Manufacturers Association (JPMA) and have always numbered fewer than thirty, behave like global companies. Vast research and resources are invested, and some products are sold overseas. In the domestic market, they are *senpatsu kigyo*, the leading producers. The rest of this sector is made up of innumerable followers, *kohatsu kigyo*. These pick up drugs that are out of patent and make their own products, called *zorohin* ("me-too" drugs). Because *zorohin* need not repeat costly trials to meet the Ministry of Health, Labor, and Welfare (MHLW) requirements, they can find a niche for their products.

However, what makes Japan unique is the distribution of its market share. Thanks to previously loose regulations on new drug patents, the conventional dichotomy of branded drugs and generic ones is not clear. From 1993 to 2000, the concentration ratio of top ten producers only rose from 31.6 to 40.6 percent, far lower than the 70 percent concentration of U.S. drug firms. On the other hand, though the smaller followers are the main body of the pharmaceutical sector, they must survive crude competition over small market share. Drugs, after all, are not like cars; the variable nature of diseases and treatments naturally makes it harder for other makers to take your established share. As a senior stock analyst specializing in Japan's pharmaceutical sector informed me, many small companies survive with only one or two generic drugs that have been produced since the company was founded.

Based upon this understanding, we can start to see the role that global companies play in this market, which is to a large degree marginal. A 1998 report shows that Pharmaceutical Research and Manufacturers of America (PhRMA) member companies have about $9.6 billion in annual sales in Japan, which is equivalent to a mere 15 percent market share. According to the JPMA profile, among the top 20 JPMA member companies in fiscal year 2002, only Pfizer (ranked 6th from the top), Novartis (11th), GlaxoSmithKline (16th), and Astra Zeneca (19th) are foreign-investment companies. Even Pfizer, the best performer, whose sales in Japan for 2002 totaled $1.78 billion, fell far behind Takeda, the leader, by $3.6 billion. In short, these global companies sweep the world, but not Japan, where Japanese companies are always the dominating players.

In contrast to the domination of local companies in Japan, it is foreign subsidiaries that control the Taiwanese market. For them, Taiwan represents a market rather than a business competitor. Despite its rising economic capacities, Taiwan has a weak pharmaceutical sector. A 1998 report shows that local companies have only 31 percent of the total market, while companies from the major global players take 64 percent, including 20 percent by the United States, 14 percent by Japan, 11 percent by Germany, 9 percent by the United Kingdom, 6 percent by Switzerland, and 4 percent by France.

In terms of recent data, in 2003 the top twenty pharmaceutical companies took 63.2

percent of total sales, which accounts for $2.12 billion. However, only three Taiwanese companies—Yung Shin, ranked 15th, Tung Yang, 17th, and Sintong, 19th—are able to make it onto this list. Beside, they are in fact producers of generic drugs, focusing their marketing on pharmacies and clinics rather than hospitals, which can afford more expensive brand drugs. Thus, it is fair say that the Taiwanese market for proprietary drugs belongs exclusively to the foreign players.

The above situation also affects the marketing strategy of U.S. firms. The international market for pharmaceuticals offers a wealth of potential for U.S. companies and it grows at double digits annually. Intensified global research and development activity, which generates a steady flow of new therapeutic products, is one of the key factors fueling the expansion. Even so, PhRMA does not spend as much on the research and development of pharmaceuticals abroad. As described in the Chapter 2, the research and development expenditure of PhRMA reached $30 billion in 2001; however, according to PhRMA's *Annual Membership Survey* (2002), only $4.56 billion, accounting for 19 percent of their R&D budget, was spent outside of the United States.

Let us now trace these budgets. Western Europe enjoyed the biggest non-U.S. investment at $2,441.2 million, or 52.3% of the total. The second and third largest were Japan's $564.1 million (12.1%) and Canada's $245.7 million (5.3%). As an emerging region, the Asia-Pacific region, which includes key states such as Taiwan, Korea and Singapore, obtained $40 million. It is clear that because of competition, PhRMA makes some investment in Japan; however, it is not comparable to the profits they earn. As for Taiwan, because of the lack of local competitors, PhRMA considers it a pure market not worth much R&D investment. It takes from Taiwan without giving anything.

Local Factors Shared by Japan and Taiwan

Although they have the most advanced products, it is not easy for global drug companies to conquer East Asian markets. In this section I will introduce local factors in Japan and Taiwan that determined the buying force and the restrictions on pharmaceuticals. These factors fall into two broad categories: the national health insurance (NHI) schemes and local drug regulations.

Japan has a long history of collective health care, the origins of which can be traced to Goto Shimpei, the founder of modern public health in Japan and Taiwan.[4] A former

[4] Goto Shimpei (1857-1929) has a long international career as a politician and public health policy maker making him a legendary figure in the modern history of both Japan and Taiwan. Among many Meiji elites, Goto was typical as a medical doctor deeply involved in political affairs. He was one of the few

student of German bacteriologist Robert Koch, Goto introduced the German model of social welfare which, as many point out (Sugaya 1977, Fann 1998, Chang 1999), helped to consolidate the newly born Japanese state (and later empire), which was faced with the impending problems of the need for a robust labor force and the possibility of class conflict. This development gained energy and was realized in Japan's first national health insurance program in 1927. The making of this law deserves another book to discuss it (for example, Sugaya 1977, esp Chapter 3); I just want to point out that the enactment of the Health Insurance Law empowered the government to dominate healthcare affairs. Using this new scheme, it integrated and took over in most cases pensions and welfare packages previously provided by cooperative societies (*kumiai*), and its importance grew. It made the state not only the ultimate protector of citizens' health and the provider of healthcare; it ensured the existence of a robust Japanese race as the biological base for this modern nation-state.[5]

The new and independent health insurance institution moved from the Ministry of Agriculture and Commerce to Internal Affairs under the newly founded Bureau of Social Affairs, and local offices were established, along with health insurance *kumiai*, as specified by the law. The coverage of the insured extended with the military government's march into the Asian continent and ended with the foundation of the Ministry of Health and Welfare (MHW) for the purpose of overseeing this task. At the end of World War II, a system consisting of 10,349 *kumiai* and covering about 95 percent of Japanese cities was formed (National Health Insurance Association 1948: 266). The American occupation following the end of the war did not interrupt the Japan's national health insurance. In fact, in *Report of Social Security Mission*, W.H. Wandel, the leader of the mission, suggested the a unified system granting universal health care service to all citizens should be offered by the government. By solving the financial problems of some *kumiai* by replacing them with a government-run organization, coverage continuously rose. In parallel with its strong economy, the Japanese government launched "insurance for all nationals" in 1961. In 1973, the so-called "opening year of welfare", the

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doctors who received formal training in Western medicine, and after studying medicine in Germany he was chosen as the Head of Sanitation Bureau under the Ministry of Internal Affairs from 1890 to 1892 and again from 1895 to 1898. The second enterprise he joined was Taiwan, where he was the Head of Civilian Administration from 1898 to 1906; he introduced modern institutions almost the same as he had done in Japan. As researchers note, Taiwan, as the frontier and first colony of Japan, granted Goto the full opportunity to realize how a state-backed public health system could be possible. Because of his success in Taiwan, he was made president of the Manchurian Railway, Japan's first national and semi-colonial business overseas, in 1906. These works proved Goto a reliable bureaucrat; his career reached its climax when he was made Mayor of Tokyo and then various other high-level posts in the central government.

[5] I am grateful to Professor Hiroi Yoshinori at Chiba University for providing me with this political economic observation.

government even proposed a free health care program for people over seventy years old.

However, this promise could not be kept easily in the late 1970s when Japan's economic growth started to slow down. The MHW, despite its increasingly complicated functioning—not unlike a combination of the FDA and National Institutes of Health in the United States—was no longer as generous as before. Worse, expenditures grew rapidly with the advancement of medical technology. As a result, expenditure for everything related to national health insurance became a major burden on the MHW. Under the increasingly harsh economic regression, the roles of the MHW as the protector of health and controller of the health budget were in conflict. National health insurance became so difficult to maintain that the MHW ended up as a bureau dealing nothing but this task.

Drugs were one of the main targets of budget control. As a single buyer, the MHW controlled drug prices though the reimbursements paid to medical institutions under the NHI. Each prescription drug had a fixed price announced every two years. After a long and difficult negotiation in 1982, when the MHW founded a committee to control medical spending, drug prices were cut by 18.6 percent of listed price in the next year, the largest cut since the pricing system was enacted in 1950; they were then lowered almost 60 percent over the next five years. It was such a harsh cutback that the industry claimed "winter" had come. The price cuts continued regardless of currency inflation during the 1990s; a 7 percent annual cut is shown in table 3.3.

Table 3.3 MHW Price Cuts, 1990-2000

Year	1990	1992	1994	1996	1997*	1998	2000
Price cut (%)	9.2	8.1	7.4	8.5	4.4	9.7	7.0

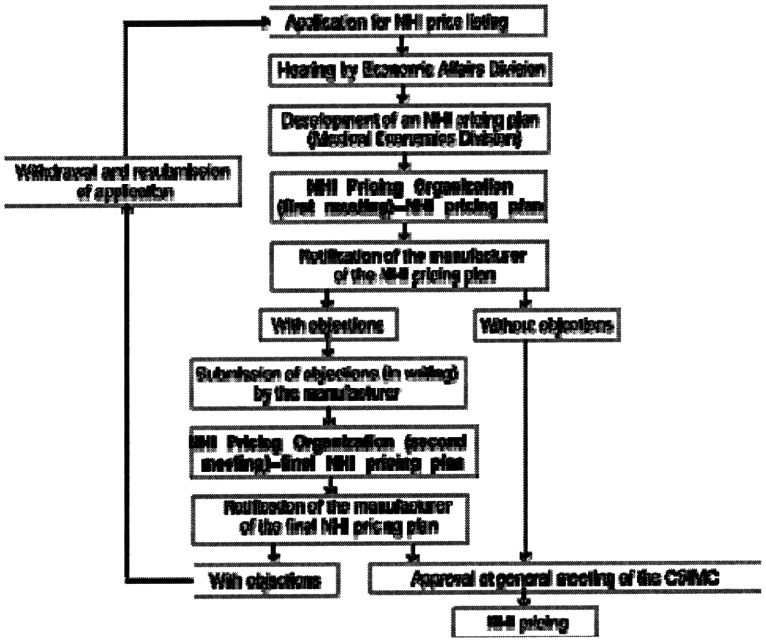
*Special cut for revised consumption tax

Source: UBS Warburg (from 1990 to 2000) and Yashiro Mitsuo, "Revision of NHI Drug Prices and Medical Fees, Fiscal 2002" (2002)

For the price cuts the MHW designed a long and burdensome process involving a very complex calculation mechanism (see fig. 3.1). Drugs are categorized into two groups, branded and generic, and different pricing systems are applied accordingly. Drugs are generally listed under the brand name for which product approval was granted. However some drugs listed in the Pharmacopoeia of Japan, biological products, and others may be

listed under a generic name depending on their active ingredients, formulation and specifications. New drugs containing NCEs can apply to the NHI drug price list four times annually at prices calculated by comparison with comparable previously listed drugs. If no similar drug is identified, the new drug is priced according to the calculation method. The prices calculated by this method are adjusted if they are more than double or less than half of comparable pharmaceutical prices in the United States and Europe.

Fig. 3.1. Process of NHI Pricing for Prescriptive Drugs



Source: JPMA website, http://www.jpma.or.jp/12english/publications/pub019d_nhi/

Before establishing its own NHI program in 1995, Taiwan had ten different public insurance schemes: Labor Insurance (1950), Government Employees Insurance (1958), Farmer's Insurance (1985), Low-Income Household Insurance (1990), and so on. Each covered a particular subset of the population and fulfilled a particular political promise in the postwar context of Kuomintang (KMT) government's control over the island. The planning stage for the NHI took seven years, from 1986 to 1993, covering the critical period of Taiwan's political transition to a vibrant democracy. To preempt the challenge from Democratic Progressive Party (DPP), which had long advocated the establishment of universal national health insurance, the KMT government submitted an NHI bill to Parliament, and it was and finally passed in July 1994, less than a year prior to the program's eventual inauguration.

Taiwan's NHI scheme covers more than 96 percent of Taiwan's citizens. Third party reimbursement is therefore an important consideration in any healthcare expenditure and in procurement of pharmaceuticals. As expected, since the very beginning, price cuts have been one of big issues with this program. Like Japan, Taiwanese government applied a centralized system to control prices. Beginning in 1997, a series of price and reimbursement controls were introduced by the Bureau of National Health Insurance (BNHI), which operates a price-setting system based on international comparisons. According to the guidance on drug prices enacted in 1999, new products without bioequivalent competition are set at a median price of the product as it is listed in ten developed markets. Basically the price is determined by a special committee and is fixed after review; but prices products whose market prices were lower than 80 percent of the reimbursed price in a price/volume survey were subject to revision. Further, there are increased use restrictions placed on new drug reimbursement. Over 50 percent of new drugs now have reimbursement limitations. In principle, the BNHI tried to make its reimbursements approach the costs of these new drugs.[6]

Although it imports many foreign products, Taiwan is criticized for its regulatory practices, the second local factor it shares with Japan that should be taken into consideration. While some progress has been made in achieving rapid registration for certain classes of drugs to treat life-threatening diseases such as AIDS and cancer, Taiwan remains a late registration market for international companies. The reviewing time taken to approve new compounds was long in the 1990s—as long as thirty months in some cases, further reducing the exclusivity period provided by patent protection. Some long reviews were related to regulatory delays in the registration of clinical trials, which were requested via notice from the Department of Health (DoH) in 1993. These clinical trails, which had to consist of at least forty subjects, were criticized as being too small to be scientifically valid. In addition to registration trials, in most cases hospitals, with government acknowledgement but not government mandate, required a formulary-listing trial before a drug could be included on the hospital's reimbursement list. It was claimed that these regulatory hurdles continued to prevent fast market entry of new drugs that had been approved in other industrialized countries. Even so, the history of drug regulation in Taiwan is relatively short. Only in 1970 did Taiwan pass its first law concerning control

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[6] On the other hand, like other countries that have national health programs, Taiwan controls its drug expenses by supporting the use of locally manufactured generic products. For bioequivalent products, BNHI allows a price (i.e., reimbursement level) close to 100 percent of the originator's. For common products (i.e., no proven bioequivalent generics), BHNI approves a price near 80 percent of the originator's. As will be discussed later in this section, PhRMA complains that these controls are discriminatory; local companies enjoy a favorable market position due to the controls' application.

of medications, and pharmaceutical firms followed by the establishment of the Good Manufacturing Practices (GMP) requirements and criteria in 1982. Taiwan had no regulations on clinical trials before the ICH.

In fact, prior to the requirement for local clinical trials, intellectual property was the issue that foreign companies were most concerned with. Before the revision of patent law in 1986, Taiwan protected manufacturing processes for new drugs, but not the end products. Many new drugs patented elsewhere and registered in Taiwan lost their market exclusivity. Of course, global companies suffered from this when some local producers were able to "copy" their products; imported drugs would not be as competitive as local ones in price. For example, Piroxiden (piroxicam) was a non-NSAIDs proprietary drug produced by Pfizer and sold to Taiwan at the price of $25 NTD ($0.63, in 1986 dollars) per capsule. However, when local copies came out in competition with the original, the price fell to only $1 NTD. Because Pfizer objected to reducing its price below $12 NTD, Piroxiden was first dropped from the general practitioner market and then badly defeated by imported "me-too" products, such as those from Cyprus, in the hospital market. Pfizer finally stopped selling this drug and retreated from Taiwan. Even after the modification of the patent law and the establishment of a non-governmental, professional institute for the technical review, PhRMA worried that confidential data it submits are not being protected by the government employee confidentiality regulations.

Foreign companies encountered the same regulatory problems they later met in Taiwan in Japan back in the 1970s, and the pace of change was slow. Prior to 1976, Japan followed the German patent law that protected only for process patents for pharmaceutical products. It meant that with "alternative production processes" for a patented drug, Japanese companies could legally manufacture and sell it in their domestic market.[7] Fighting against strong pressures from domestic industry, the MHW finally adopted product patents in an amendment of the patent law.

Also like Taiwan, Japan required registration clinical trials through the MHW and listing trails for the hospitals where the products were to be dispensed. Before the introduction of the ICH guidelines, Japan had rules from 1968 on clinical trials using local subjects. In the 1980s there were special study guidance groups consisting of "patriarch" specialists organized by the MHW. These groups drafted specialized guidelines for conducting clinical trials in fields such as cardiovascular or gastrointestinal disease, and these were imposed on any firm that wanted to sell drugs in Japan. For foreign companies, the requirements were not necessarily tough to meet; however,

[7] for another example including automobiles, see Cusumono 1989: 97-100.

because they required local subjects and the format was incomparable with FDA guidelines, these companies had to repeat all clinical trials before entering the Japanese market. Although the MHW made efforts to streamline its reviewing process in the 1990s, the delay in drug introduction still averaged three to five years. For global drug companies, the main difficulty was not with their products but with the delayed market entry due to these administrative barriers.

Let me sum up the local factors discussed above. For the global pharmaceutical companies, the policies of Japan and Taiwan that affect their interests have three roots: pricing and reimbursement, regulatory affairs, and intellectual property rights enforcement. These result from the national insurance schemes implemented in the two countries. This fact also contributes to the government's irreplaceable role as protector of people's health and wealth. It may seem odd for PhRMA to decry the Wal-Mart practice of pushing down prices by buying in huge volumes, but if we take the state into consideration we will understand the partial logic behind the argument. For PhRMA, these practices contribute to unfair competition. The market exclusivity and commercial potential of their new products are reduced by the restrictions introduced by the government, and the aim in PhRMA's mind is to favor the local competitors.

Thus PhRMA appealed to the U.S. government. The pernicious effects of foreign government price and access controls, they claimed, hurt patients in the United States and abroad, created market access barriers to U.S. exports, cost well paid jobs in the U.S., and constituted unsound economic policy, even for the countries that employed them. The government should recognize the potential harm to the U.S. trade interests resulting from some countries' market-distorting practices in the area of pharmaceuticals. For all of these reasons, PhRMA claimed, the U.S. government should make reforming these anti-innovation market barriers a top priority of U.S. trade policy.

Pressures Initiated by the United States

In this section I will introduce two legal institutions that affect the U.S. international trade policy on drugs: free trade agreements (FTAs) and Section 301 of the Trade Act of 1974 (hereafter Section 301, "Special 301," and "Super 301").[8] These two institutions

[8] In fact, concerning the institutional practice of research pharmaceutical companies trying to expand their markets, Christopher Harrison lists four routes by which this is done (Harrison 204): domestic solutions for the international market (i.e., Section 301), bilateralism without institutionalization (e.g., negotiations between the United States and other countries), bilateralism with institutionalization (e.g., Bills C-22 and C-91 with Canada), and multilateralism (e.g., WTO or TRIPS). However, in this section I will only review the two of these that are related to our Asian cases.

are different in many ways; for example, the FTA is a diplomatic document worked out based on the mutual understanding of the states involved. In contrast, Section 301 is a domestic law and the actions it induces are unilateral and uninfluenced by diplomatic concerns. However, both share the same goal: expanding the territory in which goods can be sold freely.

The history of these institutions can be traced to U.S. trade policy in the 1960s. Under the Trade Expansion Act of 1962, the U.S. established an interagency trade policy mechanism, and this mechanism later evolved into an organization consisting of three tiers of committees: the Trade Policy Staff Committee, the Trade Policy Review Group, and the National Security Council/National Economic Council. These committees developed and coordinated U.S. government positions on international trade and trade-related investment issues. The Special Trade Representative (STR), the new position created by the law, played a leading role in the development of policy on trade and trade-related investment, as well as in the coordination of the interagency process of trade policy formulation.

The STR's responsibilities substantially expanded in the 1970s through the Trade Act of 1974 and other related laws. Congress made the STR responsible for trade agreement programs and directly accountable to both the President and the Congress for these and other trade responsibilities. In 1980, the STR was renamed as the Office of the United States Trade Representative (USTR), centralizing U.S. government international trade policy-making and negotiating functions. Its mission, in a simple reflection of U.S. trade policy, is to open the world market for U.S. manufacturers as much as possible. Over the past twenty years the USTR has grown into a strong institution that has two offices working on five organizational lines; it has succeeded in making the United States party to numerous trade agreements with other countries and participated in negotiations for new trade agreements in a number of countries and regions of the world.

It is not necessary to discuss these trade agreements,[9] but three significant characteristics can be noted. First, although globalization is a term often used in international trade, it is difficult to achieve this goal, and it depends on the scale of negotiations. The larger the scale of an agreement, the more difficulties it faces. In fact, it was not the WTO but rather rising regional networks of FTAs that brought about an acceleration of international commerce.[10] Although from 1994 to 2002 no free trade

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[9] For details, see the Office of United Trade Representative's website at http://www.ustr.gov/trade_Agreements/Section _Index.html.

[10] While emphasizing the importance of bilateral agreements, I do not intend to ignore the importance of the WTO (see, for discussions, Harrison 2004, Chapter 8). As an international organization that oversees a large number of agreements defining the "rules of trade" between its member states, the WTO was also a

agreements were passed in the U.S. Congress due to pressure from domestic industries, existing organizations provide a platform by which the United States conducted bilateral negotiations, such as the U.S.-Singapore FTA, and other agreements led to broader cooperation in various regions, such as the Middle East Free Trade Area.

Second, the main goal of these agreements is to eliminate "trade barriers" for exports from the United States. Unlike the global WTO, where Europe, Japan, and the developing countries are involved, in regional or bilateral FTAs the United States is inevitably dominant. Following the principle of "diversion-and-appeasement," the United States carefully chooses countries to negotiate with such that the impact on its own domestic industries can be minimized. The U.S. believes that it can beat out all local competitors if the game rules are fair and square. The third characteristic of trade agreements is their diplomatic nature. In some cases they are pursued because of concerns other than trade. For example, in order to prevent a "domino effect" from Cuba, the U.S.-Central America Free Trade Agreement excludes this communist country.

For pharmaceutical companies, free trade is a stimulant to more sales. Over the past two decades, market access and pricing issues also have been part of the U.S. trade dialogue with Canada, Japan, Taiwan, and Korea. In the Trade Act of 2002, Congress provided additional guidance on negotiating objectives, calling for increased transparency in the pharmaceutical regulatory process, consultative mechanisms, and non-tariff market access issues such as reference pricing. Let us take U.S.-Australia Free Trade Agreement (AUSFTA) as an example. Signed in 2004, it is the first FTA to include specific provisions dealing with non-tariff market access issues related to pharmaceuticals. According to the agreement, it will eliminate over 90 percent of manufactured goods tariffs between the U.S. and Australia, including those on pharmaceuticals. However, it is likely that this FTA will badly damage Australia's Pharmaceutical Benefits Scheme (PBS). According to Kevin Outterson, because the PBS's economic evaluation produces some of the lowest patented drug prices, PhRMA hopes to do away with this system once the AUSFTA is enacted. In fact, the USTR and PhRMA have made clear that their goal was to increase Australian prices.[11] It is not surprising that PhRMA appreciates this FTA, because it "Establishes strong legal standards for protecting intellectual property, which

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target of protests by the anti-globalization movement. However, it is less related to this thesis and should be an independent topic for discussion. Regarding global health, five agreements in the WTO are relevant: the Trade Related Aspects of Intellectual Property Rights (TRIPS), the General Agreement on Tariffs and Trade (GATT), the General Agreement on Trade in Services (GATS), the Agreement on Technical Barriers to Trade (TBT) and the agreement on the application of Sanitary and Phytosanitary measures (SPS).

[11] While working together, some people have been rewarded for these efforts. Ralph Ives, the chief U.S. negotiator who added the provisions concerning the PBS into the AUSFTA, was promoted for this success in April 2004 to the newly created post of Assistant USTR for Pharmaceutical Policy.

encourages the search for new therapies and cures for patients" (PhRMA as cited in Outterson 2004).

For countries who have not yet signed agreements with the United States, Section 301 is an aggressive, unilateral weapon with which the USTR can pry open their markets. Section 301 emerged in 1962 and was designed to give the President greater flexibility in resolving trade disputes. It was strengthened in the 1970s. As amended in the 1974 Trade Act (19 U.S.C. § 2411), it is the principal statutory authority under which the United States may impose trade sanctions against foreign countries that maintain acts, policies and practices that violate, or deny U.S. rights or benefits under, trade agreements, or are unjustifiable, unreasonable or discriminatory and burden or restrict U.S. commerce (III A). In light of congressional and industry demands for more protectionist trading policies, an amendment was made to Section 301 in 1979 that authorized the filing of private party petitions with the USTR requesting investigation of foreign governments believed to be violating trade agreements or otherwise harming U.S. commercial interests. These amendments were strengthened further in the enactment of the Omnibus Trade and Competitiveness Act of 1988, which introduced the so-called "Special 301," according to which the USTR must review, by April 30 of each year, the practices of U.S. trading partners and identify foreign countries that fail to provide "adequate and effective protection of intellectual property rights," or have any acts, practices or policies which deny "fair and equitable market access to United States persons who rely on intellectual property protection" (IV B.) The USTR consults with foreign governments to resolve issues. If in the eyes of the USTR a satisfactory resolution is not reached, recommendations are made to the President for appropriate action, which usually involve trade retaliation in the form of import tariffs and restrictions.

Pharmaceuticals are a typical case of Section 301 strategy. Speaking on behalf of globally ambitious, intellectual property-intensive companies, PhRMA regularly submits material about intellectual property violations affecting their products to the USTR. Accordingly, in its annual report, *Annual National Trade Estimate Report on Foreign Trade Barriers* (NTE), the USTR places the countries it negotiates with on the "Priority Foreign Country" list or the "Priority Watch" list, depending on how damaging their apparent malfeasance seems to be to U.S. commerce, and more investigations are conducted.[12] Although the USTR will enter into bilateral negotiations with Priority

[12] The procedure is as follows: the initiation of a Section 301 investigation can be requested by an interest group, such as PhRMA, by the filing of a petition. After publishing the initiation, the USTR provides an opportunity for public comments and starts consultation with the foreign government under

Foreign Country to remedy the problem, this is backed by the threat of unilateral retaliatory action if a solution amenable to U.S. interests is not reached. According to United States Code (19 U.S.C. 2411 et seq), a retaliatory action can be taken unless "substantial progress is being made in negotiations with the foreign country; or a delay is necessary or desirable to obtain U.S. rights or a satisfactory solution" (III C.) Although in reality retaliatory actions are rare and unusual, this measure creates real and powerful pressure on U.S. trade rivals. In this sense Super 301 is the ultimate weapon in this arena. It allows the USTR to identify Priority Foreign Country practices, the elimination of which would be likely to bring about significant increases in U.S. exports. Within thirty 30 days of identification of Priority foreign practices, the USTR is required to initiate Section 301 investigations of any Priority practices identified in the report. So far no other country can trump Section 301 in trade negotiations.

Thailand is a salient example of a country that has had to face continued U.S. retaliation (for more examples see Harrison 2004, Chapter 6). Thailand, one fourth of whose export market is the United States, introduced a compromise bill on patents in 1988 after attempting to resist U.S. pressure to change its patent laws. The next year it was listed as a Priority Foreign Country. PhRMA (then the PMA) successfully urged the U.S. government to revoke preferential treatment worth $165 million that Thailand was receiving through the U.S.'s Generalized System of Preference program. The Thai government was forced to concede and passed new patent laws in 1992, which still retained legal control over drug prices. It remains on the USTR's Priority Watch list and the subject of trade retaliation. Hit by financial crisis in 1997, Thailand was unable to bear U.S. pressure and sanctions any longer and was forced to accept U.S. suggestions for further amendments to its patent laws. The amendments to its laws have resulted in inflated drug prices, terminated opportunities for the parallel imports of less expensive generic drugs. As of 2004, Thailand was still on the list as a "watch country."

As for Japan and Taiwan, Section 301 strategies have been applied from time to time since the measure's enactment. Japan has faced them in areas including steel, silk, leather, tobacco leaves, the semi-conductor industry, citrus, construction, telecommunications, satellite equipment, superconductors, forestry, automobiles, and films. Among these, satellite equipment, super conductors and forestry were the sectors that made Japan one of the two countries listed as a Priority Foreign Country in 1989.

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investigation. After the investigation, the USTR must make a determination of whether the foreign practice is actionable under Section 301. This should be done within 18 months of the initiation of an investigation involving a trade agreement that includes a dispute settlement mechanism, or within 30 days after the conclusion of dispute settlement procedures, or within 12 months of the initiation of an investigation in all other cases.

Taiwan has faced Section 301 action over rice, automobiles, customs practices, alcohol, tobacco, and later intellectual property, which made Taiwan a Priority Foreign Country in 1992. Even so, most of the time both these countries are not the main targets of this weapon.

However, PhRMA continues to keep Japan and Taiwan on the list it submits to the USTR. In its 1998 report, PhRMA took notice of Taiwan and Japan, criticizing their regulation processes and pricing and reimbursement systems. In 1999, these accusations turned into a clear wish to have both listed as Priority Watch countries. PhRMA claimed that the new pricing system introduced by the MHW would significantly diminish the U.S. pharmaceutical industry's trade surplus with this country. The same rhetoric was used toward Taiwan's "five principles" for determining pharmaceutical reimbursement prices. Furthermore, clinical trials are an issue. PhRMA thinks their elimination is important to the spirit of free trade. Regarding the importation of bulk pharmaceuticals, PhRMA criticized Taiwan's quality concerns over the ability of companies to import multisite source products for repackaging. In 2001, Taiwan showed up in PhRMA's report again, listed as Priority Foreign Country. Repeating the reasons that it had cited in its 1999 report, PhRMA concluded, "If Taiwan fails to convert its patent term length from 15 to 20 years for all patents, PhRMA member companies will face losses of $330 million from this issue alone, due to lost effective patent terms on 39 separate products. PhRMA is currently studying methodology but estimates that total losses in Taiwan can be conservatively estimated at $730 million."

On the surface PhRMA does not seem to be doing anything wrong—it fights for liberalization. Nonetheless, it is doubtful that PhRMA practices equal justice. Two Taiwanese officials told me of their uncomfortable experience dealing with a PhRMA representative. At an international meeting in Thailand a PhRMA representative caught one official who had just come into a conference hall. "Can you spare some time? We have to talk," said the representative, according to that official. Assuming it was a private gathering to exchange ideas, he agreed. "The resulted was this woman from the UK brought ten or twelve CEOs of global companies to shoot me questions about our review practices," he complained. "They put a colleague of mine and me in a corner and asked us questions for about an hour. It was very impolite. It was impolite first not to make an appointment in advance for this meeting, and so was the style in which they delivered their inquiries. I was badly insulted when the PhRMA representative threatened me [by saying] that Taiwan should eliminate all clinical trials in appreciation for the military cooperation of the United States. I suddenly stopped her and said that was none of her business. 'You are *British*.' I stared at her. After that, I will never trust her." Leaving aside

the complicated political relations of Japan and Taiwan with the U.S., which deserve their own study, the looming shadow of Section 301 alone is enough to make these countries concede what many regard as their sovereignty and their economic welfare to the U.S. agenda of externalizing its economic policies, domestic laws and businesses using the crowbar of Section 301 and creating inevitable damage in the process.

As discussed in this section, the U.S. employs trade agreements and Section 301 as weapons to open markets that its industry can then conquer with minimal resistance. Far from the superficial excuse that its actions are an effort to further world trade liberalization—apparently for the sake of developed countries—the United States exploits its global economic power in the pursuit of its own narrowly composed parochial trading interests. Complicated social and cultural concerns are reduced to economic factors, and naïve laissez-faire is the only solution they desire.

PART II
JAPAN'S HEALTHCARE: BUILDING A SYSTEM OF TRUST

Drugs in Japan: A Different Kind of Business

In 1986, the U.S. Pharmaceutical Manufacturers Association (PMA, now PhRMA) opened its Tokyo office; it was one year after the release of a report on U.S.-Japan trade negotiations on pharmaceuticals.[13] This was the first time the PMA considered the necessity of learning about this huge market so that their products could be brought in. It soon appointed Paul Reed Maurer, then the East Asian representative of Merck Co., as its Japan representative, the best choice available.[14] From this position Maurer wrote frequently on his observations about the pharmaceutical business and market in Japan for an audience of American pharmaceutical company managers. However, before long various Japanese trade magazines asked his permission to publish these commentaries as well. Before Maurer decided to turn these articles into a book, these pieces had attracted interested readers in magazines inside and outside of Japan. In 1989, the book *Competing*

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[13] This was the so-called MOSS Report. For more discussions about this negotiation and its impact on the pharmaceutical sector, see Chapter 4.

[14] Before serving in this position, Maurer had worked for two giants in the pharmaceutical sector, Eli Lilly and Merck. During his career in the pharmaceutical business, Maurer helped Eli Lilly to establish Lilly Japan, the first fully foreign-owned subsidiary since the amendment of investment regulations in 1975. In addition, with Maurer's help, Merck made an incredible majority equity position purchase in both Banyu and Torii within the same week in 1983. In the local media at that time, Maurer was portrayed as the one who could bring in a foreign giant able to break cultural and business barriers in Japan, allowing Japanese companies to "sell themselves out" to foreign multinationals.

in Japan was published in English and Japanese (Maurer 1989a and 1989b).

In retrospect, Maurer's observations were important not only because they filled the knowledge gap in English-speaking audiences about Japan's pharmaceutical business; more importantly, they were recognized by the Japanese as a reliable information resource about themselves and a worthwhile introduction for foreigners. In fact, *Competing in Japan*'s Japanese edition sold far better than its English one. One reason for this, as Maurer pointed out, is that he separated facts about Japan from the "Japan myth," a common term in the late 1980s. What he tried to achieve in this book was to provide helpful information that could be useful to both Japanese and American companies. I will not review his book in detail at this point, as many of his opinions will be incorporated into the following sections in a more systematic way. Instead, I would like to note four clarifications that Maurer made that were different from what Americans may have thought about themselves with regard to their failures in Japan and about Japan and its successes.[15]

The first is the myth that "you cannot do that in Japan" (Chapter 2). Regarding Japan's large and continuously growing market, the American companies always felt frustrated when looking for good entry strategies. They found entry was more difficult here than in other countries, and they tended to blame limitations on improper government regulations and non-tariff barriers. Although Maurer admitted that restrictions once limited options for marketing, these externally imposed barriers were no longer a factor or excuse for the retreat of American companies. The door was always open. The limitations encountered by losers, he pointed out, were those self-imposed through their organizational structures, "minor-league" commitments to a major-league market, and a lack of experience in dealing with Japanese competition (8). After indicating the signs of improvement in the Japanese market, he suggested that any company that wanted to gain a fair share in it must spend more energy and resources in order to compete with the locals. It was not the conventional scenario of American companies competing with European ones everywhere in the world; in Japan they had to face a major-league team at home.

The second is the myth of global marketing (Chapter 3). Although it is powerful for a company to centralize marketing decisions in order to perform more efficiently in its allocation of marketing resources, this does would not work in Japan if little attention is paid to the country's special requirements. In short, what is best for U.S. customers is not necessarily the best for customers in the other parts of the world; flaws acceptable in

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[15] I will use the English edition in this thesis unless I mention otherwise.

cost-benefit terms to American customers are not necessarily acceptable to non-U.S. customers who do not value this concept (19). In the case of pharmaceuticals, the typical example would be as simple as drug doses. Although Americans may not be concerned if major harm can result from an overdose, the Japanese always think the dose administered to Caucasians is too large for the body weight of the average Japanese patient. Quality is also an issue. Like oranges, bananas and eels, Japan sets a high bar on the quality of products shipped to Japan. Minor details, such as an inconsistent coloring of a material and black particles that appear in some shipments, would cause products to not be accepted by Japanese customers and badly damage the credibility of the traders.

The third myth is that of Japanese management (Chapter 6). Although it was fashionable to claim that Japan's success was due to its unique management style, Maurer has different ideas based on his observations of the drug industry. He points out two factors that readers should take into account to reconsider the competitiveness of Japanese companies. The first is regulations. Before any attempt was made to standardize local regulations, the Japanese government was infamous for its lengthy, time-consuming process of drug review. It was correct that new products generally required 18 months for a approval after new drug applications were submitted to the MHW, and price listing could require another three to four months. Even so, these regulations were not set up especially for foreign companies; all companies, including domestic ones, were subject to them. Secondly, although the manufacturing capability of Japanese industry was well known, this relative advantage was not likely to have a serious impact on U.S. firms. Pharmaceuticals are not a production-driven industry. It requires long-term commitment and up to ten years of investment in research and development before an effective molecule can reach the market. This is a rule that applies to all companies, not just American ones. No one has said competing in Japan was easy, but neither should anyone believe that there are institutional barriers to success.

The fourth and last myth is that of the competitiveness of Japanese pharmaceuticals in the global market (Chapter 16, 17 and 18). Originally, the Japanese pharmaceutical industry was not international. In the 1980s, there were about fifty subsidiaries abroad but they were accounted for by fewer than ten companies, and their exports accounted for less than 5 percent of total sales. Wholly owned subsidiaries were established primarily in those countries that were geographically and culturally close to Japan, and when signing licensing agreements, exclusive rights for the Japanese company in Japan and other Asian countries were reserved. Few people in Japanese firms had work experience outside Japan, and the number of people familiar with foreign languages is similarly small. However this did not mean that Japan would remain that way when American companies

intruded. Maurer noticed that some aggressive companies were prepared to step out while still dominating home market. Although for him it was too early to predict the outcome of their attempt, it was clear that future competition would be global. Thus it is of no use to complain and ignore Japan's important presence in the global market, where product, price, people, and profit planning are basics that can be applied everywhere.

The above opinions seem banal. Indeed, Maurer is just an experienced, keen businessman based in East Asia. Thus the importance of his words has to be recognized in the context of the tricky relations between the United States and Japan in the 1980s. James Fallows, a former speechwriter to President Jimmy Carter and a veteran columnist on Japanese affairs, commented that this relationship has

> a fragile, walking-on-eggs quality, which makes people think that it's dangerous to talk frankly in public. Many other international relationships are robust enough to survive open discussion of disagreements.... But the American fraternity of Japan-handlers, which includes mostly diplomats and a number of businessmen, scholars, and journalists, instinctively stifles outright complaints about Japan." It is a conflict that is better to face directly than to pretend does not exist (Fallows 1989).

The rest of this section is an introduction to the background of this relationship.

Although close Japan and the U.S. have been military allies since the Korean War, significant tensions arose between them over economic issues. There remains a considerable distrust between the two countries that will continue to affect relations between them. In the early 1980s, American outrage rose over the significant trade deficit and various related controversies associated with Japan. The more significant message can be read in the export performance of the individual companies. Exports as a percentage of total sales of the top ten companies in Japan are a whopping 48 percent, whereas among U.S. firms this figure is only 15 percent.

It would be unfair to blame the entire U.S.-Japan deficit on either side, and it would not be valid to take it as a purely economic problem. For example, economist Thomas McCraw identifies the shifts in the U.S. and Japan's economic structures which can explain this deficit (1986: 29-30). In addition, early instances of trade negotiations between the United States and Japan, such as those over the "textile wrangle" in the late 1960s,[16] have shown that the problem of trade friction turned out to be a combination of

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[16] The problem that gave rise to this negotiation can be traced back to 1956, when Japan's subjected its exports of cotton textiles to the United States to voluntary restraint. Because existing agreements did not encompass textiles made of wool or synthetic fibers, in the 1960s exports of such items from Japan to the U.S. increased significantly. The United States requested that Japan voluntarily restrain its exports of synthetic fiber textiles to America and was rebuffed. To secure the support of textile-producing U.S. states in the 1968 presidential election, Richard Nixon promised to insist upon Japanese restraint of synthetic

economic and political concerns. Nonetheless, the public did not conceive it this way. As the two countries became the free world's top two economic powers, it was a common thought for many Americans that this imbalance was a problem exclusive to the relationship between these two odd political partners and economic competitors. Americans believed that the Japanese were exploiting the open American market while excluding the United States from a fair chance at penetrating Japan's home market. Specific issues between Japan and the United States got tangled up in emotional negativity and stereotyping, and at times certain opinions merited the label of "Japan bashing."

In the mid-1980s negative stereotypes of the Japanese began to appear in popular books and movies, such as Michael Crichton's *Rising Sun*. Along with the "Buy American" movement, there were deep-seated fears of Japanese infiltration into the American populace. According to a *Newsweek* report (October 9, 1989), "most now view Japan as a greater threat than the Soviet Union. They consider its trading practices unfair and think Washington should push Tokyo harder to change them" (12).

Fig. 3.2. Cover of *Newsweek* (October 9, 1989) and the title page for the cover story, "Japan Goes to Hollywood."

Let us discuss in detail the cover and the title page of the cover story "Japan moves to Hollywood" from this issue of *Newsweek* (fig. 3.2). The central figure of a Japanese goddess contains multiple meanings. Columbia Pictures started using the logo of the "Columbia Lady" in 1924 in an imitation of the Statue of Liberty, the symbol of the American spirit. After over 50 years of Americans dreams and entertainment, it was replaced by Japan. When Sony bought Columbia Pictures Entertainment, the biggest

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textile exports and to make it a condition of the return of Okinawa to Japanese control. President Nixon fulfilled this campaign pledge after three years of clumsy negotiations, and Okinawa returned to Japan in 1971.

takeover ever, many thought that the Japanese had bought a piece of America's soul.

But what is more important is the way *Newsweek* portrays this conflict. It presents it as an exclusive war between two giants. For example, the person who concluded the Columbia takeover deal is shown on the article title page. He is Morita Akio, the Sony Chairman. Alongside this description of a successful businessman who Americans have not yet come to know is a biographical introduction that tells that Morita coauthored with controversial figure Ishihara Shintaro a book called *A Japan That Can Say No*.[17] Other information boxes help to clarify the binary nature of this war. One box lists two groups of people labeled as "hawks," or simply "bashers," and "the chrysanthemum club," or "apologists." Another box shows the results of a poll about whether Japan had become a threat to America. Such questionnaire themselves were a threat in my opinion; they manipulated Americans' fearful attitude toward Japan by asking whether the Soviet Union's military power or Japan's economic one was a greater threat to the United States.

The above interpretation simplifies the question of the economic disequilibria in markets and exports between the United States and Japan. While aiming its maximum exports at the United States market, which is proud of its free-trade principles, Japan did not open its market in a reciprocal manner. Where the problem arose should be solved first. Thus *Newsweek* cites the new USTR Carla Hills' comment upon arriving in Washington for a business negotiation that she came "with a crowbar," meaning the Super 301 unfair trading practices list. Opening the Japanese market was inevitable.

Only by acknowledging this background can we appreciate Maurer's comments on the Japanese pharmaceutical industry. Although his attempt to apply his observations to other high-tech sectors might not be equally successful, his observations on Japan are less emotional and prejudicial. Maurer's basic outlook is American; he sees business as nothing but business and Japan as the most difficult market—"if you can make it here, you can make it anywhere." However, Maurer did not think that Japan was so totally exotic that no communication could bridge the cultural differences between it and the U.S. "Nothing is impossible in Japan," he emphasized at the end of *Competing in Japan*, if only Americans could think about the way the Japanese do business and the uniqueness of Japanese market (166-167). Business, for Maurer, should return to basics, namely, the customers. He frankly listed these points:

> It is an easy out to blame the "system" rather than taking a hard look in the mirror and admitting you don't have the quality and quantity of people to get the job done; admitting your regulatory affairs department hardly knows the people

[17] The official English translation of this book was not published until 1991, by Simon & Schuster, but this translation is a sanitized version, including only Ishihara Shintaro's writings.

> in the Ministry of Health and Welfare; admitting you have one salesman calling on a hospital twice a week and a competitor has three people who live in the hospital every day; admitting that during the past ten years three different men were in charge of your Japanese subsidiary, and none could understand one word of a business discussion in Japanese (167).

According to Maurer, the core of business is the universal "customers first," even in the difficult market of Japan. The first step to solving problems is identifying the rules behind Japanese customer loyalty to certain products. Do not complain about the rules, but learn them.

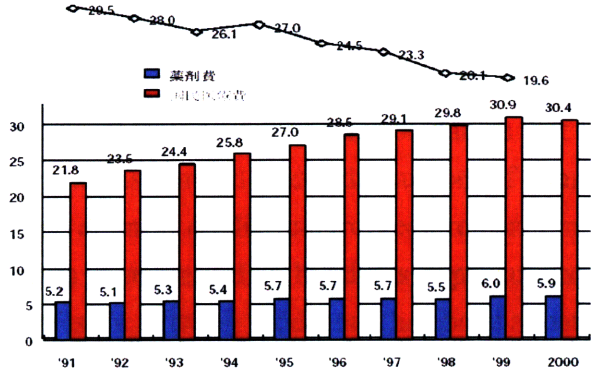
Why do Japanese drugs win Japanese customers' hearts? What are the rules behind this phenomenon, if not simple protectionism? In the following two sections I will describe the social and cultural logic behind Japanese drug consumption. Unlike the United States, which simply encourages innovation by applying high standards, I will argue that the logic that makes Japanese people continue to consume drugs is trust. As Francis Fukuyama has revealed (1995), Japanese society has a high degree of trust, and I think this observation can be applied to the business of health care. Technology innovations do not play a crucial role in creating new needs in health; instead, trust does. Through a conventional network of trust consisting of the physicians, drug companies, traders, and wholesalers, new products are produced, promoted, guaranteed, and consumed by consumers. Under this scheme, safety is always more important than efficacy, and manufacturing (GMP) more important than research and development (GCP). The initiative to improve drugs is, like in the United States, accidental misuse of drugs. Yet the mechanism is different. While the FDA creates a higher standard for drugs every time in order to control quality, in Japan the public often criticizes the system that drugs travel through, the corrupt relationship between physicians and drug companies. It is a refreshing process of social trust.

Making Sense of Japan's Drug Environment

Leaving aside international pressures, this section will analyze the pharmaceutical market in Japan from the perspective of policy making. It is well known that relative to its population, Japan has a disproportionately large drug market; but where shall we begin tackling this business? Let me introduce a simple yet often asked question: why does Japan, as one of the leading countries in terms of technological innovation, export relatively few drugs? Among researchers who have asked this question, Michael R. Reich is probably the most notable (Reich 1990). Unlike many analysts who simply apply

conventional models of protectionist government intervention and free-market competition, Reich reminds us of the importance of the medical policies introduced in a historical context, arguing that Japan's pharmaceutical industry has been nurtured and promoted through a highly regulated, well protected and continuously expanding domestic market shaped by the government's health policy.

Fig. 3.3. Medical Expenditures and Pharmaceuticals as a Percentage of Total Costs, 1991-2000



Note: Figures are presented in percentages (above) and trillions of yen (below). Blue columns: pharmaceuticals expenditures. Red columns: medical expenditures.

Source: Suzuki Hiroshi 2003, http://www.akita.med.or.jp/rikai.pdf.

Let us first look at the expansion of this market. The health economist Stuart O. Schweitzer has pointed out that the share of expenditures devoted to pharmaceutical products in the United States declined from 1960 to 1990 compared with other healthcare sectors. While expenditures devoted to hospitals hovered at 40 percent, the share for pharmaceuticals dropped by about half, to 8.2 percent, in 1990 (Schweitzer 1997: 95-96). However, Japan is different; pharmaceuticals have been a significant expense since the introduction of its universal health insurance program, constituting nearly 40 percent of the total expense. Though this percentage decreased in the 1990s due to Japan's long economic recession and subsequent budget reforms, the proportion of expenditure was still about 20 percent in 2000. Real consumption, on the other hand, increased from 40 billion yen to 50 billion yen (fig. 3.3). The Japanese even tease themselves about this high level of pharmaceutical use, saying that their bodies are heavily "pickled" in drugs (*kusirizuke*).

Indeed, in retrospect, we see a divergent trend in the growth of the Japanese and

U.S. pharmaceutical sectors in the 1970s. While the FDA and industry elevated the standard for new drugs, resulting in a double-digit growth rate in business, in Japan the same growth rate was achieved neither by the exclusion of competitors nor by the separation of the market by research-based companies. It happened by the unlimited expansion of domestic consumption. To consider the structure of this expansion, on the demand side, the rate of consumption of prescriptive drugs compared to OTC drugs rose from 48.2 percent in 1955 to 85.5 percent in 1980, creating a large space for drug development. Further, prior to the introduction of the 1997 reform, which increased co-payments for health services and drugs for the insured and the elderly, full insurance coverage resulted in visits for minor maladies making up one fourth of total medical expenditures. The same trend is also seen on the supply side. The relatively low bar for taking a drug to the market welcomed all domestic companies that wanted to develop acceptable drugs. During the past three decades the number of companies did not decrease in response to government quality control requirements introduced in the 1970s. Thousands of new products were created by hundreds of producers; most were barely qualified or were substitutes for existing products. The above situation, as many would say, is a "greenhouse" for Japanese drug companies.

Reich does not totally reject the protectionist interpretation as a way of understanding this "greenhouse." He does point out that the government protected its domestic market from direct foreign investments.[18] Nonetheless, he does not say this policy—which has benefited other industrial sectors, too—was a major influence on the drug industry in Japan. An obvious fact is that these companies, though having grown large, did not sell many of their products overseas, as is the case with companies in other sectors. According to the JPMA's report, from 1970 to 1997 the MHW approved 929 NCEs, among which nearly two thirds were sold solely in Japan (JPMA 2001: 28). In other words, Japanese firms did have a chance to sell their drugs to overseas, but they did not; even after deregulation allowed U.S. companies to import their products into Japan, most Japanese companies chose to stay in their home market.

Thus it is important to understand why Japan's drug industry is not as aggressive as its other businesses, and I will point out two characteristics that contribute to this. The first is the presence of a strong and vibrant marketing network that is directly linked to production. All major companies in Japan have their own wholesalers and sales networks, a situation that prevents latecomers from breaking into the market. Production cannot be separated from sales. This marketing orientation has its historical origins back in the era

[18] For example, until the early 1970s, direct foreign investment in and imports to Japan were restricted. This policy indirectly helped Japan's drug companies acquire the technology they were lacking.

of the Meiji Reformation, and is also tied to the origins of Japan's pharmaceutical industry's origins in drug trading (Odagiri and Goto 1996; table 3.4). Most major producers maintain their own sales departments and sales networks, which also deal with foreign products. In addition, many drug trading companies turned to importing new drugs and then establishing the production capacity to manufacture generic drugs. Benefited by the unimproved patent law, these companies chose to focus on profiting from marketing competition. Both types of companies gave rise to a complicated marketing system that distributes drugs and shares benefits with everyone in the network.

Table 3.4 Developmental Paths of Major Drug Makers in Twentieth-Century Japan

Development paths	Name of Companies
Wholesaler of *kanbo* and traditional herbs→wholesaler of Western medicine→drug maker	Takeda, Shionogi, Tanabe, Fujisawa
Government-sponsored manufacturers	Dainippon seiyaku, Maruishi seiyaku, Teikoku seiyaku, Tokyo yakuhin
New drug manufacturers	Sankyo, Daiichi, Nihon sinyaku, Morisita seiyaku, Banyu seiyaku
Importers and manufacturers	Tomoda seiyaku, Torii yakuhin

Source: Tatsuno Takashi 2001:109.

The second characteristic of Japan's drug environment is so-called "physician centralism" (*yisichusin shugi*). In Japan it was physicians, not pharmacists, who bought and sold drugs. Although there are pharmacists and pharmacies, most dispensary work is done by physicians, especially those who work for the clinics that are still the major medical providers in Japan. This phenomenon also has a historical basis. During the Meiji Era, Western-trained physicians were the only group of medical professionals presenting a style that combined intellectualism and elitism. Since the foundation of the Japan Medical Association (JMA) in 1874, physicians had formed a powerful profession. Physicians are everywhere: they are professors and researchers in universities and teaching hospitals, policy makers in the government, and, of course, healers of body and spirit. Critic Mizumaki Chusei has pointed out that the JMA (2003), as the collective

representation of Japanese physicians, has three faces: academia, policy and political manipulation. Furthermore, a good relationship with the Liberal Democratic Party and heavy involvement in local elections made the JMA the strongest lobbying group. By excluding or ignoring the other medical professions, it controls knowledge and the benefits from it.

The area of pharmaceuticals is no exception. Among physicians, pharmacists were never regarded clinical professionals, though some may think of pharmacy as an academic discipline. Although an attempt known as *yiyakubungyo* was made to separate dispensing from prescribing by physicians, this policy was strongly suppressed by physicians and remained almost functionless.[19] Though recognized in the West as belonging to a medical profession, pharmacists in Japan did not really enjoy equal status under the law. This situation has its historical roots: as Tatsuno Takashi laments, "Unlike Europe, where pharmacy and its education were generated from the apprenticeship in the guild, their development in Japan present a different path" (2001:140).

Since physicians prescribe and dispense most drugs, they profit from this business by the price differences in the drugs they dispense. Because the reimbursement scheme for physicians' service fees under the NHI is undervalued, physicians rely heavily on the "pharmaceutical margin" (*yakka saeki*) for their income. According to health insurance law, physicians there are reimbursed for prescribed drugs by insurers based on the drug list prices set by the government and reported by drug companies. However, this list price is not the one by which traders sell drugs to physicians. In order to secure the largest price difference, physicians ask drug companies to lower the sale price as much as they can. As a result, an increasing gap between drug list prices and the price paid by doctors is created. Odagiri and Goto report that such *yakka saeki* was estimated by the MHW to be worth 1.3 trillion yen in 1987, nearly a quarter of the total payments by patients and the fund for drugs prescribed by the doctors and hospitals (1996: 244-246). Although this problem has been around since the 1950s and some attempts were made to resolve it in the 1980s, nobody but the JMA and drug companies can decide the suitable (list) price for each drug.

At the local level, what makes the marriage of physicians and drug companies possible is a special group called *puropa*. Derived from the English term "propaganda," the function of *puropa* is to ask physicians to use their company's drugs, or if they already do, to use them more. Although in the United States we can find the counterpart

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[19] *Yiyakubungyo* was brought up during the American occupation by General McArthur and conditional agreement was obtained, with hesitation from the JMA. However, too many "exceptions" resulted in this policy going nowhere; over 90 percent of dispensed prescriptions were still made by physicians.

of *puropa* in medical company representatives,[20] in Japan *puropa* have a different focus, even following the introduction of a licensing system regulating them in 1997.[21] *Puropa* are hired by drug companies to maintain and expand their marketing networks and are more like salespersons than purely information providers. As in other sectors, salespersons usually do their best to please their customers. However, what make *puropa* different is that physicians are their only customers, and they are difficult to please. Thus the basic task of *puropa* is to build up a good relationship with physicians in the areas they are responsible for. Their work begins as early as the time when these physicians are still residents. To fulfill these future customers' personal needs, *puropa* do everything for them, such as copying papers, buying textbooks, bringing lunches, sponsoring after-work gatherings and holiday activities, taking care of physicians' family members, arranging visits and overseas trips, and of course, holding conferences where their drugs can be promoted. As portrayed in Yamasaki Toyoko's famous novel *Siroikyoto* (The Giant Ivy Tower, 1965), *puropa* are young, attractive women aggressive enough to be willing to sleep with their customers to obtain greater sales for their drugs.

The above social foundations have created a complicated network consisting of drug producers, wholesalers, dealers, and physicians. It is not merely a marketing system, but a system of interpersonal relationships. Only by understanding this network can we see the basis of the over-consumption of pharmaceuticals in Japan. There are three consequences. First, before intervention by the MHW, the Japanese in general had to pay higher prices for drugs than people in other countries. Although it is hard to find a basis on which a fair comparison can be made because of the different dosages Japanese people consume, Reich cites a report from 1982 indicating that drug prices in Japan were "significantly above" those in Switzerland, West Germany, United Kingdom, Italy, and France (1990: 132). Second, the volume consumed is increasing. Since the drug sales margin became the main income of local practitioners, the more drugs they prescribe, the more they earn. Doctors tend to dispense large amounts of drugs, more than patients need, to increase their income. The third consequence of the over-consumption is a high turnover rate in drugs. Policy analyst L.G. Thomas III notes Japanese doctors' "brand disloyalty" behavior: unlike British physicians, whose brand loyalty allows British drug firms to afford the extravagant cost of developing a drug with a long product life, Japanese physicians prefer the latest and most expensive product, resulting in a fast

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[20] On the subject of the culture of pharmaceutical sales practices in the United States, Michael J. Oldani provides a pioneering but excellent ethnographic account. See Oldani 2004.

[21] This system consists of examinations for people who want to be medical representatives. They are required to have basic knowledge of medicine and medical administration, such as information on packing, drug policies and regulations, and requirements for post-marketing surveillance reports.

turnover rate. The "life cycle" of drugs launched in Japan was only five years in the 1990s, compared to fifteen in the United States and twenty in United Kingdom (Thomas 2001: 65, 106). Although there are many factors contributing this phenomenon, we should not forget the effect of the marketing network. In reality, physicians are loyal to the network that brings them these products. In order to keep drug circulation active, companies have to develop new products to make physicians satisfied, even if these "second generation" drugs have only minor differences from their precursors.

As part of the social fabric, this marketing network is not closed to local and small companies, but it is closed to those companies not familiar with it. As part of the domestic drug industry, every company had its own network that does not necessarily overlap or compete with others. A firm specializing in gastro drugs will not step into the field of asthma. For them, the most important concern may not be improving their products but keeping their marketing territory. The market decides and ensures the survival of a drug company. In contrast, for foreign companies it is definitely not a system of free competition. As Maurer suggests, they have to know the rules and build up their own networks. It is reported that some international brands started to establish their own subsidiaries in Japan after the bar for foreign companies was removed. However, many of them soon found that marketing in Japan was difficult and time-consuming. Worse, they could not create crucial relationships with the doctors and hospitals as well as their Japanese counterparts could (Odagiri and Goto 1996: 246-247). This difficulty cannot be understood by the simple explanation of protectionism. In the following section I will examine the cultural roots of this network and the role government plays in it.

Trust as the Cultural Foundation of the Drug Marketing Network

Following this discussion of the drug distribution system in Japan, this section starts by looking at innovation, considered to be the core of any industry. Compared to the standard of drug innovation in the United States, discussed in Chapter 2, Japan's drug innovation is primitive, wasteful, uncompetitive, and inefficient. These differences are apparent as Thomas compares the pharmaceutical industries in Japan and United Kingdom in terms of their "ecosystems" (Chapter 3). The results are summarized in table 3.5. According to Thomas, Japan's "pathologies" include weak research and development abilities, a loose regulatory mechanism for innovation, and non-professional marketing strategies. All result in Japanese firms being behind their competitors.

This explanation implies that if global companies can build their own distribution networks and apply the same marketing skills, they should beat every local firm due to

their superior innovation ability. From this perspective, it seems to global drug companies that there is no question that, wherever they live, patients deserve the best drugs, namely, their products. However, the fact is that even after the deregulation of importation, foreign companies did not conquer Japan's market as expected. I quote a mid-1980s British industrialist: "I do not believe that selling in Japan is a matter of price.... If you sell into Japan, by and large Japanese only buy from you if there is no Japanese alternative. If there is a Japanese alternative, they will match you on price, no matter what. It is a matter of national pride" (John Harvey-Jones 1986, as quoted in Cohen 1998: 79-80).

Table 3.5 Comparative Ecosystems of Pharmaceutical Manufacturers: Japan versus the United Kingdom

	United Kingdom	Japan
R&D	global	Local
university science	strong	Weak
efficacy regulation	stringent	Lenient
pricing regulation	innovation-driven	drop with no discrimination
Marketing	evidence-based	service-based
Result	breakthrough drugs	Imitative

Source: Adapted from Thomas 2001, Fig.4.2.

To understand this situation, it is helpful to again bring up Maurer's advice that Japan has unique requirements that companies should pay attention to and respect. In other words, customer characteristics are always important, even in the field of medical care. Schweitzer points out that although the pharmaceutical market is determined mostly by professionals, it does not mean that the customers have no way to express their "demand," which is distinct from the professionally determined idea of "need." As medical economist Stuart Schweitzer points out: "market demand... entails a desire and willingness to pay for a product or service.... The difference between demand and need is more than semantic. It is important in differentiating between what 'is,' or what 'will be,' on the one hand, and what 'ought to be,' on the other" (1997: 73-74).

Putting aside the supply side discussion, we need to know Japanese customers' real demands—that is, their preferences on drugs. The Japanese's insistence on their own products may simply be a banal form of nationalism; however, I would like to suggest that cultural factors are involved in drug customers' behavior. Following the formation of connections among those who deliver prescriptive drugs, in this section I will argue that trust, as a basic concept that builds personal relationships in Japan, is the key to the logic that glues together the social fabric I described in the previous section. The question at stake is, if pharmaceuticals are not purely commodities on which a simple seller-consumer relationship is established, on what relationship can this style of business be achieved?

In the European-U.S. context there has been a range of literature addressing trust and its social meanings, among which *Trust and Power* is pioneering (Luhmann 1979). From a theoretical perspective Niklas Luhmann argues that trust is a social relationship subject to its own set of rules. It occurs within a framework of social interaction and personality. In situations when we have to act in spite of uncertainty and risk, trust means "to behave as though the future were certain" (10). Thus, as Piotr Sztompka (1999: 25) points out, trust can be defined as "a bet about the future contingent actions of others." Along with this trajectory varieties of trusts can be developed for different targets (the objects we trust) and substances (the content of the relationships); all of them are woven into the broad, collective social network called culture.

However, here I will look at trust from an "upside-down" perspective using Francis Fukuyama's well-known analysis (1995). Starting with various distinct cultures in the world, Fukuyama discusses Italy, Taiwan and Hong Kong (as Han Chinese), Japan, Korea, Germany, France, and United States. I appreciate this approach for two reasons, one general and the other specific. Generally, this study has a clear focus at the national level; Fukuyama aims to emphasize the cultural milieu where all social relationships are generated and shaped by the flow of politics and history. The second reason is related to the theme of the present study. The sociological literature presumes the concept of risk assessment and management, from which individual trust is built. Although this may be true of health discourses in the United States, as discussed in Chapter 2, it is not the case in Japan. As will be shown in this section, the Japanese appreciate natural ways of maintaining health (*yojo,* "nurturing lives"). The less intervention in the natural course of bodily recovery there is, the closer it is to *yojo*. Furthermore, they build their faith on drugs based on the network by which they are delivered. Therefore, "safety," rather than "efficacy," becomes the first priority for Japanese people who consume pharmaceuticals and for the government that regulates them.

From Fukuyama's viewpoint, Japan is a high-trust society (Chapter 14 and 15). In contrast to countries where there is trust among family members or blood relations, the Japanese have a complicated yet self-governing culture of institutions of trust. The government is not the only thing they respect. Other institutions include student associations at school, companies that provide life-long employment, and after-work social clubs; anyone who joins a social group will be protected and has a reasonable share of the responsibility and rights (the notion of *iemoto*). In fact, the Japanese are fully aware of the importance of this concept. For them, *shinyo* (trust) is the deep feeling that one seeks to feel before entering into a relationship.

Medicine is a field where *shinyo* is of particular importance. Its historical origins, as ethicist Kimura Rihito points out, can be found as early as the formation of modern institutions (Kimura 1991). In the tradition of Japanese medical practice, physicians were cast as conduits of *jin*, the Confucian ethics of benevolence, and this became the center of the medical relationship. The appropriate way of healing a person under such relationship is characterized as "the art of *jin*" (*jinjutsu*). Physicians were required to act with benevolence toward their patients and were responsible for their welfare as part of a trust relationship. As expected, this trust relationship was achieved in a patriarchal manner: physicians fulfilled their responsibility by acting in an authoritative way. Even so, as a group the Japanese are used to this. As the famous psychiatrist Doi Takeo explains, there is a unique concept by which Japanese to develop relationships with others, which he refers to by the Japanese term *amae* (Doi 1971). Doi argues that *amae* is based on an infant's relationship with its mother. Although it is not limited to family relationships, when it occurs in other relationships it is perceived in terms of the relationship between a parent and a child. *Amae* involves a "trustful dependence" through which nothing bad will happen if one person is dependent upon another person who has good feelings for him or her. Doi also points out that *amae* involved conscious awareness; that is, Japanese are consciously aware of those upon whom they depend.

The idea of *amae* can be nicely applied to the physician-patient relation. According to Kimura's interpretation, the patient's relationship to the physician is analogous to that between a child and the parent, where the latter acts to do what is best for the former. Many criticize Japanese medical practice because doctors take too little time with each patient. Indeed, a meeting of less than five minutes would seem to be too brief to develop a comprehensive dialogue by which a sound prescription could be written; however, we should take into account the social function of a clinic in terms of its accessibility in a community. Most Japanese clinics serve neighborhoods where they are familiar with everyone. In turn, the high accessibility of clinics allows patients as many and as frequent

visits to their doctors as time allows. Not all brief patient-doctor meetings are functional or necessary to curing diseases; they are also social, and they maintain patients' contact with professional who know their bodily condition well.[22] Also, as in other Japanese relationships, patients have their own will, yet these needs always have to be considered as part of the dynamics of the relationship, which Kimura calls "related autonomy." The ultimate goal for a medical relationship is a harmonious situation of *wa*, the essence of Japanese spirit.

Given this understanding, we can now consider why some "backward" parts still exist in the field of medical care in Japan. For example, until the early 1990s, many Japanese still utilized the so-called "stored drug" system (*okigusuri*). It has a long tradition originated from Toyama, where local traders sold boxes containing frequently used drugs together with brief instructions. They distributed these boxes (or sometimes bags) to families so that they could take the proper medications whenever they had minor problems. The vendors would supply the amount of drugs to be taken and clear the balance with their customers every year or six months. The "stored drug" system was widely used and formed a national sales network lasting well beyond the end of World War II; even after that, it was active in some areas for domestically produced OTC drugs.

To answer why the Japanese still supported this system, we have to remember the relation of *amae*. Toyama vendors were not purely salespersons. The book *The Medicine of Toyama: Pioneers in Marketing* (Endo 1993) carefully documents how these vendors built up trust relationships with locals, such as via acquaintance with local dialects or never claiming money before customers mentioned it. Once the relationship was built; it lasted forever. This model can also explain why many small companies are able to survive with only one or two generic drugs, and are pleased to do so. "Why don't they have any intention of improving the drug and expanding their company?" I once asked an insider. "Well, if you understand the Japanese," he said, smiling, "you will find that, for these people, the drug is not a business per se. It is a service, relationship, and network, in which they situate their lives and feel comfortable. They are happy with this lifestyle

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[22] An interesting and often discussed example of the traditional physician-patient relationship is *sharei*, the reward for receiving medical care. This is widely considered by outsiders as both distinctive and negative, because physicians should not accept any reward other than their deserved payment for service; however, the Japanese have long taken *sharei* for granted. If we understand this behavior as part of a social network bounded by the spirit of reciprocity, we find it is just a modern variation and extension of this social relationship. The price of a reward may not be crucial, but the social meaning it carries counts. As the same researchers realize, *sharei* is everywhere in medical practice, ranging from a large amount of money to a bottle of salad oil or whisky for a *bonkure* (a traditional Japanese holiday) occasion. The gift-like *sharei*, just as in tradition social settings, smoothes the relationship between the physician as a craftsman and the patient who needs help.

unless someone pushes them to change."

The advent of the modern state imposed an institutional shell on these relationships. As discussed in Part I of this chapter, the NHI unified various welfare schemes and made the state the ultimate insurer for all citizens. Under this patriarchal and nationalist structure, the *amae* tradition was preserved by the practice of community-based care, with a non-profit spirit and an elite-led essence. Two unique concepts are introduced here as salient examples of the government's mentality of intervention. The first is the idea of *yiryohojin*, meaning "juridical person of medicine." Unlike in the United States, it is illegal to operate healthcare facilities on a for-profit basis in Japan. When modern institutions grew too big to be controlled by a single person, corporate-style organizations called *yiryohojin* were introduced to solve these problems while allowing institutions to retain their non-profit essence. This is done even though in reality these *yiryohojin* operate with the same financial incentives as a for-profit enterprise.

Another example is the regulatory restriction on the transfers of *shonin*. *Shonin* are manufacturing approvals granted by the government to local traders to make sure they take responsibility for a certain product. For foreign companies, it is an unreasonable system, since this approval has no relationship to patents and similar proprietary rights held by firms. Even a simple change to a new import requires submission of data and information and the acquisition of a new *shonin*. The revision of the Pharmaceutical Affair Law in 1983 allowed foreign manufacturers to hold *shonin* in their names when importers in Japan imported their products under other certificates called *kyoka*; nonetheless, only firms that previously had either licensed production in Japan or marketed in Japan through Japanese firms holding *shonin* could take advantage of this. In short, as the gatekeeper of its citizens' health, Japan trusts no foreigners. For the MHW, it is entirely appropriate to require the manufacturer or importer, who is within the Japanese jurisdiction, to bear all responsibility for efficacy, safety and quality of a product in order to protect the health and safety of the Japanese people. In that sense the present legislative framework is most efficient, reasonable, and practical for the purposes of protecting the health and safety of the general public.

From this perspective we know why safety, not efficacy, is always the primary concern in Japanese drug regulations. For the Japanese, health is not an ideal status to pursue; in contrast, it is an effort made to compliment the natural course of life. This notion is realized by the state and reinforced through regulations. Sociologist Nakane Chie (1970) points out that Japan as a whole is a segmentary system consisting of clusters of hierarchies, each of which has a clear boundary to its territory (Chapter 3). Thus, in the field of healthcare we see players such as the MHW, JMA and JPMA fighting against

each other over various issues. Nonetheless, the distinctions between their territories, though clear, are dynamic; under the scheme of the Japanese state they are all aware of being members of a group when confronting foreign entities. In this sense the government is recognized as an apparatus for ensuring the absolute safety of its people.

Numerous measures are taken for this purpose, and this has constructed a self-contained system in which risk is out of the question. Every foreign firm should have a "guarantor" in Japan, and everything foreign must be checked by a trustworthy process. It is with a similar mentality that a "Japanese-style" clinical trial is conducted. Before the ICH, clinical trials in Japan were comparative studies with existing products controlled by a few professors at top universities. Cases were collected from various places under the assignment of the senior professor in charge. Although few physicians involved in the trials knew the details of the study, they were concerned for the safety of their patients throughout the clinical trial. On the other hand, the practice of physicians at the trial sites was seldom checked and qualified; the drug companies, though they sponsored these trials and took care of all administrative work, were not allowed to question these physicians, because this would damage their professional dignity and break the trust relationship. In short, it was a system in which trust was placed in individuals, rather than evidence, to ensure the safety of an unknown product.

Finally I shall introduce the way this system evolved. As described in Chapter 2, the FDA elevated its standards for drug approval after several disasters in which mistakes were made and unsafe drugs were approved. It was the same in Japan, where drugs that harmed patients triggered the evolution of the regulatory system. However, there were differences in the consequences that followed. Instead of the higher and tougher standards employed by its U.S. counterpart, the MHW was conservative in the way it improved its regulatory system. First, in terms of administration, the MHW slowed down the registration process for new drugs and added more mechanisms that increased the credibility of each review. Second, it required stricter measures for the reporting of adverse effects. Even so, the patient harm from drugs did not cease. In contrast, according to Takano Tatsuo (1981), from the late 1967 to the late 1970s such cases increased with the increasing consumption of pharmaceuticals. The more cases were identified, the more intensive were the measures that were introduced.

The consequence of Japan's institutional changes, compared to the United States, was the establishment of an institute for monitoring adverse drug reactions. A semi-governmental fund was first founded in 1979 to provide benefits to sufferers of adverse pharmaceutical reactions that occurred in spite of appropriate use of medicines, and this was enlarged into a new institute, the Organization for Pharmaceutical Safety and

Research (OPSR), after two colossal disasters: transfusion-caused AIDS (1985-1992) and herpes drug-caused sudden deaths (1993-1996). For the former, the reform included the research and development of medicines and medical devices, and for the latter, full responsibility for technical reviews of all new drugs. In 1997, the OPSR began new activities around clinical trial guidance and compliance reviews for new drug approval applications in line with government efforts to improve the evaluation of new drugs.

Though it resembles the FDA, the OPSR has a different orientation, as stated in its objectives:

> Relief of adverse drug reactions suffered by providing benefits including medical expenses, personal damage pensions and bereaved family pensions. Enhancement of people's health by providing services for the promotion of technological development and services to improve the quality, efficacy and safety of medicines and medical devices. (OPSR website)

Its effects can be seen on new drug reviews. When user fees were instituted in the United States in 1992, the FDA successfully shortened the NDA review time from twenty-three months in 1993 to fourteen months in 1996. However, the reviewing time in Japan has in fact been prolonged to as long as forty-four months in some cases. The case of Vioxx, as reviewed earlier, exemplifies the necessity of this delay. With its tough safety-checking process, the OPSR can satisfy the Japanese in many ways. Yet it is certain that global companies would prefer that these barriers set by the national government in the name of health and welfare were not present.

PART III
HEALTHCARE IN TAIWAN: POLITICAL PROMISE AND ITS LIMITATIONS

Promoting the Health Miracle, Promoting Taiwan

Just a week before the 2004 World Heath Assembly, the Organisation for Economic Cooperation and Development (OECD) chose "Health of Nations" as the theme of its fourth international forum. Since its launch in 2000, this forum has been a summit that brings together business and labor leaders, civil society figures, government ministers, and leaders of international organizations to discuss key issues of the twenty-first century. This was the first time that it had chosen a topic other than economics. In conjunction with this first-ever meeting of health ministers was the initiation of a three-year project focusing on measuring, analyzing and improving the performance of health systems. All this makes this forum a must-attend event that attracts both government officials and

pharmaceutical industry leaders.

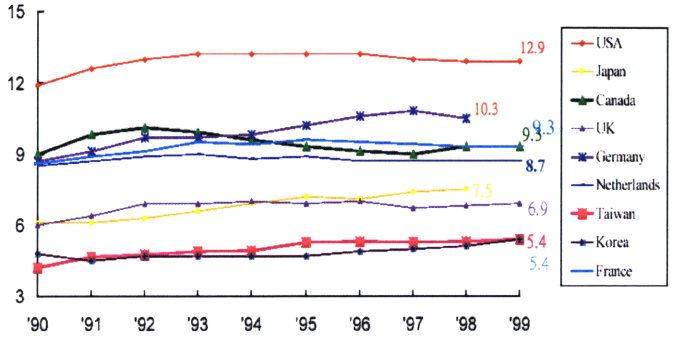
Among the few Asian speakers invited, Kim Dae-jung, Nobel Peace Prize winner and former President of South Korea, was certainly the most well known. He was the keynote speaker addressing "East Asia in the Twenty-First Century." However, it was Chang Hong-Jen from Taiwan's BNHI who provided the forum audience with examples of competitiveness for the future. Indeed, according to the UK-based Economist Intelligence Unit, in 2000, among all developed and newly industrialized countries, Taiwan's healthcare performance was second in quality only to Sweden's. Among Taiwan's healthcare achievements, its NHI program is the most obvious.

Chang appeared on a panel discussion on "e-health," an emerging concept concerning the growing use by patients of the internet to gather information on diseases, medications and treatments. Chang's report, titled "Where Are We in IT [information technology]: Taiwan's National Health Insurance," presented an important aspect of the BNHI's recent project of recording medical information on smartcards (credit card-sized devices embedded with small microprocessor memory chips). He explained, "Using German technology, we implemented a €3.3 billion investment to equip Taiwan's 23 million people and healthcare workers with smartcards. This program has already saved three times the amount invested." As expected, his words moved the audience. Daniel Viel, the director of the French industry periodical *Pharmaceutiques* and the moderator of the panel, suggested afterwards that Taiwan would be the first country that to make such a system workable (Taiwan implemented this system later in 2004). Of course, Chang's presentation style was unforgettable. In his early fifties, Chang had already served as a senior M.D.-bureaucrat, and had a great deal of government experience. He is one of the few Taiwanese medical elites who chose to pursue a career in public health in the early 1980s and one of the promising officials promoted to deal with foreign issues. Furthermore, he is talented at rhetoric. His Harvard-cultivated English nicely matches the sharp ideas he delivers, giving listeners the refreshing feeling of a sip of hot Taiwanese Oolong tea.

Even so, good speeches do not consist of empty words alone. Chang used a half of his presentation to introduce Taiwan's NHI, the fundamental framework that contributes to the success of Taiwan's public health. It is an exemplary combination of a socialistic program with the spirit of capitalism. As discussed previously, before Taiwan's NHI was established, 41 percent of the Taiwanese population was uninsured, and the majority of these were children under fourteen and adults older than sixty-five, whose need for healthcare was greatest. Yet political tensions pushed President Lee Teng-Hui to decree that the NHI begin operation by March 1995; its hasty inauguration followed amidst

chaos and confusion. However, the public warmly supported the outcome of this program. As famous writer and human rights activist Po Yang commented in an often quoted line, it was "the first time in our history that people dare to be sick, can afford to be sick, and be sick without any worries. They can accept whatever diseases that attack them."

Fig. 3.4 Per Capita Healthcare Expenditure as % of GDP, 1990-1999.



Source: Adopted From OECD Health Data 2001.

Indeed, from its birth Taiwan's NHI was the focus of experts in health policy, especially at about the same time that President Clinton's ambitious plan to provide comprehensive health insurance to all Americans lay in ruins. Showing the picture of Taipei 101, the tallest skyscraper in the world, in the title slide, Chang's presentation adeptly pointed out two sources for the increasing rate of public satisfaction with NHI—from 39 percent at the beginning of the program to 60 percent after six months and 70 percent or higher thereafter. Its bold promise of mandatory enrolment (over 99 percent of population was covered) and the wide range of coverage (no gate-keeper system) explain this welcome. On the financial side, the NHI's performance is bright. The national expenditures on health did not rise significantly with the addition of this burden. These expenditures consume from 5.27 to 5.29 percent of Taiwan's GDP, a number lower than many benchmark OECD countries that provide the same kinds of services.[23] This is worth noticing, because we can compare it with the performance of the United States, whose per capita health expenditure is over 2.5 times greater at 12.9 percent, as shown in fig. 3.4. The BNHI seems to have achieved an impossible goal. It claimed that it was able to establish an affordable, universally accessible, high public satisfaction framework with an acceptable quality of care. The story of Hu related at the beginning of

[23] The reason for this lower rate, as Chang summarized, is that Taiwan's NHI exercises a precise mechanism of budget control characterized by cost sharing for ambulatory and inpatient care and drugs, a comprehensive benefits package, and a fee-for-service approach, all under a global budget.

Chapter 1 is testimony to this promise.

Of course, there are many factors that contribute to this. Some factors are institutional, such as the bargaining power of the BNHI in dealing with global pharmaceutical companies, and a free market on the health delivery side that allows competition among health providers. Also there are social and cultural factors in Taiwanese medical practice. For example, Taiwanese physicians work very hard for a relatively low physician's fees.[24] In addition, it is Taiwanese custom for families to provide daily care and company to hospitalized family members. Finally, the Japanese style of doctor-patient relationship can be found on this island as well. The traditional image of physicians is authoritative, and that of patients is compliant; a trust-like relation shapes the needs and demands of medicine. These factors result in a relatively stable environment for medicine, upon which the NHI was put into practice.

Even so, the Taiwanese government plays a role even more crucial than Japan's does, specifically in introducing the NHI scheme, and we see this intention in Chang's presentation. Given the fact that Taiwan just underwent transformations of democratization, the government's ability to execute this program, and its past accomplishments in health policy, show its competence in this area. Chang knew well that from its beginning the NHI was not just a health program but a political promise, leaving behind the previous corrupt regime and building a new statehood on the ability to improve the people's welfare. Yeh Chin-Chuan, the first CEO of the BNHI, emphasized this objective: "We all hope that coming generations can live in a fair and just society, forever free from disease, fear, and menace. This is precisely the objective of the NHI: equal opportunity medical care and the highest ideals of individual and public health for future generations in the Republic of China [Taiwan]." It seemed that Chang was proud of this vision and of the fact that it was triumphantly fulfilled.

However, these accomplishments were not enough. In addition to demonstrating its competence to its citizens, the Taiwanese government was concerned about making its achievements recognized by other countries. In this sense, the NHI was not a political promise but an agenda for health that made Taiwan visible in the global context. Thus, in addition to spreading the "gospel" of the NHI, Chang was an active participant in other presentations. For example, when Per Wold-Olsen, president of Merck's Human Health Europe, Middle East and Africa division, reported that the Internet has been critical in providing up-to-date information to AIDS and osteoporosis patients, Chang added that Taiwan has promoted public education on the control and prevention of AIDS through the

[24] Taiwanese general practitioners usually work more than 12 hours a day, from 9 AM to 10 PM, and see as many patients as possible at a rate of about US$3-10 per patient per visit.

Internet since 1997 and was the first Asian country to use this new technology to publicize medical information.

This desire for recognition was strongly displayed in Taiwanese newspapers, which cast Chang's appearance more heavily with a different focus than the international media. For example, one newspaper emphasized the seemingly minor point that Chang was introduced as being from "Taiwan" instead of "Chinese Taipei," the name used in some formal international settings. Some newspapers focused on Chang's aggressive promotion of Taiwan's success in the past, which seemed irrelevant to his presentation. According to them, Chang reminded the audience of the panel on infectious disease control of Taiwan's pioneering experience in malaria eradication in the 1950s and 1960s, when Taiwan was still a member of the WHO—in 1962, with the help of the WHO and other international organizations, Taiwan claimed to be the first developing country to eradicate this insidious disease. These reports give the impression that Chang was not promoting the NHI but Taiwan itself. As one newspaper report concluded, "In just over a week [at] the World Health Assembly, Taiwan was able to make its presence felt in the development of health systems. What made this global exposure more meaningful was the ministerial meeting, which was held at the same time as the forum."

Confused by the complicated relations between health and politics demonstrated in local media, I talked to Chang Hong-Jen one day after a lecture at the National Yang-Ming University, his alma mater. He quickly clarified two points. First, it was indeed the first time the OECD invited speakers from Taiwan, and it was the Taiwanese government's efforts that made this happened. Because Taiwan's sovereign status is politically repressed by the PRC, the point was not whether its NHI was important enough to deserve a presentation; rather, Taiwan has always been promoting itself to confirm its existence. Chang recalled and explained the process. Although still not a member of the OECD, Taiwan is a specific observer in its Global Forum on Competition. Thus as soon as the Taiwanese government knew the theme of the forum, it strongly sought a chance to present its health insurance program. Because of the OECD's political commitment that no Taiwanese ministers would be allowed to attend the meetings, Chang, who had just left the position of Deputy Director General of Taiwan's DOH, was chosen for this job. "So you see I was there as a compromise," he concluded as if it was nothing special.

The second yet equally important point is the topic Taiwan chose to present. Chang emphasized repeatedly that "political" reasons notwithstanding, Taiwan's NHI deserves global visibility. For him and for Taiwan, international conferences are tricky. They are not places where people meet and exchange ideas. For Taiwan the conference was an

arena and Taiwan was the gladiator; every appearance was a cruel battle to be noticed and remembered. Thus, Chang told me, "You have to be strong on some topics to earn people's attention." Of course, he did not reject the reality that sometimes opportunities for visibility are not given for the best topic or at the best time, yet when they arise, Taiwan has to do its best. "I am happy that I know Taiwan's health insurance is one of the best we can contribute to the world," Chang said. "Taiwan does not have many things that it can share with advanced countries, and I think health insurance is one of them, like our semi-conductors, monitors, and bikes. Therefore, I never feel a lack of confidence when I present our program to them."

Since Taiwan cannot participate as a country, its appearances have to be achieved by individuals like Chang. As a medical technocrat he knows clearly what he is able to present to the world and what is possible. Malaria eradication, though old, is one item that is presentable. However what surprised me was the fact this episode was not only history but are also a vivid memory in people's minds that helped construct the dignity of the state. When asked why he changed his career from medicine to public health, Chang referred this period as the "golden age" of Taiwan's health policy. It was the time when internationally reputed scholar of public health Cheng Kung-Pei (KP Cheng), who was a senior WHO consultant, led this field in Taiwan. "It was a time of victory. We were full of energy and thought that we could do everything," Change recalled excitedly. As he spoke, Chang gave me a sense that what he was talking about was not Taiwan's health but the island itself, making me to think of health policy as something other than simply improving people's health or welfare.

A couple of questions need to be asked: 1) with regard to the issue of drugs, I wonder whether Taiwan has formed as "presentable" a policy in this field as it has in health insurance; 2) concerning individual agency in making heath policy decisions, I wonder what medical elites like Chang think of their careers—do they serve people's health needs as well as the excellence and advancement of Taiwan, and are these goals achieved without conflict? 3) concerning the visibility of Taiwan through its health performance, I wonder if there exists a drug policy that could serve the needs of the Taiwanese people, and what social and cultural factors might limit its achievement. In the rest of this section, I will discuss these issues in order to enrich our understanding of health in Taiwan.

An "Imperfect Copy" of Japan? Taiwan's Drug Industry and its Failed Attempt to Catch Up

Let us return to the social characteristics of Japan's health care. If we look deeply into the social fabric upon which Japan and Taiwan's NHIs operate, we find astonishing similarities in medical culture between the two countries. Like in Japan, Taiwanese physicians dominate all healthcare affairs. They are social elites who have survived a series of cruel competitions starting in kindergarten. Most of them have the same life path. They are born in middle-class families, many of which are physician families, and have received the best education afforded in the areas of their residence. General examinations for entrance into high schools and universities confirm their superior intelligence, and medical schools, as the first priority for those who are interested in medicine and life sciences, are the destination where these talented individuals meet their future colleagues and shape their imaginations about the business they are going to serve. Considered the best on the best, these medical graduates are the expected leaders in medical care and in society.

This idea was reflected in the landscape of Taiwan's medical environment up until the mid-1990s. It was characterized by numerous clinics, which provided a wide range of services to their community. In 1994 there were 74.41 medical institutions for every 100,000 people, and of these about 95 percent were clinics. The real number was larger than this, since small private hospitals were in reality extensions of clinics and controlled by individual physicians. Most physicians chose to establish their own clinics, usually at their homes, after receiving resident training. This type of career is called *kaiyeyi*, literally meaning "doctor with his/her own operation." These small, single-handed clinics spread everywhere, especially in urban areas, delivering the full gamut of primary care service to their neighbors. When physicians felt the need for larger facilities, they enlarged their clinics by adding more beds and spaces in the existing infrastructure. In Taiwan, hospitals are defined as medical institutions with beds, but until recently, clinics were free to add beds to "upgrade" themselves to small hospitals; these "hospitals" are bigger clinics where physician is still the manager.

Another career track for medical graduates was to be hired by hospitals. Unlike with hospitals in the United States, no open system is found in Taiwan. Dual practice in both hospital and clinics is prohibited for physicians employed in hospitals. Lacking a functional differentiation among different types of hospitals and a referral system, most hospitals provide various services, from outpatient care and admissions to intensive care. The salaried doctors working in these hospitals enjoy the advanced facilities and continue their specialty training. However, there are tradeoffs in this pyramid of power/knowledge. Salaried doctors have to keep competing with each other in order to be promoted to higher, more powerful positions. As described in Ho Wen-Yung's popular novel *Baisejuta*

(The Hospital, 1999), the inside of this "white ivy tower" is full of power struggles, corruption and factional fighting.

No matter where these physicians choose to work, basically they are the only people who determine which drugs should be prescribed to patients. Like in Japan, until very recently the separation of drug dispensing did not exist in Taiwan. This was even more so for *kaiyeyi*, most of whose income came from the sale of drugs. In this trading network, we can easily find all the terms and behaviors that have been discussed previously. For domestic drug companies, Taiwan has dealers who bring their products to hospitals and clinics. Other dealers work for foreign companies importing drugs into Taiwan. Alongside the wholesalers, companies have their own sales representatives (*propa*) to promote their products directly to doctors. They do the same as their Japanese colleagues, copying textbooks and papers for junior residents and tending to various personal needs of senior visiting staff.

The direct consequence of this, as we might expect, are seen in drug prices. Due to the single payer system introduced under the NHI scheme, Taiwanese physicians tend to ask companies to lower the prices of their products in order to earn more from the difference between the amount they pay and the amount paid by the BNHI. Taking the antidepressant Sinzac for example, it is reported that a private hospital buys this drug at $2.4 NTD (about $.07 U.S.) per dose, but the BNHI pays $41.5 NTD (about $1.22 U.S.). There are mainly three areas of contention. First, when healthcare providers buy large batches of medication, pharmaceutical companies give them discounts, but these are not reflected in the fees charged to the BNHI. Second, general practitioners provide only basic reports on total pharmaceutical use, rather than case-by-case reports, and there is a gap between the amount paid by the BNHI for daily doses and the actual costs of the pharmaceuticals. Third, healthcare providers use low-cost substitutes but charge the BNHI for the high-cost originals. All this results in a difference even larger than Japan's *yakka saeki* that is criticized as a "black hole" (*yaojia heidong*) of pharmaceutical costs.

The facts reviewed above might give the impression that Taiwan has copied the way Japan developed its medical care, and this is not surprising: it was Japan that built the modern medical institutions in Taiwan during its occupation of the island from 1895 to 1945. The influence from Japan did not wane when the KMT regime took over. Taiwan's foundational medical institutions from before the war continued to be robust and thoroughly disseminated into the Taiwanese's everyday lives.[25] As the table 3.6

[25] For example, Taiwan inherited the Japanese categorization that considers vitamins a drug and not a nutrition supplement. The Japanese historically have used three criteria for regulating vitamins: the shape or form of the product, whether a dosage is specified, and whether the manufacturer makes a health claim.

shows, there are various time lags by which the major reforms were transferred from Japan to Taiwan. If we consider pharmaceuticals as a part of an advanced industry, it is easier to relate this impression to a broader framework, which Ezra F. Vogel calls "waves of industrialization" (Vogel 1991). According to his interpretation, Japan, the "late developer," resumed its industrialization efforts in the first decade after the end of World War II and returned to its former status as the leading power in Asia. Yet over the next three decades, four small, nearby "late late developer" states, of which Taiwan was the leader, made their own breakthroughs. If this pattern of development can be applied in the pharmaceutical sector, we could expect that with a similar medical environment, Taiwan would enjoy the same development as Japan did in the 1960s.

Table 3.6 Major Reforms in the Regulation of Pharmaceuticals, Japan and Taiwan

Year of introduction	Japan	Taiwan
NHI scheme	1961(1928)	1995
Mandatory clinical trials for pharmaceutical products	1968	1993
Good Manufacturing Practice (GMP) validation	1974	1982
Revision of Patent Law from process patent to entity patent	1975	1986
Policy intervention on drug prices	1978	1998
Fund for the relief of adverse drug effects	1979	2000
Approval system for foreign-produced drugs	1983	1991
Dispensation separation	1986	1997
Clinical trail guidelines	1989	1993
ICH guidelines implementation	1991	1998

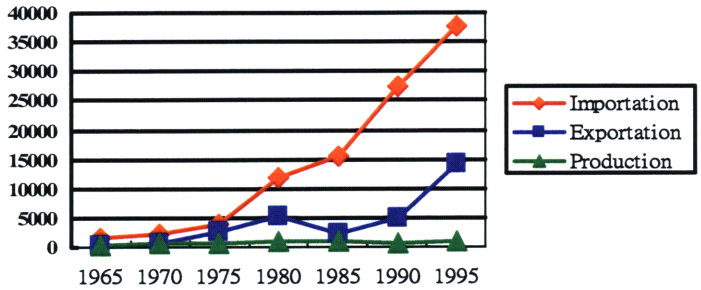
Source: compiled from various sources by the author.

Unfortunately, it did not. Up until the mid-1990s Taiwan was still considered a country of generic drugs. According to the United Nations Industrial Development organization (UNIDO), Taiwan is a category C2 country, recognized as one that produces only generic drugs and not bulk pharmaceuticals (for the details on this categorization,

According to the MHW, if any of these criteria are likely to provide the average person with the understanding at the time of sale that the substance has a medicinal purpose, then it is classified as a drug.

see table 2.2). Its industry is composed predominately of small-scale generic manufacturers, except for twenty-eight foreign-investor plants that formulate and produce drug products. Although in the 1990s there were 406 registered manufacturers (producers of non-Western products are excluded), the number of companies that had passed GMP validation was few.

Fig. 3.5. Production, Exportation and Importation of Western Pharmaceuticals, 1965-1995 (in millions of NTDs)



Source: Adopted from Hsieh 1999, Fig. 3-1.

Considering this structure from a historical perspective, we can identify a three-stage trend in the evolution of Taiwan's drug market and industry (fig.3.5). In the first stage, from the 1960s to 1980, the volume of drugs consumed (indicated by the importation figures) did not rapidly increase compared to the take-off of Taiwan's economy. Although some foreign companies, mostly Japanese ones, established subsidiaries in Taiwan, their numbers were few. The second stage is characterized by the rapid increase in the consumption of drugs in the 1980s. In this decade the drug market increased five-fold. Even so, Taiwan failed to develop any research and development-based companies of its own. Because of the government's policy on foreign investment and technology cooperation, the number of foreign pharmaceutical companies increased form seventeen in 1977 to twenty-eight in 1989. These newcomers were mainly 100 percent Western-owned companies; they soon beat out their Japanese competitors.

Along with the increasing living standard and increasing need for high-quality medical care, the drug market and the amount of importation both grew in the 1990s; yet only foreign companies benefited from this. On the one hand, the implementation of mandatory GMP validation in 1987 eliminated about 200 local companies by badly weakening their competitive abilities. In addition, the surviving firms were not well protected while they updated. In 1991, the government terminated the free importation

policy on drugs. While this policy mainly kept out more foreign companies, it did not protect local ones. Thus only tough drug producers, such as Yung Shin, Tung Yang, Standard, and CCPC, survived competition with foreigners in the big hospital and medical center markets. It was reported in 1996 that only seven local producers had plans for research and development.

What was worse for local companies was finding their niche in this physician-dominated market. Although the Taiwanese NHI scheme has been criticized by PhRMA for its reimbursement policy that favors local competitors—for example, both high and low quality (i.e., not bioequivalent) generics that are reimbursed at prices near the level of products made by research-based firms—the GMP companies know that salaried physicians do not favor the high quality generic drugs made by local companies. First of all, global competitors can afford a greater budget for the promotion of their products, both branded and generic, than the locals can. More importantly, Taiwanese physicians, especially those in big hospitals, simply distrust local products. As elites practicing high-standard medical care, they tend to believe that local products are inferior, and they are willing to "sacrifice" larger profit margins in order to maintain their credibility with patients. On the other hand, although private hospitals and clinics prefer local products, they would only choose those offered at the lowest price for the drugs they need. For them, cost-benefit, not quality, is the first concern. Thus, as Hsieh Shing-yen points out, even after the introduction of GMP validation, some small companies that failed to produce high quality drugs only survived by a low prices and flexible production strategies. They produced various types of drugs, from generic to OTCs, and even herbal medicine, and changed their main products according to the needs of the local market. Thus, in the 1990s some GMP companies collapsed after losing the quality battle to global companies in hospitals and the price battle to small companies (Hsieh 1999: 190-191).

Let me sum up this section. Despite many similarities with Japan, Taiwan's pharmaceutical industry is weak. It has no research-based companies and even the GMP-validated (now current GMP) companies are in danger of extinction. If Japan has successfully created some companies that are strong enough to resist the West, Taiwan, like an imperfect copy, has no idea what to do with itself in the era of globalization.

The Fragile Foundation of Trust and the Role of the Government in Health Policy

In this section I will discuss two interrelated characteristics that made Taiwan develop so differently from Japan in the drug business. The first concerns the social

foundation of trust. Jerry Chiu of Nomura Research Institute explains this difference in terms the different mentalities toward drugs. While the Japanese rely as much as they can on domestic products, the Taiwanese would like to use as many foreign products as possible (*Bio Era* 2002). In other words, the Taiwanese do not trust their products. However, trust is a social behavior. As Fukuyama claims, trust is "the expectation that arises within a community of regular, honest, and cooperative behavior, based on community shared norms, on the part of other members of that community" (26). According to Fukuyama, these norms can be about subjective values such as the nature of God, but they can also be secular ones such as professional standards and codes. If we consider Japan has a group-oriented cultural norm that goes beyond single individuals or the state, apparently Taiwanese customers seek another norm of trust.

In Part II of this chapter I discussed how the Japanese conduct drug business by forming personal networks in which everyone trusts each other. It is the rule that PhRMA's Maurer emphasizes repeatedly in understanding the Japanese market. The "exotic" standard imposed by global pharmaceutical companies, though scientific, met trouble in fitting into this network. In Taiwan we seem to see the opposite. The Taiwanese physicians, though they enjoy high profits from prescription drug price differentials, insist on costlier foreign products. Personal networks may determine their choices of brands (i.e., no brand loyalty), but they would not make them "convert" from foreign products to local ones. It is the same mentality on the patients' side. Unlike the Japanese, who think that Japanese drugs best serve Japanese bodies, the Taiwanese believe that imported drugs are always superior to domestic products.[26] In other words, while the Japanese trust in the social norm of personal networks, the Taiwanese trust the norm of science embodied by "foreign" drugs. If patients receive medicines and find that they are domestic, they will think they are not being well treated or do not have a good relationship with their physician. I once heard a comment in a clinic in Taipei that physicians only prescribe foreign drugs to those they want to have better results.

On the surface this seems superstitious. A former Taiwanese DoH official, a medical elite of course, complained to me that ordinary people have no idea of what "foreign" means. Drugs marked "imported" can be from a wide range of countries, from the United States at the top, to Italy or Spain in the middle, down to Cyprus. He did not understand why Taiwanese drugs, supposedly better than many foreign products, failed to win people's trust. When I quoted studies and public opinions about the problems in the government's practice of GMP validation in Taiwan, he looked irritated and replied:

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[26] For an example of such public opinion, see *Zongguo Shibao* [China Times], March 31 2004.

"Who, who said this? You cannot question our government. We should trust in its ability to protect people's health. Let me say, if a product can show acceptable bioequivalence and bioavailability to the originals, I do not see any reason why we cannot say it is equal to these foreign products." It seemed to this official that it is people's misunderstanding that makes difficulties for the government. Professionally, everyone knows that the government maintains public health, and thus people should follow and appreciate what the government does for them but not criticize it from the outside. This was what he meant.

His response drew my attention to the second social characteristics that makes Taiwan's drug business distinct from Japan's—the role of the government in health policy. According to Fukuyama, Taiwan belongs to the category of Han Chinese societies, which are characterized by their low degree of trust (1995: Chapter 8, 9). In the PRC, Taiwan, Hong Kong, and Singapore, kinship is highlighted as the first avenue of building up trust among people. Fukuyama cites Gordon Reading's observation on Hong Kong business to describe the "radius of trust": "The key feature would appear to be that you trust your family absolutely, your friends and acquaintances to be the degree that mutual dependence had been established and invested in them. With everybody else you make no assumptions about their goodwill" (75). Therefore, it is paradox for these companies to enlarge while maintaining family-style management. It is also a paradox for the governments of these countries to establish themselves as worthy of their citizens' trust. Fukuyama reminds us of the dominant role that the government plays in a low-trust, family-based society in order to allow for large-scale business. The state must step in to help create trust through subsidies, guidance or even outright ownership (30). Nonetheless, Fukuyama does not further question on what social basis the state, an artificial apparatus beyond all blood networks, legitimates control over society.

From this perspective we can see, in terms of the social/domestic and historical/international, profound differences in medical policy between Taiwan and Japan. First, concerning the constitution of society, the difference is nicely captured by the famous author Lin Yu-tang, who comments that Japanese society is like a piece of granite while Chinese society is like a loose tray of sand, each grain being an individual family. Given this, in Japan the state is merely a political shell around this social granite, but in Taiwan the state has to seek external supports in order to exercise its power. From this viewpoint we can see the reason for the Taiwanese's deep distrust in local products. They do not trust the products' quality or the government's credibility. On the basis of their everyday experience Taiwanese people think they know how these drugs are produced and how they pass validation. In contrast, they believe that all foreign products

have passed quality control before being sold and are therefore trustworthy. Apparently, the ICH is the latest reason for the Taiwanese to choose foreign goods.

The problems of trust and the state can be well demonstrated in the case of Japan and Taiwan's NHI programs. In Japan, before the establishment of the NHI scheme, there had already been many self-organized cooperative societies (*kyosaikumiai*) dealing with issues concerning the social welfare of their members. The national program just incorporated these existing civic communities with a light touch. However, this was not the case in Taiwan. Except for some local organizations, such as farmers' and fishers' associations left by the Japanese colonizers, Taiwan did not have any societies of this kind. The Taiwanese, especially people of Hakka ethnicity, have a strong supporting network based on familial ties, but they do not extend this trust to any group outside the family, including the government. Without this kind of institutional support, the social foundation of the NHI in Taiwan is fragile.

Thus we are compelled to ask what makes Taiwan's NHI program successful. Concerning the secret behind the high satisfaction rate and low expense, I argue that for the Taiwanese the idea of risk sharing is foreign. It is the concept of *kinfun* that makes possible the calculation of how much Taiwanese people pay and expect to get from the NHI. Roughly translated as "discrimination," the operational meaning of *kinfun* is holding the best for oneself rather than sharing with others. The reason why the NHI program is welcome is because it offers much greater value than what it costs.[27] The NHI even offers services for those who were residents but have left Taiwan for years, like Hu, whom I mentioned in Chapter 1. As a top BNHI officer once teased, it the Taiwanese are pleased when they can have everything but pay very little for it, which he called the culture of "all you can eat." Quality is not expected. A popular rhyme makes this point: "Taiwan has three 'treasures' [*bao*]: labor insurance [*laobao*], health insurance [*jianbao*], and all-you-can-eat buffet for only $299 NTD [*chidaobao*]!" Sometimes superficial criticisms of the NHI can be heard, especially comparing it to other countries; however, in reality people do not truly expect it to improve because they do not want to pay anything extra. In fact, since the enactment of the National Health Insurance Law in 1994, some clauses concerning the reevaluation and readjustment of the payment rate have never been put into practice due to public resistance (Clauses 19, 20, 21, and 34, for example). As Yeh Chin-chuan comments regarding the definition of Taiwan's NHI, "It is

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[27] It is notable that at the beginning of Taiwan's NHI, many people resisted paying because they thought the program would soon go bankrupt. However, when it entered its second year, these people asked government to add them in and wanted to waive the penalty. Another example is the lowest ever public satisfaction rate reached in fall 2002 (59.7%) when the Minister of Health attempted to raise both premiums and co-payments, which had not been done since the NHI began. See Yeh 2002, pp.17-18.

like a blank check.... Our government is not allowed to tax more, to raise payment, but has to provide the best service continuously. The NHI is an unlimited company that has only obligations but no rights" (2002: 113-14).

Finally, let us discuss the difference between Taiwan's and Japan's health policy internationally. It cannot be understood without tracing how Taiwanese medical elites form a career consciousness about their role in health policies in history. This consciousness can be traced back to Taiwan's past achievements in its "golden age" of public health. It is known that before the abolition of martial law in 1987, Taiwan was an authoritarian state thoroughly controlled by the defeated KMT; interestingly, however, the KMT did not show much interest in public health up until the 1970s. No big projects were conducted and no serious attention was devoted to this matter. In this "hands-off" environment, the people in charge of public health affairs were all Taiwanese medical elites, which was unusual, and their works were to a degree independent from other departments under this regime. While the KMT exploited ever means it could in its fight with the mainland, Taiwan's public health was restored after the various wars it endured by international forces. These institutions, which included the Joint Commission on Rural Reconstruction (JCRR), WHO, UNICEF, and the Rockefeller Foundation, provided almost the entire budget for its health policies before 1972.

I have discussed the international public health collaborations of the early postwar era in depth elsewhere (Kuo forthcoming). The United States first helped Taiwan to build up a network of public health units through which two kinds of policies, problem-oriented projects and public health demonstrations, were applied. In the following fifteen years, various achievements were made: malaria was successfully eradicated in the 1950s along with many other infectious diseases, and the birthrate was efficiently controlled in the 1960s. Alongside these changes, the most important impact of the new public health policies was the emergence of a group of local people, whom I call health technocrats, on the decision-making level. Functioning as liaisons between the U.S. aid institutions and the KMT, these medical elites found a position from which they could maintain their professional pride while fulfilling their passions for social reform after the Japanese colonization.[28] Of course they were practical and loyal, to a certain degree, to the KMT, but at the same time they maintained good relations with U.S. aid institutions and international health organizations, from whom they sought world-class public health for Taiwan. Thus, their attitude toward public health was not one of serving but to rather

[28] It would be interesting to consider this idea as a continuation of the "in-between" identity of Taiwanese doctors after the Japanese colonization. For more a more academic analysis of this identity and its relations with colonial theory, see Lo 2002.

educating their people. Taiwanese physicians had a tradition of leading social movements, but the new rulers simply repressed all possibilities that might threaten their control. After the February 28 Incident of 1947 and the "White Terror" that followed,[29] most Taiwanese medical elites retreated from participating in public affairs. Even so, in the emerging field of public health, they found access to social participation as policy makers.

This consciousness makes these elites' role in the making and execution of health policy tricky. Unlike Japan, where medical policy does not carry much meaning outside of its own field, Taiwanese medical elites expect these policies to be a part of larger projects of social reform. Although it was hard to win local people's social trust and the legitimacy of the ruling power was questionable, Taiwanese health officials shared a patriotic, progressive belief that these policies were necessary to improving the quality of society on the one hand, and to making Taiwan able to contribute to the world on the other. They may not have liked the KMT regime or any political power, but they genuinely thought that they spoke for an ideal Taiwan that would soon be globalized and developed.

Only with this understanding can we understand why Chang Hong-Jen wants to defend the NHI. He told me, "To make Taiwan a developed country we had to introduce [the NHI] anyway. We cannot wait for the people to understand what we are doing." Facing endless criticisms of the NHI, Chang was confident about overcoming people's distrust while imposing regulations that could improve Taiwan's international status. Echoing former DoH director Hsu Tsi-chou's tenet on public health, Chang said, "I do not care if people blame me. My goal for Taiwan is always clear—to be one of the best in the world."

CONCLUDING REMARKS: PROBLEMS WITH DRUGS AND THE STATE

In this chapter we have heard the "local tones" of our non-Western characters. This chapter starts with a quick view of the pharmaceutical markets of Japan and Taiwan from

[29] The February 28 Incident is in fact an uprising that occurred on February 27, 1947, when a police agent attempted to confiscate black market cigarettes from an elderly Taiwanese woman. After an onlooker was accidentally shot to death, a crowd demonstrated next day (February 28) demanding a trial for the agents. The KMT governor-general, in response to their anger over its monopolistic control, chose to declare martial low and enforced curfews immediately. During the following months, many Taiwanese medical elites, most of who were selected to negotiate with the government, were arrested and executed without trials. The initial purge was followed by the time of repression known as the White Terror, which lasted until martial law ended. Thousands of Taiwanese were imprisoned or executed for their opposition, real or perceived, to the authoritarian KMT regime. Even after democratization this is still a highly volatile political issue.

the viewpoint of global companies, and then it turns to considering how they see themselves (their monologue, or "voice one," as discussed in Chapter 1) by introducing their related medical environments and focusing on their different social and cultural backgrounds. I will sum up the issues raised here and mention how they relate to the chapters that follow.

For some U.S. policy makers, Japan is a mysterious state. It has the most advanced agricultural technologies, but it seldom exports its products. The Japanese government is hesitant to open its market to foreign countries, even when the price and quality offered are cheaper and better. U.S. policy makers tend to give the simple explanation of protectionism to this problem. In the case of pharmaceuticals, while Japanese regulators protect their domestic industry, they seem to put their patients in jeopardy by delaying access to the most advanced medicines through lengthened review times and specific requirements for clinical trials.

Although this chapter has pointed out the social factors that should be taken into account in considering Japan's "irrational" behavior, this problem does exist. As Thomas claims, a "new drug lag" is appearing. For example, of the 149 drugs approved in the U.S. between 1992 and 1996, 51 percent were not available to patients in Japan by 2000. Even ordinary Japanese people are aware of this.

For example, in *Say Hello to Black Jack*, probably one of the most popular *manga* on medical issues in Japan,[30] an episode appeared on the issue of drug lag. While treating a woman suffering from pancreatic cancer with chemotherapy, Dr. Saito Eiji, a young intern in the cancer ward, is discouraged to discover that in the repertoire of chemotherapeutic agents effective against pancreatic tumors, only the out-of-date Gemzar (gemcitabine) can be used and paid for by Japan's national health insurance. Doctors know this reality, and the main problem resides not in their ignorance but in the reviewing process for new drug approval. When the astonished Saito asks his adored advisor Dr. Zyoshi Naoki about this problem, Zyoshi tells him the cold facts: "This situation [that only one chemotherapeutic agent is available for a certain cancer] is not restricted to cases of pancreatic cancer. Japan does not recognize many anti-cancer agents that have been used overseas" (fig. 3.7). An even more sad statement follows: "For today's bureaucratic system of the WHLW, these drugs require at least ten years to be

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[30] The "Black Jack" in the title refers to the superhero physician of Tezuka Osamu's classic strip. Created in January 2002 as homage in *Shukan Morning*, this comic has sold over 4.5 million copies in total. Because of its popularity, it was adopted to a TV drama serial by TBS in 2003 and won several awards at the 37th Academy Awards for television programs. Its impact is not limited to the domestic realm. It has been translated into French, German, Chinese, Spanish, and English, and is available to *manga* readers overseas.

recognized."

Fig. 3.7. Scenes from the episode "What's inside a smiling face" (*egao no uragawa*) in *Say Hello to Black Jack*

Source: *Say Hello to Black Jack*, vol.5, Episode 46.

We have learned the advantage of holding clinical trials from the Vioxx case, and now we learn the opposite scenario. Can the Japanese government keep its promise of protecting people's unique health needs while encountering bio-globalization? How can Japan play the game with global pharmaceutical companies by its own rules? On the other side, can global companies be patient and appreciate Japan's custom of medical care? Etienne Labbe, medical director of Synthelabo Recherché Japan, once stated, "For the time being, to overcome difficulties in conducting clinical trials in Japan, one must remember three rules: 1) stay calm, 2) try to understand the Japanese way of thinking, 3) respect the local rules" (1995: 32). However, as we will see in the next chapter, these capitalists did not do so. For them, the ICH has become a battle in which Japan will finally be captured by globalization.

And we turn to Taiwan. As described above, Taiwan does not have a strong pharmaceutical industry, nor does its government have the people's trust. However, as policy makers, the Taiwanese medical elite try to both improve the quality of medical care and educate their people. For them, the state is crucial as a tool for catching up with advanced countries and as a means by which to improve people's lives. The "golden age" of public health, when Taiwan was globally known for its achievements in health care, is the source of their energy.

Ironically, the Taiwanese state is their biggest obstacle. In 1965, the United States announced the end of its financial support to Taiwan. In 1969, the last and the biggest problem-oriented public health project, the Family Planning Program, reached

completion. These factors forced Taiwan to step into a new era of independent health policy. However, just as it began to pursue better public health for itself, other countries severed their international political relationships with the island, ostracizing it from the rest of the world. In 1971, seven months after the Department of Health was founded, Taiwan was expelled from the United Nations. It was no longer recognized as a state; the "golden age" of public health, though great, was gone.

Thirty-five years have passed since then; Taiwan's public health system became strong and independent in its own right. But it had been, and still is, isolated and totally ignored by the world. As we see in Chang Hong-Jen's presentation to the OECD, returning to the "golden age" is no longer a feasible way to improve Taiwan's health status; this action has clear political implications involving rehabilitation of relationships, as a normal state, with others. How do these medical elites "save" Taiwan from this complex situation? How can they deal with the capitalists' requests alone, given that their government is not globally recognized? As we will see in Chapter 5, the ICH, as an international forum, gave these people a chance to speak for themselves as well as for their muted motherland.

PART TWO
Marching in East Asia, Struggling toward the Global

On a hot, humid summer morning in August 2002, I took the subway to Nihonbashi, the heart of Tokyo's business district, to visit the Japanese subsidiary of an American clinical trails services company, which I will call P International. Along with higher technical standards for clinical trials, the rise of contracted research organizations (CROs) responds to an increasing need for pharmaceutical companies, especially those who cannot maintain a big department to deal with the complex requirements for drug approval, to turn to other, specialized firms to provide diverse clinical trials services from laboratory to bedside. The goal of this division of labor is to smooth the entire clinical trial process from beginning to end through the management of placement, principal investigator recruitment and training, contract and budget negotiation, regulatory affairs, coordinator assignments, patient recruitment, data collection, quality assurance, and compliance.[1]

Occupying two floors in a small building in a quiet neighborhood, the world-reputed P International has a quite modest presence in Japan. Before meeting John, the director of this office, I assumed that I find the company headquartered in a huge building named after it, as is the case with many Japanese companies. John received me in a small conference room where he briefed me on his company. He told me that it was a recent decision for P International to open its Japanese subsidiary in 1997. Apparently, the ICH was the reason, and John described its influence. On the U.S. side, the ICH offered pharmaceutical companies a technical instrument by which the Japanese market becomes accessible at reasonable cost. On the Japanese side—more importantly, in John's opinion—the conference presented a platform from which Japanese companies could see and realize the imminent arrival of globalization. The collapse of Japan's bubble economy made the high-level decision makers of the P International hesitant to rush into investment, but the guideline that attempted to bridge racial differences changed their mind. Asia may have been a market for pharmaceutical companies for years, but only after the ICH did it offer an opportunity for CROs, since both sides needed a mediator capable of dealing with local regulations and scientific requirements. Japan, which has the biggest market and the most advanced pharmaceutical industry in the region, was chosen as the beachhead for P International.

Though the above reasoning sounds perfect, it does not match my observations. In fact, I had heard some of the realities behind globalization from a friend of mine, a stock

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[1] The increasing role of CROs in clinical trials outside of the United States, though important, has not garnered much attention in the medical anthropology literature. Although because of volume limitations this thesis must leave it a topic for future study, I recognize Adriana Petryna's pioneering work in this area, which calls attention to the ethical meaning of human subjects in global clinical trails (2005).

analyst who introduced me to John, and John told more over our thirty-minute conversation. The mutual understanding and communication, according to John, do not exist. In contrast to big companies that have their own business partners for this task, P International had hard time finding its niche in this market. Racial difference is still considered an essential factor in drug review; the new guideline does not make it easier, but rather more difficult. John was impeded in persuading local companies to sell their drugs overseas and in conducting local clinical trials under the new guideline to get drugs approved in Japan more quickly. The former effort, John concluded, was hopeless. Except for few big names, such as Takeda and Yamanouchi, Japanese pharmaceutical companies are weak. They fail to produce really innovative products that can pass the global standard, and they cannot compete with other companies in overseas markets. More crucial is the fact that they are not aware of the importance of high-quality clinical trials, which are most important in the drug business. "Japan's companies are never R&D oriented," John said.

On the other hand, the main office of P International does not support John's efforts to establish sites for clinical trials. The cost of doing clinical trials in Japan did not decrease after the implementation of the ICH guidelines. Clinical trials using Japanese subjects are required for most cases and are still difficult to conduct. Having lived and worked in Japan for years, John thought that he knew the problem. He told me that Japan's clinical environment is primitive; clinical trials are still controlled by professors in university hospitals and their methodology needs improvement. Moreover, like foreign pharmaceutical companies in this country, foreign CROs that lack established local connections can rarely gain any ground. Quality does not seem to be the main concern for Japanese companies' choice of partners. John did not say that the ICH or the guidelines were of no importance. "At least a channel is there," he stated. However, a legal channel could not promise any cooperation unless real exchanges of understanding took place. Looking around this office where only six people or so worked, I read a deep frustration in John's face.

To relieve this heavy atmosphere, I switched the topic to other Asian countries. "If Japan is so difficult, why not try other places?" I asked. John quickly answered that for the CROs Japan must be the first in East Asia, since it has the largest national market and is the only country that does not accept clinical data produced in other Asian countries. The conventional logic for other commodities does not apply to drugs, where consumer power matters. For P International, the ideal situation would be to apply Japanese data to other Asian countries, not the reverse. Even so, John felt pressure from the CROs in these countries. John was impressed by the aggressiveness of Albert Liou's Apex in Taiwan and

Robert Teoh's Propharma in Singapore, in contrast to Japan's conservative, mind-your-own-business attitude; the former has established subsidiaries in Korea and the PRC, and the latter is trying to secure a position as the Asian representative for global companies. Recently they both showed strong interest in the Japanese market. It may not be P International's explicit policy to have Asian strategic alliances, but it would not exclude this possibility if the shortest way to doing business in Tokyo had to be through Taipei or Singapore. When the interview came to end, John gave me Albert's contact information and asked if I could visit him if I stopped by Taiwan. "Let me know what he thinks," he said.

On the way back to the other side of downtown, where my host institution was located, I thought of the best way to make sense of the situation John had explained to me. It seemed like Japan had had a chance to meet the global at the ICH but had failed to seize the chance because of its old-fashioned methodology, backward clinical trials environment and bureaucracy. On the other hand, other Asian countries, though not the main target in this global plan, tried to take advantage of the situation and make their markets more appealing. All these dynamics have to be traced back to the ICH and the debate on the issue of racial difference, and this is the starting point of my investigation in the following chapters.

Chapter 4
Weaving Quarrels into Harmony: Presenting Japan in the Bio-Global

> [I]f we pass from the white man to the black or the red man, through all the intermediate variations, it is no longer the difference, but the analogy, which strikes us. ... Thus, the European, with his graceful and elegant forms; the Negro, characrterised at once by the colour of his skin and the peculiar contour of this head; the American Indians, with a red skin and Herculean form, and, lastly, the Chinese, with a yellow tint and oblique eyes; are all derived from the same stock, and form a single chain. ... Such is the solution science gives of this interesting question of the primitive unity of man.
>
> Marcel de Serres (1845)[1]

> The ICH harmonisation process has not only promoted a much more harmonious and productive relationship between MHW and companies of all the three ICH regions, but also helped to improve access of innovative new drugs for patients, as intended, through the effective use of clinical data across the three regions. I hope ICH will continue to work to the benefit of patients worldwide by rationalizing new drug review on the common scientific basis reached by ICH.
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> Osamu Doi (2000)[2]

PART I
COMPETING VOICES/INTERPRETATIONS: A MODERN FORM OF RACIAL DEBATE

Pharmaceuticals and Race: Ambiguity Across Culture and Health

This chapter will look ethnographically at how Japan joined and presented itself in the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), the bio-global stage set for the world of proprietary drugs. In a "slow-motion" fashion, the chapter will first deal with "pre-ICH" negotiations with the United States around 1986 on the acceptance of foreign clinical data, and then with the debate over racial difference with other parties in the

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[1] In "On the Unity of The Human Species", reprinted in *Race: The Origins of an Idea, 1760-1850*, edited by Hannah Franziska Augustine, pp.201-202.

[2] In Nutley ed., "Benefit and Value of the ICH," p.4.

Expert Working Group (EWG) meetings in the ICH from 1992 to 1997. The reason for marking two distinct periods is two-fold. Not only is it essential to capturing the complicated origins of how race is conceived in drug regulation; it also explores two modes of negotiating, one bilateral and the other global. Ethnographic inquiries of voice and setting are foregrounded as necessary to deepen understandings of how Japanese resistance to the bio-global has crystallized around the notion of "race."

This thesis has no intention of analyzing the complicated intellectual background and development of the concept of race, which could be the theme for another thesis. Nonetheless, it shall outline in brief the differences in concerns about race and drugs between Japan and the Western world (i.e., Europe and the United States), to which end I think the above quotation from Marcel de Serres is useful. De Serres, then teaching at the University of Montpellier in France, published a paper in the *Edinburgh New Philosophical Journal* about the possibility of forming a scientific basis for the comprehensive unification of all races into a single species with a single origin. Having mastered comparative anatomy, de Serres tried to provide in this paper a spectrum-like scale by which all variation in the external characteristics of existing races could be located and measured. With skin color, for example, he rejected the notion that variation was due to differences in living circumstances or evidence that different races were different species. The way that de Serres explained the primary unity of human races was a biological, thus scientific, one. He argued that between the second epidermis and true skin there existed a thin pigmental apparatus that determines the coloration of the skin. Thus, different degrees by which this organ develops make distinct the skin appearance of the major races—white, black, red, and yellow. Yet the boundaries can be crossed if we observe all the different races together with the "intermediate" varieties between them. The races can thus be considered a single species consisting of a series of subgroups that have variously tinted skin; on one end of this spectrum stand the "elegant" Europeans and on the other the "peculiar" blacks.

Although this pre-Darwin text made the effort to group all races into one species,[3] one thing we should know is that like all his Victorian contemporaries, de Serres was intensely aware of the differences among humans and intended to argue against those who treated them as total distinctions. In addition, it is remarkable that he reasoned the fundamental unity underlying superficial differences, which latently reflected a parallel trend of biological or scientific racism. Although all human beings belonged to a single species, the reference or measure for differentiating these races was an imaginary

[3] For a concise review of the various ideas about race and racial difference in the early nineteenth century, see the introduction to *Race: The Origins of an Idea, 1760-1850.*

Caucasian man. Although it had been powerfully proven that the different races were fundamentally the same, the possibility of crossing the boundaries between them also created a tension whereby the superiority of a race was not essential and permanent. This kind of racist ideology, as we know, resulted in some extreme forms of such sentiment, including the Nazis' "cleansing" of some "inferior" races during World War II.

However, after World War II, racism as a political concept transformed from a national ideology aimed at justifying superiority in the world to an ideology used by dominant ethnic groups to legitimize their relationships with minorities in domestic affairs. Meanwhile, the role science played was transformed. Instead of proving the biological and intellectual superiority of a certain race, science now tended to hide cultural prejudices with the production of supposedly "objective" knowledge. A clear distinction between "superior" and "inferior" races was blurred and a simple proposition for science and racial politics evolved into a complicated landscape of ethnicity and society. It was no longer proper or politically correct to exclude any ethnic group from the human species; but along with this transmutation of the broad realm of "human beings," new boundaries, categories or standards began to emerge.[4]

Concerned with the entangled meaning of biology and society in an American context, Donna Haraway provides us with a seemingly odd yet powerful frame of mind for appreciating the twentieth century world (Haraway 1997: Chapter 6).[5] According to Haraway, biology or bodily knowledge is not merely a meditative discourse that can be separated from society. Instead, it is "a linguistic sign for a complex structure of belief and practice through which I and many of fellow citizens organize a great deal of life, ... a complex web of semiotic-material practices that emerged over the past 200 years or so, beginning in 'the West' and traveling globally"; it "emerged in the midst of major inventions and reworking of categories of nation, family, type, civility, species, sex, humanity, nature, and race" (217). This argument is followed by three period-paradigmatic configurations in which race, population, and genome figure as "key objects of knowledge" (table 4.1); the first two objects are discussed in this chapter.

The first configuration, from 1900 to the 1930s, is characterized by a clear distinction of human races I have mentioned previously. What is worthwhile discussing is the second configuration, dating from the 1940s to the 1970s. Technically speaking, a

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[4] The same kind of unity/demarcation can be found in the debate over bodily origin and gender difference in Enlightenment Europe. The emerging modern anatomy saw that males and females had the same bodily composition, but men were the only reference. See Laqueur 1990, Chapter 3.

[5] I thank Professor Haraway for reminding me of this historical shift, which helps me to locate Japan's approach to the world of pharmaceuticals. For discussions concerning the "delay" of the genomic step in pharmaceuticals and Japan's intentions toward genomic research in the pharmaceutical field, see Chapter 6.

population differs by one or more genes from other groups of the same species. The gene is a rhetorical idea and a material unit that defines characteristics of a population. The frequency of a certain gene within a population presents the status of population and the possible paths of its evolution; the flow of genes between populations creates population differences that also bind the species together. Following this argument, we find in the medical field a new way or a new language to connect population and disease.[6] Although genes might be too new a tool to widely be used in clinical practice, their functional phenotypes, along with various factors identified by the established epidemiology, served to separate out the characteristics of medicine and society and the dynamics between the two realms. These practices constructed the identity of a population by linking the frequency of some factors to a certain disease; meanwhile, they constructed the identity of a disease by tracing the phenotypes of patients in a certain population.

Table 4.1 Configurations on the Biological and Society in the Twentieth-Century United States

Dates	1900-1930s	1940-1970s	1975-1990s
Key object of knowledge	Race	Population	Genome
Data objects	Tree genealogies, taxonomies	Gene frequencies	Genetic databases
Legal and political documents	Eugenic sterilization laws are passed by 30 state legislatures in the United States from 1907-1931	UNESCO statements on race, 1950, 1951, are written from point of view of population genetics and modern evolutionary synthesis	The Biological Diversity Convention, NATFA, GATT, and the WTO include provisions on patenting biological materials
Status of race as epistemological object in science	Race is real and fundamental.	Race is an illusory object constructed by bad science, while remaining prominent in domains of social	Race reemerging in medical discourse albeit being a hotly contended issue in cultural, political struggles.

[6] Haraway chooses to highlight this period in *Family of Man* as the time when the norms of the nuclear family, heterosexual marriage and gendered labor division were constructed. However, using her perspective, this thesis will try to explore how population as a "key object of knowledge" is related to medical discourse.

		science.	
Paradigmatic technical practice	Craniometry	Measure marker (HLA, ABO blood) frequencies	Genetic mapping
Rhetorics of unity/ diversity	Family trees	Universal family of man	Human Genome Project (HGP) and Human Genome Diversity Project (HGDP)
Ideal of progress	Everything moves in stages from primitive to civilized. Hierarchy is nature at all levels of organization	The universal sharing way of life is at the origin. System management should produce cooperation	Multiculturalism and networking are ideo-logically dominant in sciences, business and liberal political practice

Source: Adapted from Haraway 1997, Table 6.1.

Considering people who take drugs as a whole, race disappears into the notion of population and is reconstructed as one factor, like gender or age, which affects the performance of drug. In the pharmaceutical field, such differentiating within a population in this way is new. In pharmacologist Werner Kalow's pioneering study, pharmaco-anthropology is defined as a branch of clinical pharmacology that deals with inter-ethnic differences in the response to metabolism of drugs. In drug development, racial difference is usually dealt with in terms of categorization into the main races—Caucasians, Asians and blacks.[7] The way to tell the difference between them, as expected, is by frequencies of genetic expression. Kalow claims in a later study that the inter-ethnic differences in drug-metabolizing capacity are now "a well-established fact." The only things scientists need to know are as follows: how frequent or how widespread the genetic differences are; to what extend these differences are of medical and

[7] Pharmaco-anthropology is an interesting field, one in which medical research and social science encounter each other. Yet our concern here is by which route each discipline approaches this field. While many anthropologists stopped pursuing a biological definition for "socially constructed" race, life science researchers such as Kalow claim their authority over this field by using the language of science. However, what is problematic here is how Kalow can make this claim without having an acceptable definition of race. For this reason an STS study on race is necessary. In Chapter 5 of *Emergent Forms of Life and Anthropological Voice*, Michael Fischer has done a detailed analysis of such discourses. This chapter, with the same intention yet on a different trajectory, will try to show how this scientific discourse gets "stocked" in the ICH, forcing it to reveal the cultural assumptions behind it.

toxicological importance; under what circumstances these differences should be considered; and which populations should be included (Walker, Lumley and McAuslane eds. 1994: 28). From this viewpoint, the discussion over race becomes detached from ethnicity. Under the scheme that takes a population as a whole, the term "race" refers to all factors that are clear genetic traits, whereas "ethnicity" encompasses traits linked to other factors, such as lifestyle and environment.

About the same time, some administrative attempts were made to deal with concerns about racial differences. Among these, those taken by the European Community (EC), which hoped to form a single market for pharmaceuticals, were pioneering. Although the establishment of common rules and regulatory requirements created a homogeneous background for this ambition, some biological differences could not be easily reduced. Recognizing the heterogeneous nature of a European population divided into politically determined states, the goal the EC sought in terms of racial difference was an integrated regulatory system in which all clinical data produced could be used across the region by mutual recognition among local authorities. From this viewpoint, race was a different problem. Unlike the pharmaco-anthropology, which considers differences within a drug-testing population, the EC aimed to form an administrative platform by which clinical data from the populations of the member states could be made reliable and thus able to be shared. In this sense, the problem of racial difference is one of identifying if race might be a problem in the process of mutual recognition and if the genetic differences due to race may be ignored. According to Rashmi Shah of the Medicines and Healthcare Products Regulatory Agency (MHRA), UK, concern over racial difference was first raised by the European Committee for Proprietary Medicinal Products (CPMP). Since 1985, the European Cooperation in the field of Science and Technology Research has conducted a project titled "Criteria for the choice and definition of healthy volunteers and patients for Phase I and Phase II studies in drug development," in which polymorphism in drug metabolism is one topic (Walker, Lumley and McAuslane eds. 1994: 22). These attempts resulted in European conference on pharmacogenetics in 1990 as well as a draft on ethnic difference by the CPMP before the foundation of the ICH.

However, the above approaches concerning racial difference met problems in Japan, an Asian country consisting of an Asian race. For global companies, it is a totally exotic population, in terms of both its regulatory system and its racial composition. It is different from the problem of minorities, such as Asian Americans, in the United States, which started to gain attention in clinical trials from 1988 when the FDA requested data analysis for drug efficacy and safety with respect to race and gender (Walker, Lumley and McAuslane eds. 1994: 112). Although U.S. minorities may be genetically different from

Caucasian Americans, basically they live in the same medical environment, such that less than 5 percent significant difference was reported (113).

On the other hand, Japan's drug registration system is different from those in Europe and the United States. Using the United Kingdom as an example, Hirokawa Kazunori and Colin Dollery compare the top fifty drugs in Japan and UK, finding that the differences between the two countries is complicated (Hirokawa and Dollery 1994). The features of Japanese clinical trials, as I have partially discussed in Chapter 3, have much to do with their debatable methods, such as the use of multiple endpoints and vague indices. Apart from these differences, there are also many other social and cultural differences that are hard to reduce to adjustable factors. Most, if not all, differences are the result of a divide between Japanese conceptions of the body and foreign ones. As the authors of the study remind us, "the possibility of genetic differences in sensitivity to drugs should be taken seriously." The bodily sensitivity described here seems to be superstitious, but it is real. For instance, anti-ulcer drugs are widely prescribed under the hypothesis that the gastric mucosa of Japanese is more sensitive and irritable (81). Thus the European approach of forming an administrative platform linking Japanese and Western population s would inevitably turn to an approach based on the racial differences between Asian countries and other countries.

Even so, as discussed in previous chapters, global pharmaceutical companies have to conquer the second largest national market in the world, even though it may be culturally and socially exotic, and they hope to do this as soon as possible. For the reasons outlined above, the issue of race emerged in Japan's relationship to the world of proprietary drugs, and the ICH is the global stage for this drama. The conventional accounts we know from the Western side tend to describe this encounter as a process of political negotiation refereed by science. This is understandable, for the West itself is an area where cultural prejudices concerning nationalism and race have existed for centuries, and the realm of pharmaceuticals is no exception.

Lionel D. Edwards of Hoffmann-La Roche, Inc. recalls his experience of racial and national differences in accepting foreign clinical data in the 1970s, when he was told by a UK regulator that "English data was very good, Scottish reasonable, Welsh data was acceptable, and that U.S. data was not helpful for an English population" (Walker as quoted in Lumley and McAuslane eds. 1994: 10). However, acknowledging that the Western world has had rich experience dealing with such conflicts, Edwards knows this attitude would not be acceptable today, at least for Europe or the United States. In other words, like many Westerners we will hear from in the rest of this chapter, Edwards regards the orientation of ethnic problems in clinical trials as an administrative or even

political one. Assuming the existence of a primary unity among populations (i.e., assuming a heterogamous yet united human species), Westerners like Edwards tend to believe that unless evidence can be found attributing differences between Asians and Caucasians to scientific factors (e.g., genes) or to subjective factors (e.g., life habits, risk factors, or medical practices), clinical data produced in the West should be acceptable in other places in the world. Japan's resistance, according to this theory, is not scientific, but based on a feeble belief in its racial uniqueness.

The above voice, which I call the "Western/capitalist view," is consistent all the way through negotiations before and during the ICH. Guided by this assumption, Western negotiators applied strategies to force Japan to become "enlightened" by scientifically accepting foreign clinical data as well as culturally accepting the idea of the fundamental unity of all human populations (i.e., by being administratively united with other regulatory authorities). Nonetheless, this chapter has no interest in repeating the traditional narrative about how the light of science "penetrates" dark and mysterious Asia and makes it willingly accept; that narrative will merely serve as the background or "counterpart" to this chapter. Instead, in the hope of to portraying the subjectivity of the state, I will explore the process of cultural encounter in a slow-motion fashion, following every step of the capitalists in order to make sense of Japan's responses to the call for unification. The "slow motion" ethnographic approach is necessary because the scientific facts are not in serious dispute, but the explanation and interpretation are.

Furthermore, we must not reject some conventional observations on the frictions between Japan and the United States, such as those by the veteran political scientist Stephen Cohen. Cohen comments on the unfairness that Japan perceives regarding the U.S.'s use of trade protocol Super 301 (for more, see Chapter 3), which allows the United States to perform the roles of prosecutor, judge, jury, and executioner in determining what is acceptable trade behavior by other sovereign states (1998: 47). What I would like to do is to address where these narratives fail to interpret the "deadlock" of a negotiation. As we will see in the debate over racial difference in clinical trials, the lack of interpretive power of discourses relying on Western concepts such as "health" or "consumers' rights" returns us to "old-fashioned" frameworks such as the nation-state from the first configuration Haraway describes when these discourses are applied to how Japan chooses to present itself when encountering globalization.

On the other hand, this chapter has an ethnographic concern that should be taken into consideration about Japan's voice of resistance: that is, the place where the negotiation dialogues occurred. If we read the secretariat of the Ministry of Health and Welfare (MHW) Osamu Doi's praise of the ICH quoted at the beginning of this chapter

carefully, we can see that he does not totally reject globalization; instead, he welcomes it. According to Doi, Japan did appreciate having a fair chance to speak directly to the global, and the rhetoric of public health and science was also good for it. In other words, from an ethnographic point of view, it is necessary to separate the action of Japan's resistance into two parts: the place the debate was conducted and the content of the debate. Apparently, Japan welcomed the former but disagreed with the latter.

In order to tell the difference this chapter is divided into two parts. Part I deals with the "pre-ICH" negotiations, particularly the U.S.-Japan Market-Oriented, Sector-Selective Discussions (MOSS) held in 1986. The second part deals with the EWG meetings on racial difference, the so-called "E5 working group," and the making of the E5 guideline. This chapter not only describes two periods in which this problem was formulated; it also shows two modes of negotiation, with a shift in scene from a bilateral meeting to a global conference. The originality of this ethnography thus not only resides in its empathy in listening to the non-Western voices, but also in its awareness of the situation in which voices were presented and heard.

Echoes of the Past: The Dualistic Nature of Differences in the U.S.-Japan Context

This section will discuss the cultural background of the "pre-ICH" dialogue over racial difference. It starts with a conversation disclosed by *Yakujinippo* [Pharmaceutical News] on October 5, 1998, which featured Doi Osamu and Professor Mizushima Yutaka of St. Marianna Medical University. In this conversation both individuals reviewed the foundation of the ICH, its impacts on Japan's clinical trials, and how Japan confronted the wave of internationalization. However, what caught my attention was the historical analogy the newspaper used in the title of this conversation: "ICH is the 'Black Ship' of Drug Regulation." The symbol of the "black ship" is commonly used in many references to globalization and carries multiple meanings, as Mizushima pointed out: "Perhaps it [this analogy] is a bit over used, [but] the ICH, so to speak, is like the black ship..., thus it is unavoidable to use a universal standard for the sake of ethical concerns as well as scientific requirements in clinical trials." The black ship metaphor refers to the arrival in 1853 of four American warships in Tokyo Bay. The ships were led Commodore Matthew Calbraith Perry, who became the first foreigner to open Japan to trade after a 250-year isolation.

In fact, Mizushima's statement is not alone; the analogy of the black ship is often seen in reports about globalization and the ICH. The meaning that this analogy delivers is

manifold. On the metaphorical level, it indicates a situation in which contact is unavoidable. As read in this conversation, Japan was hesitant to change. Doi remembered that when he brought the idea of Japanese participation in the ICH back, globalization was a "taboo-like" issue. It seems that the ICH pushed Japan to face globalization unwillingly, but this is not true. It does not mean that before the foundation of the ICH, Japan did not import any drugs from foreign countries. According to a survey by *Yakujinippo*, in 1984 Japan imported 1.77 billion yen worth of drugs from the main global producers, an amount that is small compared to other sectors, yet still significant. The analogy should be considered as dramatizing the point where Japan had to start to deal with globalization: to resist it or accept it.

In the context of global commerce, the analogy of the black ship implies an origin which results in this situation. Stephen Cohen has pointed out that this common rhetoric is widely used in describing U.S.-Japan trade. Remembering Commodore Perry, Japan envisioned the reappearance of the "black ships" when the United States requested a more open market in the 1980s and accused the U.S. government of not understanding how to master its market (Cohen 1991: 194). In this sense, the ICH seemed to be another American ship, one that would open up Japan's drug market. The United States was both the cause of and the obstacle to globalization. On the one hand, it catalyzed Japan to face the world, yet on the other hand it limited the way it was possible to deal with Japan.

It is interesting to look at Japan's two-stage encounter with globalization via the black ship analogy. In fact, the historical contact between the United States and Japan has been heavily dramatized and reconstructed by the way that the Japanese have formed their image of the United States. Let us just take this one example to see how this contact is told and retold. It is said that Perry brought a letter from U.S. President Millard Fillmore to the Emperor of Japan, hoping Japan would agree to open certain ports to American vessels so that trade could begin. However, in one of the new history textbooks for Japanese junior high school, this story has had a new focus added to it: a passage saying that the Shogunate could not reject this letter because it was threatening. It is said that along with this letter, Perry handed Japan's emissaries two white flags and a letter of his own stating that "We are ready to attack you in case you fail to open your doors to us, and victory will surely be ours. We are, however, willing to make peace with you, if you raise the white flag indicating surrender." The textbook passage concludes, "Such a threatening diplomacy, forcing a country to accede to demands by use of armed force, is known as 'gunboat diplomacy,' an approach frequently resorted to by the Western powers

in their dealing with Asian countries."[8] Though interesting, according to historians Masato Miyachi and his colleagues, the above interpretation is weak on the historical source it uses (2001: 46). I am not an historian on Japan or diplomacy, nor do I have any intention of entering the debate about whether Parry's letter really existed. But what I want readers to pay attention to is the way Japan formulates its past experience about rejoining the world: namely, why it suffers and casts the United States as its unfriendly mediator. The history may be adjusted, but the intention is real.

On the other hand, the United States has its own historical and racial locus by which it formulates its image of Japan. This past, as historian John Dower nicely traces in his *War Without Mercy* (1987), is the Pacific War from 1941 to 1945, an episode in which both the Americans and the Japanese racially subjugated their respective enemies. Dower reminds us that for Americans the image of Japanese brutality and bestiality was closely related to Japan's actions in the invasion of Asia, such as massacres in Nanking and Manila. Among Americans these accounts seemed to insinuate "the field day they'd [the Japanese] enjoy if they marched through the streets of Washington" (17). Of course, Americans tended to racialize this war, and through this process they treated the Japanese state and the Japanese people as two sides of the same coin. The legacy of this treatment has survived into the postwar period; Japanese nationalism became the starting point by which the United States constructs its image of Japan.

Here is one example, taken from an issue of *Time Asia* on August 16, 1999. This issue, titled "Japan Returns to Nationalism," shows on its cover a young Japanese man decorated with *hinomaru* flags, his mouth open as if he is shouting to the world of Japanese nationalism's resurrection. Articles in this issue successfully delivered the patriotic, though selective, picture of the Japanese in the era of globalization. By singling out recent "right-wing" phenomena, such as the wish to take back territory lost to Russia, commanding schoolchildren sing the national anthem that honors the Emperor, rearming the country's military force, and, most importantly, revising the "peace constitution" created during the American occupation, the issue presents an image that readers can easily relate to the military nationalism of World War II. According to *Time Asia*, the unsettling reality that nationalism is on the rise again, as suggested in a comment by a political analyst: Japan "will make laws that enable them to do whatever they want to do" (18). Some borderline-racist arguments can be found to support the above observation.

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[8] *Atarashii rekishi kyokasho* (New History Textbook), p.176. Quotation from an alleged letter of Commodore Matthew Calbraith Perry, translated by Miyachi et al. in Miyachi et al. 2001: 44.

The fiery writer and mayor of Tokyo Ishihara Shintaro's *Japan That Can Say No* series[9] is one of the symbols of these right-wingers. Also heavily cited is the recent series "'Haughtiness Manifesto" (*gomanizumu sengen*) by cartoonist Kobayashi Yoshinori.[10] The magazine quotes Kobayashi's famous comments on the actions of Japanese soldiers in World War II, which is regarded as politically incorrect: "Let's be proud of our grandfathers who fought against white imperialistic Europeans and Americans" (17). It is understandable the issue of history textbook; any attempt to downplay the violent behavior of the Japanese military would be interpreted as a recurrence of nationalism and therefore harshly criticized.

The contrasting images that Japan and the United States have constructed of each other from histoircal memories resemble the dualistic nature of Japan's worldview. It is seen in *nihonjinron* (theories of the Japanese), which characterizes Japan as "the self" and foreigners or the West as "the other." As Peter Dale points out, it is a "dialectics of difference" and is articulated in the form of the uniqueness of the Japanese (1986: Chapter 4).[11] The Japanese have constructed an image of the West so as to clarify the boundary between "Japanese-ness" and "Western-ness." Like the arrival of the black ships in the past, the West and the United States are dangerous because they bring contact that would force Japan to accept foreign standards that do not fit the people well. The uniqueness of the Japanese can only be justified by this dualistic order supported by cultural and historical manipulations.

However, it is equally important to note the same tendency in the United States, which has created a stereotype of Japan that is essentially racial. The U.S. tends to ignore Japan's intentions and self-conception and interprets everything as military nationalism. The interpretation of *nihonjinron* is an example. Despite noting Japan's nationalist threat,

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[9] The first book of this series is *"No" to Ieru Nihon* (A Japan That Can Say No. Tokyo: Kobunsha, 1989), coauthored with Morita Akio. This book was followed by three others by Ishihara and other authors, *Soredemo "no" to ieru Nihon* (A Japan That Can Still Say No. Tokyo: Kobunsha, 1990), *Danko no to ieru Nihon* (A Japan That Can Absolutely Say No. Tokyo: Kobunsha, 1991), and *Amerika sinko wo suwate yo* (Dumping the Myths on America. Tokyo: Kobunsha, 2000).

[10] Kobayashi began to serialize *Gomanizumu sengen* or "*Gosen*" in 1991 in the weekly magazine *Spa!* The cartoon boldly defied taboos in Japan and established his Kobayashi's fame as a critic. The title of the series, "Haughtiness," is from his final remark—"can I be haughty?"—in every episode, and the first special edition was *Sensoron* (On War), published by Gentosha in 1998, made him a national phenomenon. After that about every year he produced a special edition of *Shin gosen*, such as *Taiwanron* (On Taiwan, 2000), *Sensoron 2* (2001), *Sensoron 3* (2003), and newly published *Okinawaron* (On Okinawa, 2005).

[11] As Dale points out, from this viewpoint, the world consists of two parties—Japan and everyone else— that are always comparing themselves to and mimicking each other. A list of comparisons by which Japanese uniqueness (as well as the homogeneous "other") is characterized, ranging from geographical conditions to intellectual style or mentality, can be found in Dale 1986, Chapter 4. In short, the two parties have nothing in common.

in this same issue of *Time Asia*, Japan expert James Fallows ignores the sensitivity of the Japanese's notion of self by dividing *nihonjinron* into two opposing schools of thought. One side is formed by a large outpouring of books and articles, almost all in Japanese, about the reasons that Japan and Japanese people are unique. On the other side are a smaller but more splenetic stream of rebuttals, mainly written by foreigners who have read *nihonjinron* and mean to expose its lunacy to the outside, English-speaking world. In short, assuming a universal standard for judging all people and cultures in the world, the United States tends to polarize its relation to Japan, casting itself as "rational" and the other as "subjective."[12]

It is not the goal of this thesis to analyze whether the United States employs "gunboat diplomacy" toward Asia, nor do I presume to know whether Japan wants to resume the military nationalism by which won it an empire, a humiliating defeat and occupation. I do want to point out the dualistic nature of the encounter between the two countries. For Japan, the encounter forces this Asian power to remember the hostile arrival of the American ships, which symbolized the presence of "the other" and led to an unwilling opening to the world. The two-stage process of globalization is thus predestined. For the United States, it was an odd meeting with a country that was both familiar and strange to it. Japan did not follow any rule the United States applied to other countries, which were either too similar or too weak for any differences between them to be noticeable. Japan was an enemy, it surrendered, and it is now a political partner and an economic competitor; however, it is sill a mystery rather than a simple portrait of nationalism.

Unavoidable Encounter and Circles of Negotiations

The "pre-ICH" encounter of Japan with the global took place under the structure of MOSS. Part of the reason for these talks was commercial conflict in the mid-1980s, as reviewed in Chapter 3. Following the discussion of the dualistic nature of the dialogue,

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[12] A typical interpretation of this division is Stephen Cohen's *Cowboys and Samurai* (1991), which portrays samurai and cowboys as characteristic of the fundamental differences that divide Japanese and Americans. Cohen traces Japanese behavior back to its pre-modern period, when "the samurai of the Tokugawa era seem to have been transformed into the new breed of managers and bureaucrats who guide modern Japanese corporations and government agencies" (73). In the same manner, he portrays America this way: "It is the youngest of the major industrial countries. It is one of the few countries born out of genuine revolution. It is the only country in the world to be formed by people from every other country in the world; one of a handful of countries without feudal or class patterns, having been founded by immigrants who came overwhelmingly from the lower classes" (98).

this section will focus on the political background on which the dialogue took place and the conventional accounts of these negotiations.

In his famous book *A Japan That Can Say No*,[13] Ishihara Shintaro suggests a bilateral talk exclusively between the United States and Japan—which he calls the "G2", following the formulation of the then group of seven (G7) structure—so that a frank dialogue can be established along with a clear Japanese identity.

> When there are only two parties meeting, Japan will have no choice but to say "yes" or "no" without resorting to gray areas. Japan must be equipped with logic and reason whenever it says "no." Best of all, by holding a G2, Japan will only have itself and the U.S. with which to be concerned, making it easier to stick to the "no." (Chapter 11)

When stating this, Ishihara assumed this ideal situation was yet to come. However, this was not quite true. The political atmosphere of the 1980s had stimulated such a meeting. It was created by former Prime Minister Nakasone Yasuhiro, who aggressively dealt with the United States and established good relations with then U.S. President Ronald Reagan. Thus it was expected that an exclusive conversation between these two world powers would take place sooner or later under such a "G2 establishment" (*jitsu taizei*).

However, having a conversation does not mean that will be fair. Apparently, both sides thought this relationship was not fair to them. On the Japan's side, Ishihara charges that during the "Ron-Yasu" (Ronald and Yasuhiro) era Nakasone behaved like a "lowly yes-man" to Reagan's suggestions on topics ranging from global deployment to economic policies (Chapter 9). A negative term, "G2 problem" (*jitsu mondai*), was coined to indicate the possible frictions in this relationship, the most noteworthy example of which is perhaps the yen-U.S. dollar agreement of 1987, in which the yen was forced, through bilateral U.S.-Japan talks, to a value of 140 yen to one dollar, as compared to 264 yen to one dollar in 1985 (for details on this valuation, see Funabashi 1992, III-3).

The United States was not satisfied with these negotiations either. As mentioned in Chapter 3, it was threatened by Japan's sky-rocketing economy and frustrated in its efforts to conquer its market. To the Americans, Japan always seemed to protect its producers rather than its consumers; it has never conformed to the free-market, consumption-oriented model. These negotiations did not bridge the gap in U.S.-Japan relations, which, as Cohen concludes, got even wider over the last three decades: "In 1969, the United States was annoyed with Japan's import barriers, export aggressiveness,

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[13] Here I use a complete yet unofficial English translation available on a website. It was done back to 1989 shortly after its original was published.

and $1 billion bilateral trade surplus with the United States. In 1997, the United States was annoyed with Japan's import barriers, export aggressiveness, and annual bilateral trade surplus in the range of $50 billion" (1998: ix).

From these long-existing problems and failures of negotiation, Cohen summarizes a model which he calls "negotiating in circles." Based on the assumption that Japan's hesitancy toward the global takes the form of protectionism, Cohen describes two scenarios for negotiating patterns—or two strategies that Japan employs to beat the United States in U.S.-Japan negotiations: the United States protectionism version and the import market access version (1991: 151-152). According to the discussion in Chapters 2 and 3, the issue of pharmaceuticals belongs to the latter. Its scenario, modified from Cohen's model, goes as follows:

Scene 1: The Pharmaceutical Research and Manufacturers of America (PhRMA) complains bitterly of the lack of reciprocity in Japan's trade practices. Overt barriers, cultural practices, industrial structure, and dirty tricks are cited as restricting market access.

Scene 2: The United States Trade Representative (USTR) applies pressure, saying that grave consequences are in store for Japan if it does nothing to correct its trade disequilibrium by allowing other countries to sell more to it. The Japan Pharmaceutical Manufacturers Association (JPMA) complains of the reappearance of "black ships" and accuses the United States government of shamelessly and misguidedly meddling in Japan's domestic affairs.

Scene 3: The "internationalist" MHW quietly thanks the Americans for the vivid threats, saying that they are useful levers in internal debates. They point out to the Japanese protectionists that export growth is at risk if no international standard is set. The MOSS negotiations begin; the Americans are advised that they need to invest more energy in understanding the Japanese market.

Scene 4: Negotiations between Japan and the United States face problems. Other issues are brought up and no concrete agreement is reached. The Japanese definition of implementation bears little resemblance to the United States definition. There is almost no measurable subsequent increase in U.S. market share.

Scene 5: The PhRMA expresses dismay that Japan did not truly obey the spirit of the agreement to liberalize the market. The MHW responds that it should respect local customs. Private lobbying continues.

Scene 6: After a brief interlude, both sides express dismay at the continued enormity

of the bilateral trade surplus. Return to Scene 1.

It seems like there is no way to break the circle; however in practice it is possible. Karel Van Wolferen's *Enigma of Japanese Power* is one book that provides a solution to this problem. According to Van Wolferen, Japan would never accept a deal provided by a weaker party. With Japan's stubborn political system, free talk is impossible. Only by showing dominance can the United States force Japan to accept a request or at least make some compromises. This book's popularity is apparently understandable, because it serves the agenda of powerful lobbyists who believe that the U.S. should retaliate against Japan's economic success. "It has nothing to do with threats," said a Pfizer Japan officer. "We just wanted to sell our goods to this country. We want to play a fair game."

The practice of the MOSS negotiation should be understood by this logic. As Cohen points out, the advent of MOSS is "the most important development in the bilateral dialogue" at this moment (1991: 43). The purpose of this new negotiating format was to avoid tedious case-by-case complaints and vague accusations on issues of principle. The MOSS talks were designed to address all identifiable, particular Japanese trade barriers in areas in which American businesses were thought to be internationally competitive and yet unsuccessful in Japan. The public watched the progress of the talks closely, and many writers addressed its impacts (for the U.S. side, see Cohen 1991 and 1998, McCraw 1986; for the Japanese side, Masuda and Tsuchiyama 2001, Funabashi 1992, Tanaka Naoki 1989, and Takenaka 1991).

The MOSS talks limited to four sectors: telecommunications, electronic products, pharmaceuticals and medical devices, and forest products. Even so, the talks were difficult. In late September 1985 an interim report on MOSS talks results was announced, but it reportedly took four days of nearly round-the-clock negotiations before both sides were willing to sign the report (*Nihon Keizai Shinbun* (*Nikkei*) [Japanese Economic News], October 2). During the talks, the U.S. government had warned that if satisfactory progress was not made, they would retaliate using Article 301 or some other means. It also indicated that it had new items it wished to have addressed in the MOSS talks in 1986. Talks in the electronics and telecommunications fields had positive effects. The forestry products negotiations were a total standoff. The MOSS talks concluded in August 1987, having achieved only modest Japanese concessions, mostly in the form of tariff reductions and some relaxation of regulations.

Some policy analysts saw the results that the MOSS talks achieved positively. They believed that MOSS had successfully forced Japan to face its excessive exports to the

United States and its restricted domestic market. Although ultimately the negotiations did not achieve the $1000 million rise in imports expected by the U.S. side, it at least established a precedent for effective negotiation that could be followed up.

In fact, the United States did follow up as soon as it finished the first round of MOSS. It said that Japan had not delivered on what it had promised. MOSS did yield some progress, but not enough. Some critics did not give any credit to the meetings. As Cohen cites, some U.S. negotiators' frustration and cynicism toward Japan were expressed in the joke that "MOSS really stood for 'more of the same shit'" (1991: 43). This seems to be a consequence of the United States' disappointment with Japan's repeatedly broken promises about opening its market. The Maekawa Report,[14] for example, released in 1986, presented a typical exercise in Japan's promise making. The basic policy suggested in the report was to transform Japan from an exporting nation to an importing nation, but the report was severely criticized for its lack of specific, concrete measures.

Based on this, the United States again brought out the threat of trade retaliation. On May 25, 1989, when U.S. Trade Representative Carla Hills, in accordance with Section 301 previsions, singled out Japan, Brazil, and India as having engaged in unfair trading practices, U.S.-Japanese trade relations came to their toughest point. After several clashes, the so-called Structural Impediments Initiative (SII) was created to save the fragile relationship. It was a breakthrough, as Cohen recalls (1991: 49). Five negotiations were held from September 1989 to June 1990,[15] and Japan was dropped from the list of countries being sanctioned by the United States. In the 1990 report on U.S.-Japanese relations by the Edwin O. Reischauer Center for East Asian Studies (1990), subtitled "A new world environment; New questions," trade friction was still the most important issue for both countries; the MOSS negotiations was nothing but an episode in the long march of the United States to the Japanese market.

Pharmaceuticals in the MOSS Negotiations: Similarities and Differences

Strangely, the settlement whereby foreign clinical data were accepted does not

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[14] The full title of the report is "Report of the Economic Structure Adjustment Study Group for Integrating the Economy into the World." It was prepared by a study group led by Maekawa Haruo, then the Bank of Japan Governor, after which it was informally named.

[15] The first round of negotiations was held in September and November of 1989 and February of 1990. The results it achieved are summarized in an interim progress report released in April 1990. Before a final report was signed and released in June 1990, two more meetings were held. For a brief summary and a short commentary on what SII achieved, see SAIS 1990: 44-46.

follow any of the scenarios portrayed in the previous section. The first contact between Japan and the United States concerning the clinical standard for pharmaceuticals and the issue of racial difference was initiated during the MOSS talks, according to Naito Chikayuki, one of the key persons in charge of creating the Japanese guideline for clinical trials.[16] However, it was neither front-page news attracting public discussion nor a controversial issue in the related literature about U.S.-Japan trade friction. Like other sectors, the talks about pharmaceuticals and medial devices stared in January 1985. But despite the newness of the issue when it was first slated for negotiation, it only took nine months to reach an agreement.

This does not mean that issues in the pharmaceutical sector were simpler than those in other sectors. In fact, as discussed in Chapter 2, the drug industry is a rather more complicated issue for negotiation than other industries because it involves both equipment in factories as well as human subjects and lives. However, we also find some similarities between pharmaceuticals and other sectors. For example, under the scheme of standardization of products, the same rationale applied to settling concerns about racial difference can be seen in the negotiations on telecommunication equipment. The Japanese agreed to accept the results of certain equipment-testing procedures conducted in the would-be exporter's country and to set operating standards for telecommunications equipment more closely comparable to those in the United States. The same kind of negotiation was also seen in the area of wood products. The problem with pharmaceuticals and medical devices was whether foreign data was acceptable in Japan or if a universal standard was possible. Even so, an agreement was soon achieved.

Some believe that the reason for this quick settlement was the fact that Japan imported a relatively large amount of drugs. *Nikkei* predicted before the negotiations that "since Japan's deficit on pharmaceuticals is so large, basically the MHW should not be a spark for the Japan-U.S. economic frictions" (January 26 1985). Since Japan had imported pharmaceuticals from foreign countries, the agreement would not contain any numerical targets that might create penalties, a practice common in negotiations in other sectors.

Basically this observation was correct; however, I would like to point out that the Japanese delegation had an important factor aiding this success: this was the first time the MHW was formally involved in this kind of negotiation. Certainly it was not unusual to invite Ministries other than the Ministry of International Trade and Industry (MITI) and the Ministry of Foreign Affairs (e.g., the negotiations on rice import). However, it was

[16] For brief background on MOSS and its relationship with the acceptance of foreign data and racial difference, see Naito 1991, esp. 188-189.

unusual not to have the MITI as the "quarterback" in this negotiating team.[17] Unlike the U.S., which organized the standard "triad" team of Treasury Department, State Department, and U.S. Trade Representative for commercial negotiations, on the Japanese side the MITI was actually absent.[18] In short, this time the Japanese did not want to deal with business but with health.

This unusual scenario made the negotiation on pharmaceuticals take a direction unfamiliar to those who were acquainted with Japan-U.S. negotiations. For example, Stephen Cohen has pointed out that the U.S. team usually behaves like a "three-way cleavage" (1995: 196).[19] This time, however, the chorus played in unison. The Treasury Department was the choir leader and the team fully reflected its will to open Japan's market based on standard consumption-oriented rhetoric, as discussed in previous chapters. On the other side, detached from the conventional image of Japanese aggressiveness, the Japanese team led by Vice Minister of the MHW Yoshimura Hitoshi was self-controlled. It accepted almost all the suggestions from the U.S. side, including approval and licensing processes, listing, and other administrative issues. As reported, among the topics discussed, particularly good progress was made in the area of pharmaceuticals and medical equipment. This was the only sector that reached a concrete agreement. What made pharmaceutical issues easier to resolve, in my opinion, was mainly the nature of the MHW bureaucracy. It is not an institution for commerce but for health. For the MHW, the standard of pharmaceuticals was a problem of science and could be solved scientifically.

In this atmosphere the issue of the acceptance of foreign data was introduced. Although the related regulations had existed since 1976 and three modifications had occurred in 1980, 1982 and 1983, it was acknowledged that the range of acceptance was quite limited (only phase I data under some restrictions). Thus Japan did not accept any clinical data made in other countries before the MOSS talks; all clinical trials had to be performed on Japanese subjects before a drug was allowed to be marketed in Japan, irrespective of its testing history in other countries.[20]

The U.S. team explained two market effects that these testing requirements caused.

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[17] According to the *Report on Market-Oriented, Sector-Selective (MOSS) Discussions*, the Japanese team was led by the MHW with the assistance of Ministry of Foreign Affairs, Ministry of Finance, and the Embassy of Japan to Washington, D.C.

[18] An OPSR expert told me that it was the Cabinet that referred the request to the MHW. It was an unusual arrangement and it surprised the FDA when they were contacted by the MHW for discussion.

[19] Funabashi adds in his analysis that the Whitehouse was an additional factor that shaped the U.S. policy of foreign business and frictions. See Funabashi 1992: 79-87.

[20] For details about the drugs abandoned or suspended during their applications, see Naito 1991 (1985): 482-483.

First, the extremely costly duplication of testing placed a burden upon foreign firms that their domestic competitors in Japan did not have to face. Second, duplicative testing in Japan delayed product marketing. On Japan's side, the fundamental concern was the difference between the Japanese and Caucasian Americans. The MHW expressed its worry that a lack of Japanese clinical data might endanger drug users. Even so, conversation was still on the right track; no one drove these disagreements in the useless direction of arguments over capitalist hegemony or nationalist resistance. In the first vice-ministerial meeting of the negotiations, held on March 12, 1985, the U.S. side suggested that waivers for local clinical trials be given to those drugs that would not be impacted by racial differences.

As the negotiations moved from commercial question about waiving clinical trials to the matter of which trials related to racial difference, they became easy. The Japanese had assigned a group of scientific experts to study this matter under the heading of "testing and test data" before the negotiation.[21] Expert-level discussions between the MHW and the FDA regarding each nation's policy were held on May 26. With some conditions, the MHW agreed to accept foreign clinical test data for regulatory approval of pharmaceuticals, medical devices, and in-vitro diagnostic reagents (*Yakujinippo*, July 4 1985). The results were as follows:

1. With regard to pharmaceuticals, foreign clinical test data will now be accepted for all examination/testing requirements except for the following three items where there are immunological and ethnic differences between Japanese and foreigners: comparative clinical trials; dose finding tests; and absorption, distribution, metabolism, and excretion tests.
2. Foreign clinical test data will now be accepted for in-vitro diagnostic reagents except those with new parameters (i.e., those that measure an entirely new substance as a diagnostic indicator), and those in which immunological reaction problems could occur with the materials to be tested.
3. Foreign clinical test data will now be accepted for medical devices, except those implanted in the human body and those affecting organic adaptability. (14)

The above resolution was approved by both sides in June 1985 talks in Tokyo. The relevant regulatory action taken was Notification No. 660 for the "Handling of Foreign Test Data for Pharmaceuticals, etc.," dated June 29 and effective July 31, 1985. It was one of the first and fastest-resolved issues in this set of negotiations.

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[21] This was "The study group for the evaluation of the foreign clinical trial data," led by Naito Chikayuki, then the director of Department of Internal Medicine, Tokyo Teishin Hospital, in 1983. The evaluation report was released in May 1985.

Under overwhelming politico-economic pressure from the United States, the case of pharmaceuticals seemed to present a "win-win" situation for Japan, allowing the country to make its first step toward the global. Earlier the United States had changed its regulations to allow non-U.S. data as the sole basis for approval; Japan reconsidered now the possibility of accepting foreign data based on this.[22] It might be said that medicine is science, separable from politics, but in fact it was not that simple. Reading the notification carefully, we can find the cultural boundary that the MHW drew for this acceptance.

Two points should be noted. First, it excluded all test waivers related to human bodies. For example, on pharmaceuticals the MHW asked for a near-repetition of phase II and III clinical trials, which are done on human beings. On in-vitro diagnostics it mentioned in particular the necessity of collecting domestic data for blood testing reagents. And on medical devices it required domestic clinical trials for all devices implanted into human bodies, such as pacemakers, intrauterine devices, contact lens, and breast implants.

The second point is the trust-building endeavor on pharmaceuticals. As discussed previously, Japan's medical care, along with its social system, is based on trust. Thus while it accepted foreign data, the MHW demanded "picky" requirements. Foreign applicants not only needed to comply with existing guidelines between Japan and the country where the clinical trials are done—the acceptability of their data was also judged on the basis of medical practice. Also required was the building of credibility: all investigators had to be listed with full resumes of their achievements in the field related to the tested drug, and all the institutions involved as well.[23] When these documents were translated, which was also required, the resumes of the translators were also listed in order to make sure that the translation was faithful.

Indeed, the deepest concerns about clinical trials rested on issues surrounding the body which could not be easily reduced to regulatory terms. In this sense, the MOSS settlement did not change anything. As commented on by Shintani Tetsuro of the JPMA, "it is not exceptional for Japan to conduct separated tests to fit its own nationals' body physics (*taikaku*) and predispositions (*taishitsu*)" (*Nikkei* January 30, 1985). However, it is hard to say whether the MHW was practicing a protectionist trade discourse or protectionism of body and health. It clearly stated that its position opened the gates for

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22 For details of this change, see FDA 1985.

23 It is interesting that for situations where the signatures of investigators were not available, such as their deaths, additional documents had to be provided by applicants explaining the reasons.

international trade, but it also guarded its people's bodies and health. The MHW stated, "Holding maintenance of people's health and safety as its supreme end, [MHW] is making a serious effort at smoothly admitting foreign products while trying to understand foreign requests" (WGDA 2000: 233). As we will see in Part II, the MHW's position did not change behind the scenes when the issue of racial difference was debated. In just three years the stage was transformed from the bilateral MOSS negotiations to the more complicated ICH negotiations.

PART II
RACE AND GLOBAL PRESENCE: DEBATING RACIAL DIFFERNCE AT THE ICH

From Bilateral to Global: Forming a Conference for Regulatory Experts

Part II will address Japan's encounter with the ICH and the temporary settlement of the racial difference issue in the E5 guideline "Ethnic Factors in the Acceptability of Foreign Clinical Data." It deals with, in order of appearance, the creation of the ICH as a global forum, the formulation of the racial difference problem and scientific research on the issue, and the political arrangements needed to make a temporary settlement. Unlike the "pre-ICH" mode of its negotiations with the United States, Japan took the initiative and brought the sensitive issue of racial difference to the broader, technology-oriented ICH, turning around their approach to this problem.

Even so, there were some concerns that remained unchanged in this new mode, such as the "dialectics of difference" discussed in part I. Although all participants agreed with a vague interpretation of the biological essentialism of race, quarrels over the definition of racial difference and its clinical significance continued as the field changed from culture to science and then from science to politics. The original break over which standard (Caucasian, Asian, or a mix) should be used for studies haunted the conference. Worse, in terms of administration, a nationalist concern over how a universal standard could incorporate subjects from a specific country (i.e., the Japanese) was added. All these made the final result, the E5 guideline, nothing but a reflection of the complicated nature of this problem. In this sense, globalization did not gain anything by fusing things together; instead, it wove conflicts and contradictions into a superficial harmony named "the guideline."

Let us first return to the bilateral mode. While regional experts still urged the United States to "push harder on trade" or encouraged the Japanese and the Americans to deal

with their trade problem rather than "pretending it didn't exist," the discussion on pharmaceuticals and the acceptance of foreign clinical data had silently departed from the MOSS negotiations and was no longer a cause of trade friction. Although the MOSS follow-up meetings continued, as shown in table 4.2, they did not involved important issues, including the acceptance of foreign clinical data. The discussion deviated further and further from the "regular track" of bilateral business negotiation; this was because the global ICH rather than the trade-oriented MOSS became the scientific and administrative platform for discussion.

Table 4.2 MOSS Follow-up Meetings, 1986-1996

No	Time/place	Main topics discussed
1	August 1986/ Washington, D.C.	Confirmation of MOSS agreed topics Drawing up of approval standard for vitamins as OTC drugs
2	March 1987/ Tokyo	Confirmation of MOSS agreed topics
3	April 1988/ Tokyo	Confirmation of MOSS agreed topics Calculation of formula for prices of new drugs
4	March 1989/ Washington, D.C.	Calculation of formula for prices of new drugs Acceptance of U.S. quality management data for medical devices
5	May 1990/ Tokyo	The Central Social Insurance Medical Council Setting reimbursement rates for implantable medical devices
6	November 1991/ Washington, D.C.	Highly advanced medical technology Proceeding period of in-vitro diagnosis
7	June 1992/ Tokyo	GIP (Global Internet Project) Highly advanced medical treatment Standard proceeding period of In-vitro diagnosis
8	November 1992/ Tokyo	Specific therapeutic materials GIP
9	April 1993/ Tokyo	Guidelines for customary dealing of medical devices GPMSP (Good Post Marketing Surveillance Practice)
10	October 1993/ Tokyo	Classification of medical devices
11	December 1994/	Specific therapeutic materials

	Washington, D.C.	Highly advanced medical treatment Request for the relaxation on drug regulations Hard Gelatin Capsules
12	July 1995/ Tokyo	Hard Gelatin Capsules Introduction of insurance system for new techniques Specific therapeutic materials
13	March 1996/ Tokyo	Hard Gelatin Capsules Insurance reimbursement

Source: adopted from the Drug Administration Working Group, Japan 2000: 235-239.

In Chapter 2, I reviewed the foundation of the ICH and its motivations on behalf of global drug companies and business (Chapter 2, part III). However, commerce does not represent all the concerns of this conference. In this section, I will review the ICH from the viewpoint of the regulators and medical technocrats. I argue that it was their wish to form a global platform that made the establishment of the ICH possible.

It is hard to trace the exact historical origin of the ICH, but it is was surely no later than the first MOSS experts' meeting held in Rockville, Maryland, in May 1985, where MHW experts learned from the Food and Drug Administration (FDA) of the Western style of drug regulations. The FDA did not have a major presence at the MOSS negotiations, yet they appreciated this dialogue when they met the MHW experts directly. It was reported that the experts from both sides discussed "the possibility of setting bilateral or multilateral common standards for the acceptance of foreign clinical data." Afterward, the FDA and the MHW agreed in principle that "it is desirable to work toward a system of international harmonization" (MOSS Report 1986: 14).

The meeting had more impacts on the Japanese side. Before MOSS, the MHW was a very "domestic" ministry. Besides, as mentioned in Chapter 3, it was already occupied in the routine duty of administering national health insurance. However, the MOSS talks broadened the horizon for the MHW. One former MHW official remembered that the MITI complained when the MHW was assigned for the negotiation, but they insisted that they were able to handle this task.[24] This action also marked a shift of the people in

[24] The replacement of the MITI by the MHW had to do with what Chalmers Johnson has observed regarding the fragmented nature of Japan's bureaucracy, which itself has a long history dating back to the Meiji period. Each *jikohonyi*, or ministry, has its own territory and looks after only that territory. I will

charge. I have mentioned that in Japan, physicians play a dominant role in all medical affairs, including drugs. However, when dealing with foreign countries, another group of experts specializing in drugs was responsible. These *yakkeigikan*, pharmaceutical affairs technocrats, are very different from the conventional idea of Japanese bureaucrats. Although they are not at the highest level of the bureaucracy, they are in charge of regulatory issues. Cohen is right when he observes that the MHW technocrats chosen were smart, outstanding, and curious to know new things. It was during the MOSS negotiations that these officials witnessed a different system of drug approval. "Only since then have I realized how 'Japanese' we are in such a business," one regulator remembered.

More stimulation came from the MOSS-like negotiations with the EC starting in December 1986. Like the United States, the EC requested a market-oriented negotiation that included cosmetic products, pharmaceuticals and medical devices. Two experts' meetings were held: one for medical devices and cosmetic materials in June 1987, and the other for pharmaceuticals in September 1988. Agreement was reached to omit "unnecessary" clinical trials when the MHW officials met with their European colleagues, who were mainly experts from the EC commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA), which represents the European pharmaceutical industry. The time was right to create a forum of these experts.

Chapter 2 reviewed the official origin of the ICH, the International Conference of Drug Regulatory Authorities (ICDRA) held in Paris in 1989. However, this description does not say anything about the mechanism by which such a program was initiated. In fact, the ICH had a "non-commercial" and "non-political" beginning that had nothing to do with the ICDRA. Organized by the WHO, the ICDRA had been held since the 1980s, yet not much had been done concerning regulations that improved the safety, efficacy and quality of innovative medicines. The idea to form a conference on this matter originated from a private meeting of experts on drug regulation from the United States, Japan and Europe occurred. There seemed to be a spontaneous need for these regulators to do something for themselves. They were science people with scientific thoughts. It was a brainstorming meeting in a small room, Elaine C. Esber, then the FDA representative and one of the few people who has participated from the foundation of the ICH, remembered. Esber was not able to remember who exactly was present: "I can count, five or six, not many" she said of the meeting excitedly. But what was clear to her was that a consensus was soon arrived among these regulators. They agreed that international standards for

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argue that since drugs were not considered a "business," the MHW, which was a more health-oriented institution, was not much influenced by the MITI or the Ministry of Foreign Affairs.

new drugs were not only desirable but necessary. "So, let us do it!" was the conclusion reached.

However, the ICH could not be realized without administrative backing. Esber said that she then brought the proposal to harmonize regulations on drugs back to the FDA, asking for its support. Following the agreements between Japan, the United States and the EC, the latter two signed an agreement in November 1989 to hold biannual expert meetings on scientific and technical regulation of food and pharmaceuticals (*Nikkei*, November 14 1989). Two officials were key to realizing this concept: F. Sauer, who was involved in the harmonization of the rules among EC countries, and Nelly Baudrihaye, Director of the EFPIA, who had worked closely with the EC Commission. These officials proposed that three regions—the EC, U.S. and Japan—discuss how to stop the duplication of so many studies by harmonizing requirements. They got the advice of the WHO, the support of the International Federation of Pharmaceutical Industries (IFPMA), and the agreement of U.S. and Japanese regulatory bodies. Meanwhile, experts continued to work on issues and topics they could bring to this conference. As written in the proceedings of the first ICH conference, its preparation owed much to "the many technical discussions between experts which have taken place at international symposia dealing with regulatory requirements" (D'Arcy and Harron eds. 1992: xix). Their efforts finally resulted in the first ICH conference in 1991.

Now let us return to the shift of the dialogue channel from the MOSS to the ICH. Chapter 2 discusses two characteristics of the ICH that provide the reasons for replacing bilateral negotiations such as the MOSS. First, the ICH's membership is exclusive to the countries able to produce and consume proprietary drugs. Thus instead of making agreements one by one, this forum was expected to be able to generate more timely and productive results. Second, the ICH made possible direct conversation between industry and regulators. If the MOSS talks had to have the involvement of political parties, such as trade representatives and The Ministry of Foreign Affairs, the ICH presented a more direct means by which the needs of producers and regulators could be clearly heard. However, here I would like to discuss the MHW's attitude toward this conference. How did Japan perceive this gathering?

Many might be surprised that the MHW in fact showed substantial interest in this conference. Elaine Esber mentioned to me in an interview that Kurokawa Tatsuo, then the MHW representative to the ICDRA, cordially supported her scientific proposal from the beginning. This information is confirmed from the Japanese side. For example, Kurokawa reported that at the third EC-Japan experts' meeting, which was held

immediately after the ICDRA, the EC representatives asked Japan to join the endeavor (ICH-Japan Study Group 1993: 7). Doi Osamu, then the director of the new drug division of the MHW, commented of this request that Japan was in fact invited as a *gaiatsu*, or "external pressure," in order to keep German and French pharmaceutical companies at the negotiating table. Doi also noted that it was the MHW's experiences at the MOSS and other bilateral negotiations that made it realize that a forum dealing with both Europe and the United States was inevitable (1999:10). Therefore, we are compelled to ask, why did the MHW decide to turn to the global while at the same time globalization was attempting to capture Japan?

This question can be answered by three aspects of the conference. First, from practical aspect, the MHW understood and appreciated the operation of *gaiatsu*. It is a common negotiation practice in Japanese culture. From a domestic perspective, although the MHW does not have much of an obligation to protect domestic industry, it did have reason to welcome the *gaiatsu* of the ICH. This pressure would help the regulatory authority's international connections and give it the scientific requirements it needed to flight against the conservative medical authority of clinicians and professors, which was considered an obstacle to reform. Besides, in an international context, the MHW was happy to be a *gaiatsu* for other countries. It was a logical dimension of international politics to them, and it demonstrated Japan's significance in world affairs.

Related to the political operation of *gaiatsu*, the political aspect of the MHW's active participation reveals an unspoken wish to "escape" from the bilateral framework of negotiation in which the United States was always dominant. As Cohen observes, there was a trend for Japan to move from bilateral to multilateral negotiations in the 1990s (1998: 28-30). According to Cohen, Japan's strategists assumed that they had a better chance of wining if disputes were arbitrated on a multilateral basis. In addition, since the late 1970s Japan had wished to improve its foreign relations from bilateral to multilateral. As Tanaka and Miyazaki both point out, the key to this change was Europe's position as a reemerging market and negotiator. Europe not only relieved the direct tension between the United States and Japan; it also became an important part of global market (Tanaka 1989: 73-40; Miyazaki 1990:45).

From all this we can see two reasons for the MHW's participation in the ICH. The passive reason, as Bernd Knabe points out, is finding an ultimate solution to all the economic frictions occasioned by drug approval requirements (Knabe 1988). Nonetheless, the ICH was also an active means of avoiding a market-driven conflict in which the United States tried to force its drugs on Japan and Japan responded by putting up non-tariff barriers. The MHW's major concern instead was whether the ICH's scientific

and technological orientation would be accepted and abided by the U.S. and drug companies, or whether the latter would try to exploit it for their own purposes. In fact, Doi recalled the FDA's hesitation over founding the forum. He reasoned that the U.S. hoped to universalize its standards and thought that a multilateral forum might prevent it from reaching this goal (1999: 10-11). This wish can be read also in Kurokawa's comment on Japan's relationship with Europe and the role it played in its inclusion in the ICH.

Finally, on the cultural and ideological level, joining the ICH coincided with the Japanese worldview. The words "international" and "harmony" in the ICH's title caught the MHW's imagination. Partially because of their inexperience in international negotiations and partially because of the title of the conference, the MHW truly believed that in the field of health and body, harmony (as distinct from unity in a Western sense) could possibly be achieved. The term *wa*, translated as "harmony," carries special cultural weight for the Japanese. It is the best way in communication: when divergent viewpoints are integrated into an acceptable solution, then *wa* emerges. Another concept related to *wa* is mutuality and reciprocity. Kawashima contrast the role of *wa* in Japan with individualism (1967): "*Wa* is not mechanical co-operation, starting from reason, of equal individuals independent of each other, but the grand harmony (*taiwa*) which maintains its integrity by proper statuses of individuals within the collectivity [and] by acts in accordance with these statuses" (264, as quoted in Gudykunst and Nishida 1994: 24). Thus the making of harmony is considered a social process confirming each participant's status. As the only non-Western party to the conference, Japan treasured this opportunity and expected to confirm its status as an equal to the United States and Europe in every international stage; this was the possibility it saw in the ICH.

The above explanations are key to understanding why Japan was comfortable with joining the global. In contrast with conventional perceptions of Japan regarding protectionism and globalization, I did not hear any objections or suspicions from the technocrats about joining the conference. The MHW even expected this conference to be "also a help for making our pharmaceutical industry international" (MHW 1990: 187). In fact, before joining the ICH the MHW had asked the JPMA do a survey of all member companies concerning overseas markets and sales (JPMA 1989). The results indicated that about 90 percent of companies had considered the future unification of the European market, and many had established bases in either the United States or Europe. However, thirty-three out of forty-two companies that answered the questionnaire complained that the absence of a bilateral or trilateral agreement on the related regulations would be a big hurdle (39). Although the MHW had little experience in business, this result was enough

for it to join this conference.

The same tone can be also read in the 1990 *MHW Annual Report*, which does not mention the ICH by name, but includes a chapter titled "Japan's Contribution to the World" that says that "the MHW is joining actively an international conference with the United States and EC, along with others, for the harmonization of standards. It will contribute to the making of this scientific, appropriate standard" (MHW 1991: Chapter 6). With this optimism, the problem of racial difference was handed over to a group of experts and regulators.

Bringing Culture into Science: Formulating Racial Difference in the ICH

In the following three sections, I will trace how racial difference was discussed at the new conference. As discussed in Chapter 2, the EWG meetings were the main arena where debates over each guideline took place, and the E5 guideline, though it took much longer than the others, was no exception. From the viewpoint of scientific controversy the debate process can be divided into three rounds, each with a distinct focus (for information about these meetings, see table 4.3 and table 4.7). The first round began with the first EWG meeting September 1992 and lasted until the release of a position paper in August 1994. It focused on the scientific evaluation of whether racial difference had any significance in drug development. From this time until ICH3 was held in November 1995, a second round of discussion took place that featured heated debates over whether factors other than genetic polymorphism should be taken into consideration. The third and final round was built around a workable proposal for dealing with racial difference. It proceeded by establishing an operational definition of racial difference as a factor that could be "bridged" by the extrapolation of clinical data from one country or population to another. This thesis will go through these discussions round by round. However, along with analyses of conflicting arguments, ethnographic concerns will lead it to examine the dynamics of discourses in which race was not a biologically fixed point of reference, but a field defined and shaped by the actors involved.

This section is an introduction to the topics and initial investigations. Since race is so obvious a subject, people might think it is an easy topic to start discussing. However, this was not the reality. Two considerations needed to be taken into account in addressing race. The first was a technical concern that the cultural intuition of "racial difference" makes no sense in a scientific context. In order to initiate a scientific discussion, race had to be given a form that was scientifically arguable. Maybe we should think of it this way: in this instance of drug regulation, how can concerns about racial difference be presented?

The second concern had much to do with the existing complicated relations between science and culture. As a controversial issue in both realms, it was hard to keep the topic in only one realm when it is discussed. Thus if the ICH wanted to examine this issue, the question had to be asked as clearly as possible in order for there to be no unwanted complications.

Although racial difference was not given as an independent subject for discussion at the beginning of the ICH conferences, tensions concerning the issue were apparent. Originally, in preparatory meetings the issue was considered to be ethnicity and was put on the agenda for a panel on "studies in support of special populations"; yet following consideration of possible cultural implications, only aging people were selected for inclusion in this discussion. At ICH1, a panel on "design/requirements for dose responses trials" was arranged for under the category of efficacy. Presenters from the United States and Japan recognized the fact that the Asians tended to administer smaller dose regimens than Americans (D'Arcy and Harron eds. 1992: 479-511). Therefore, the category of efficacy and the issue of dosage seemed to be a natural starting point to exploring differences between the three regions. Even so, people on this same panel expressed worries. William Wardell of the Warner Lambert Company, for instance, argued that harmonization should start on two fronts: medical and cultural, and "we need to clarify any medical-scientific difference and to understand cultural difference." It is obvious that medical difference is a subject of scientific investigation, but the reason for studying international cultural differences in medicine and therapeutics was to enable researchers to "separate the cultural from the scientific differences, and so use valid scientific data in support of international application anywhere" (488).

Wardell's caution reflected the tense political background to the subject of racial difference in relations between Japan and the United States in the 1980s. It was reported in 1983 that Nakasone Yasuhiro said of Japanese racial homogeneity that "the Japanese have been doing well for as long as 2000 years because there are no foreign races" (quoted from Fallows 1986: 41). He infamously commented in 1986 that Japan's racial homogeneity had helped it become a more "intelligent society" than the United States, "where there are blacks, Mexicans and Puerto Ricans and the level is still quite low" (Wysoski 1986). Thus I was told by conference participants that the United States did not want Japan to bring up the issue of racial difference, at least not in a form that could be related to Japanese nationalism. In short, Wardell and others hoped that Japan would separate its state from its people.

On the other hand, the MHW insisted on the importance of this issue. Presenting at the opening ceremony of ICH1 (D'Arcy and Harron eds. 1992: 24-26), Doi Osamu

elaborated the Japanese perspective in two ways. First, rejecting conventional thinking on globalization that assumed a one-way distribution from the West to the East, Doi argued that the mission of the conference should be to achieve "mutual acceptance" of foreign clinical data. "We are not yet satisfied with the present status of global harmonization through scientific discussion at this ICH meeting," he said. Second, Doi considered racial difference to be an essential issue that impeded the promotion of mutual acceptance, and believed it could be solved by scientific investigation. He claimed, "I believe and I hope that this issue will be discussed from a scientific point of view at the ICH meeting and in its expert group meetings." In other words, while the United States and the EC tried to "incorporate" Japan into their proposals for globalization—namely, to have either a restricted racial consideration in each trial or an administrative integration that would compromise Japanese sovereignty—Doi insisted on Japan's national presence within the global scene. He did so based upon his strong belief that the Japanese nation and race could be defined by science.

Because of Japan's insistence, the issue of racial difference was first brought up at the topic-searching meeting held in Washington, D.C., in March 1992. It was softly rebuffed by the European Union (EU, formerly the EC) and the United States in the first round, but as soon as this was heard by MHW expert Naito Chikayuki, Doi Osamu, the leader of the MHW delegation, urged that the issue be put back on the list. Naito remembered: "It was noon; I had lunch with other MHW delegates. I reported to Doi that our proposal of racial difference was declined earlier this morning, but he insisted that it must be in. I did not know exactly how they made it; the only thing I heard is that the MHW went to meet the FDA to talk over this issue, and it was finally added as the third priority in the category of efficacy."

Of course, Doi's fervent insistence might be due to his personality, but it could also be understood as an assertion that has multiple implications. On the subject of clinical trials, the MHW had been accused of not keeping its promise to accept foreign data; in fact, Japanese regulations required every foreign applicant to repeat almost all clinical trials they had already done somewhere else.[25] Thus the issue needed to be reconsidered in one place or another, and Doi intentionally chose to make the ICH the place. This decision had political implications, as it was an escape from the MOSS framework and moved the crucial issue of racial difference to a new platform. The MHW hoped that by resolving the matter of racial difference it would no longer be an excuse for protectionism

[25] These are the so-called "three repeats": the absorption, distribution, metabolism, and elimination tests of phase I, the dose finding tests of phase II, and the comparative clinical trials between Japanese and foreigners of phase III.

and "Japanese style" clinical trials.

Table 4.3 Timeline of Discussions on the E5 Guideline, 1992-1995

Time	Event	Achievements
March 1992	Steering Meeting in Washington, D.C.	Subject accepted
September 1992	First EWG meeting on E5	
October 1993	ICH 2 in Orlando, Florida	Retrospective study on racial difference reported by Japan and EU
March 1994	EWG meeting in Tokyo	Draft 1 drafted
August 1994		Position paper released
October 1994	EWG meeting in Brussels	Draft 2 formed, in which "triage" was proposed
February 1995	EWG meeting in Athens	Draft 3 formed; temporary settlement of the acceptance of phase I and II data
March 1995	EWG meeting in Washington, D.C.	Draft 4 formed in which bridging study was proposed
July 1995	EWG meeting in Brussels	Draft 5 formed; "triage" and bridging study approaches used simultaneously
August 1995		Draft 6 circulated
November 1995	ICH 3 in Yokohama	Draft 7 formed; temporary settlement of the acceptance of phase III data

Source: adopted from Koyama 1999: 58, Table 1.

In an atmosphere that mixed optimism and suspicion, racial difference entered the field of science in the context of dose-response trials. Although aware of the genetic polymorphism and environmental components of racial difference, at the first EWG meeting the experts only agreed to conduct comparisons of Japanese and Caucasians in the area of pharmacokinetics. Specifically, these studies mainly focused on the absorption, distribution, metabolism, and elimination (ADME) of drugs among these two groups. The

MHW undertook a retrospective study, looking at differences in results from healthy volunteers and patients for products submitted for approval in Japan since 1985. The Center for Medicines Research (CMR) carried out a survey in the United States and Europe, collecting data from phases I, II, and III.

Even considering only the biological factors, these comparisons had a hidden agenda: they were intended to see whether there was any collective significance to race by weighting individual and interethnic differences.[26] On the surface they seemed to echo an American approach to the evaluation of how much weight should be placed on race in clinical trials; however, the FDA showed little interest. An FDA expert shared with me his opinion on racial and individual difference. "You ask me why we did not care much about racial difference," he said. "I will tell you that it is because it is less important than many other factors, all of which compose a complex situation concerning what we call a disease and a person. If we do want to take racial difference into account, I will say, for example, in the field of cancer research everybody is in fact a race. All patients are unique in some ways. They should be considered as individuals and every disease should be treated accordingly." As a scientist he thought the E5 EWG asked the wrong questions. Nonetheless, in the context of the dialog this agenda was very important. Since Japan conceived of state and race as bound together, the other parties to the ICH saw it as crucial to refute the myth by blurring the boundary that separated Japan from "the other." In short, they wanted to play a "zero-sum" game. Dose-response was no longer a focus; the concept of nation-state was.[27]

The results of the first scientific investigations were a surprise. The MHW assigned a study group to conduct scientific studies,[28] but their results did not support the Ministry's "nationalist" assumptions. Yasuhara Hajime's retrospective study on eight new chemical entities (NCEs) shows that, in spite of some hormonal differences and genetic polymorphism, such as cytochrome P-450 enzymes, intra-ethnic differences in the ADME data were greater than interethnic differences (D'Arcy and Harron eds. 1994: 440-442). Using differences in AUC (area under concentration of a drug in the body) and C_{max} (maximum effective concentration of a drug in the body) as parameters, it was

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[26] It is not a fortuity for these scientists to apply this approach to clarify whether racial difernce exists. According to David S. Jones's current study on the history of medical researches on racial differences, it is a tendency shown in these studies that they emphasize more on the importance of difference among individuals than that due to different racial groups. I thank Professor Jones for this important information.

[27] The subject became an independent topic titled "Dose-response information to support registration" (E4). It reached step two in March 1993, and the step four draft was signed off by the ICH Steering Committee on March 10, 1994.

[28] It began with studies of the anti-TB drug INH, a dose-response study on NASID drugs, and P450 polymorphism.

reported that for most drugs, the differences in AUC and C_{max} between Japanese and people of other races were within a two-fold range, meaning that no significant difference could be found. The other study showed more striking results. The data of a methenytoin-type drug, UL-01, showed significant differences in AUC and C_{max} between the two groups tested that might have been contributed to by racial differences. However, comparing PK parameters, Yasuhara found extraordinarily high values in two Japanese subjects and one non-Japanese subject; these values' difference from the mean values of their respective groups were even larger than the interethnic difference. In short, the findings betrayed the Japanese belief in a homogeneous racial group.

It was so dramatic a result that the E.U. experts extended its implications to their own studies. Stuart Walker of the EFPIA pointed out at ICH2 that interethnic difference only accounted for approximately 11 percent of total individual genetic variation. He boldly concluded that the varying frequency of genetic polymorphism of the cytochrome P-450 enzyme is likely to have "considerably less impact on drug kinetics and dynamics than other non-racial genetic factors or environmental influences" (D'Arcy and Harron eds. 1994: 444). Since then, the UL-01 study has been widely cited as a "classic," scientific proof that racial difference is of no clinical significance. It was believed that if Japan did not accept this result it would be accused of being irrational and unscientific.

Did Japan really have no way to escaping this dilemma? Scientifically, yes; culturally, no. Yes, because Japan did have some ways of arguing against the implications of the UL-01 study. JPMA representative of the EWG Uwoi Tohru, for example, pointed out that the results were badly analyzed due to the improper use of statistics (Uwoi 1999: 45). Not only did this study not enroll enough subjects to prove the results they claimed (six Japanese and twelve Swedes), but the way the data were interpreted was misleading. Uwoi admitted that there were indeed two Japanese individuals with high AUC and C_{max} values; however, for the comparison to show racial difference, it was necessary to stratify the population and balance out these anomalous figures. For Uwoi, there was no statistical sense to the claim that there was no racial difference.

Nonetheless, Japan did not respond this way, for it would have been culturally unacceptable. In order not to challenge the presumption that the Japanese were unique *as a group*, the MHW chose to accept the conclusion of the UL-01 study, "abandoning" that part of PK testing for mutual acceptance. In other words, the MHW chose to break the process of clinical trials into pieces instead of breaking the definition of race itself into individual pharmacokinetic factors. For the sake of administration, the MHW insisted that anything proved racially insignificant (in comparison with individual variations) should

be subject to mutual recognition between Japan and the West; however, this result could not be applied to other areas of clinical trials unless more studies showed similarities between Japanese and Caucasians. For example, in the same presentation Yasuhara pointed out the racial difference found in PD data, another biological indicator used in phase I studies. Later he found more genetic polymorphism indicating racial differences in metabolism, such as N-acetylation, debrisoquine hydroxylation and S-mephenytoin hydroxylation (Yasuhara 1994).[29]

Some might think that Japan violated rules of science, but it did not. Science should bring light to cultural controversies, but the results of these studies revealed how limited it was. Perhaps, as Donna Haraway claims in her three period-paradigmatic configurations (see table 4.1), in the stage when population, not race, featured as the "key object of knowledge," race was cast as an "illusory" construction by bad science and only remained prominent in domains of social science. In fact, having been controversial in bio-medicine for a long time, race was a topic which Western scientists did not know more about than their Japanese colleagues.[30] It is convenient to simply make the criticism that that Japan's racial discourse has no scientific foundation. However, relying on a naïve category to divide all human beings into Caucasians, Asians, and blacks, the Western agenda on race, which is based on the primitive unity of all races, is also problematic. The division between the West and Japan is not due to the fact that the former is more "scientific" than the latter. Instead, it is a conceptual one: while the West hopes to separate the concerns about race from those about the state, Japan goes in the opposite direction.

It became clear that the Western concepts of race and state were of little to no help in dealing with this problem. Japan was invited to the ICH for negotiation as a state, and all parties agreed to consider the Japanese a distinct group; however, the two sides of this debate had different presumptions. In opposition to Japan were experts who assumed the "primary unity" of human beings and considered all races to be the same unless differences could be clearly identified or proved or the integration of regulations could be worked out so that no significant difference was found. However, for the MHW, the presumption was that the state and race were inseparable. Bodily factors, such as "Caucasians are taller and heavier," "eating habits are different," "Japanese have a less tolerant gastrointestinal tract," and "Japanese are more liable to depend on medicine and

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[29] The frequency of poor metabolizers was, respectively, 10%, < 1%, and 20% in Japanese people and 50%, 10%, and 5% in Caucasians.

[30] For a critical review on the concept of race in scientific studies, mainly in the Western world, see Duster 2003.

more sensitive to side-effects" (D'Arcy and Harron eds. 1994:434), were real to the MHW. Unless similarities could be shown that proved otherwise, the Japanese should be considered different from others. As Naito wrote in the first annual report of the ICH study group concerning racial difference, it was dangerous to simply accept the clinical trial data done in foreign countries: "No matter how advanced they are, we cannot accept them without having any clinical trials done in our country" (ICH-Japan Study Group 1995:82). The PK was just a start. For the Japanese, racial difference from the West must be found somewhere else if it was not present in PK levels. This division also marked the end of the "zero-sum" game and led the EWG to a tug of war over the definition of race, described in the next section.

From Racial to Ethnic: The Tug of War on "External Factors"

Upon the preliminary settlement of the issue of PK testing, the battle moved on to whether more tests could be waived. This was important for global pharmaceutical companies because it took much more effort to fulfill the requirements of these trials; waiving the duplication of testing on local subjects would save lot of money and time (for more analysis, see Chapter 2). From the viewpoint of commercial negotiation, the first round showed that Japan's bottom line was the PK data; it would trade this and close the conversation in order to preserve control over phase II and phase III trials. On the other side, the West was eager to break Japan's line, trying to push harmonization further into phase II and/or phase III. Since Japan could not easily accept the notion of the racial unity of all human beings and waive all local tests, the game could not be brought to an end.

However, the situation was more complicated. In fact, nobody knew that the ICH would develop into a long series when it began. Although people thought one ICH conference could not solve all problems, three were thought to be enough. As predicted by FDA representative Elaine Esber, "[for some areas] specific areas for action and methods for resolutions were identified with anticipated timetables for resolution in at most within two years (ICH2) and others by 1995 (ICH3)" (D'Arcy and Harron eds. 1992: 551). On the other hand, the MHW hoped to maintain this conference as long as possible. According to Doi, the EC and European industry that did not want to continue the conference; however, "to promote our industry to overseas, the MHW needs a platform on which conversation can be conducted ... With the help of the FDA and PMA [PhRMA] the rule to have the ICH held every two years was determined" (Doi 1999: 11).

Now the impasse in reaching a settlement on racial difference provided a reason to keep the ICH going. The question was how to continue the discussion. Let me summarize

what was obtained for the prolonged game. At the fifth EWG meeting the first draft agreement was drafted, yet nobody was satisfied. Japan agreed to waive the PK study when applicable, but asked to have dose finding and clinical trials done in Japan. The EU and U.S., in contrast, wanted to grant full waivers to some drugs that were the least likely to vary racially. As shown in table 4.4, the Japanese representatives showed a negative attitude toward waiving trials. They did not assert that the Japanese were different from Caucasians, but they claimed that the matter was too complicated to be studied. On the other hand, Stuart Walker of the EFPIA believed that the results of UL-01 study could be applied to tests in other phases of clinical trails. He agreed that there were some differences found between the three regions, but he thought that they could be accounted for.

Table 4.4 Comparison of the Interpretations of Racial Difference by Japanese Representatives* and Stuart Walker

Stages		Japan's interpretation	Walker's interpretation
Phase I study	PK	No significant difference	No significant difference
	PD	Differences observed (P450, NASID)	No significant difference (P450)
Phase II study	Dose finding	Differences found; racial difference suspected	Differences found; can be harmonized methodologically
Phase III study	Clinical trials	Related to both genetic and environmental differences; too complicated to waive	Related more to environmental differences; can be methodologically harmonized

*Japanese presenters on the panel on racial difference at ICH2: Naito Chikayuki, Yasuhara Hajime and Kumagai Akira.

Source: summarized from D'Arcy and Harron eds. 1994: 427-468.

Staring with this understanding, environmental factors were introduced into the discussion. Forgetting the possible implications of culture, each side developed its strategy on the use environmental factors to help understand racial difference. Stuart Walker, for example, argued for these factors a subject for study because all differences in clinical effectiveness appeared to be due to "methodological differences between the

three regions and the use of lower doses, rather than a real difference in how the patients were affected or responded to the drug" (D'Arcy and Harron eds. 1994: 451). Disregarding the role biological difference played in phase II and phase III studies, he focused on social factors, such as medical practice, dose regimens, and trial design, and thought that these could be corrected by statistical means and thus harmonized. Obviously this approach echoed the EU's administrative concerns about its multi-state situation.[31]

On the other hand, the MHW referred these "non-racial" factors back to racial differences. Naito Chikayuki, for example, commented that to study environmental factors was unrealistic and time-wasting: because "environmental factors consist of many aspects, such as culture, medical traditions, philosophy of doctors on drug treatment, diet, religion, doctors' and/or patients' education, doctor-patient relationship, climate, body size, and so on, we thought that it would be very difficult to assess them properly and to reach some degree of harmonization" (D'Arcy and Harron eds. 1994: 429-430). The complexity of these factors was not the point; the point was that a substantial number of local subjects were necessary to make the various factors testable *as a whole*. In order to make possible the determination of the best dose without adverse effects, race was a crucial factor in "balancing out" other variables.

In this unusual context, the battlefront on racial difference extended from the exclusively biological to a broad concept that included the cultural and the social. As soon as these "external factors" started to be taken into consideration, the racial differences in drugs' behavior (ADME) were no longer a main concern.[32] The consideration of race turned into the consideration of ethnicity. Robert T. O'Neill of the FDA reported the EWG's decision to make an "operational definition of ethnicity" that could be practically implemented (D'Arcy and Harron eds. 1996: 430). Even so, the conceptual division remained. While the EWG led an analytical drive, using algorithmic tools to try to exhaust the influence environmental or "non-racial" factors, a holistic appeal was put forth by the MHW. The MHW argued for the evaluation of net drug effects through the accumulation of data from clinical testing based on existing racial categories, namely, Japanese, Caucasian and black. What should be incorporated into the

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[31] Marisa Papaluca even pointed out the fundamental role regulatory authorities played in the harmonization of drug information, which could be "an important factor leading to actual 'non-ethnic difference' in clinical responsiveness across Europe for the analyzed new drugs" (D'Arcy and Harron eds. 1994: 462).

[32] According to Naito, ADME was not an important issue at all in accounting for racial difference. He reminded me of the MOSS talks, where he had suggested that the MHW drop the requirement for repeating ADME tests. However, he emphasized that upon the advice of one FDA expert the MHW decided to add ADME to the list of factors to be considered.

list and what should not? The tension was so high that it prompted the EWG to turn to anthropology, the discipline of the study of human beings. As rapporteur Naito Chikayuki summarized, "The so-called ethnic difference might be sometimes deeply influenced by environmental factors rather than genetic ones. Therefore, when we consider ethnic factors in a long-term perspective, we may have to take account of anthropological approaches" (D'Arcy and Harron eds. 1994: 430).

As a result, the definition of race was loosened. Etienne Labbe and Jean-Marc Husson of the EFPIA voluntarily worked out a draft list of factors to be considered, but this led to nowhere. Compiled with the help of one representative whose wife was an anthropologist, it might have been a good chart for academic use but was definitely not practical for forming a practical guideline. As stated in the position report released in August 1994, about forty factors were mentioned under the categories of either "objective," "pharmacologically related" or "subjective," and related studies were cited (a summary of this research is listed in table 4.5). Everything could be racially related. While the EU and U.S. experts assumed they were working on an operational definition for negotiation, the MHW regarded this attempt as a list of priorities for topics that should be discussed first. The MHW was unsure of the extent to which these external factors could be accounted for and remained passive in this part of the discussion.

Table 4.5 Ethnic Factors considered

Objective differences

	Topics selected	Study cited
Population composition	Majority and minority	Edwards 1992
	Genetic diseases such as sickle cell disease, thalassemia	Vesell 1989
PK and PD	Pupil dilation	Chen & Poth 1929
	Liver enzymes	Drayer, et. al. 1977
	Acetylator	Wood, et. al. 1991
	Drug induced SLE	Hess 1982, Rieder, et. al. 1991
	Debrisoquine-sparteine metabolism	Wood, et. al. 1991, Zohn, et. al. 1989
	Mephenytoin metabolism	Kupfer, et. al. 1988
	Phenothiazine metabolism	Kumana, et. al. 1987
	Propranolol and imipramine metabolism	Eichelbaum, et. al. 1990

Drug reaction	Clozapine	Leiberman, et. al. 1990
	Drugs on central nervous system	Wood and Zhou, 1991, Poland 1991
	Tricyclic antidepressants	Strickland, et. al. 1991
	Lithium	Jefferson, et. al. 1987, Lin, et. al. 1986, Takahashi 1979
	b-blocker and ACE blocker	Hall 1990, Fries, et. al. 1986, Kiowiski 1985, Osler, et. al. 1987, Zhou, et. al. 1990
	Ca and K channels	Kiowiski, et. al. 1988

Pharmacologically related differences

	Topics selected	Study cited
Alcohol	Diet and metabolism	Medoza 1991
Geographical, nutritional, and others	Sickle cell disease	Medawar 1961
	Diltiazam-induced PR prolongation	Rubio, et. al. 1992
	Antipyrine metabolism	Lin, et. al. 1986, Henry, et. al. 1987
	Myocardial infarction rate	Robertson 1977
	Felodipine and nifedipine bio-availability	Baily 1991
Age, height and weight	Weight variations	Metropolitan Life Insurance 1980
	Age variations	World Almanac 1992, WHO 1992

Subjective differences

	Topics selected	Study cited
Medical practice	Dose administration, therapy preference, doctor-patient relationship, report of adverse effects, expectation of drug effects	No study cited
Adverse Effects	Monitoring	EU study 1993
Policy	Efficacy versus safety, tolerance of adverse effects	No study cited
Terminology	Names and definitions of diseases, range of hypertension, description of syndromes, expression of pain, religious beliefs	Dziewanowska 1992, Cannon 1957, Zola 1972, Eisenberg 1973

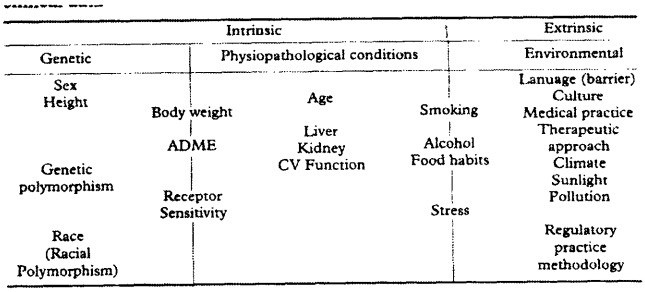
Dose arrangement	Different concerns on efficacy, safety, toxicity, etc.	Edwards 1993, Papaluca 1993

Source: Adopted from ICH2 E5 EWG 1995[1994]: 286-289.

The EU and U.S. experts knew this problem, but they did not know how to solve it. Even after intensive revision, as shown fig. 4.1, there were still many factors. Originally the EWG members considered having an anthropological investigation before the discussion continued, yet ultimately this was not realized (Uwoi 1998a). Furthermore, it was noted that if the topic of racial difference was delayed, it would need to be considered within all the completed guidelines, such as E1 (population safety exposure), E2 (clinical safety data management), E4 (dose-response information), E6 (GCP), and E7 (studies in geriatrics) (ICH2-E5 EWG 1995[1994]: 285). This development realized Naito's prediction for ICH2: E5 was an issue encompassing everything.

The E5 met a deadlock. There was indeed a growth of knowledge on race, yet no substantial progress was made. To address too many factors meant to address nothing. Things seemed to go back to the original point and everyone fell into deep frustration and distrust. Etienne Labbe expressed to me his sense of powerlessness: "I was alone in EU ..., nobody wanted to take care of this difficult topic. ...I read a lot of papers to try to identify those 'ethnic factors' that could explain the differences and preclude the acceptance of high quality Western clinical studies, and prepared a table today attached to the GL [guideline] E5. Many factors are mentioned in it, but, except for some rare cases of genetic differences, no one really impacted the clinical data but one: THE CULTURAL DIFFERENCES" (emphasis original).

Fig. 4.1. Intrinsic and Extrinsic Factors Concerning Ethnic Difference in the Acceptability of Foreign Clinical Data



Source: D'Arcy and Harron eds. 1996:435.

On the other side, Naito complained about the rudeness of the global pharmaceutical industries: "They only wanted to waive all required clinical trials that should be done in Japan before going to the market. It is very unscientific and I cannot stand it. I do not know why they hesitate to do clinical trials in Japan." He commented on the attempt to make these racial factors clear: "The fact that the racial differences are resulted from factors other than genetic differences, in contrast, became an overwhelming hindrance to the harmonization" (ICH-Japan Study Group 1995: 137). He thought that in such circumstance, guidance, not a guideline, was the best solution, because "we thought we were facing up to very difficult problems to be solved by the time of ICH3, which was, at that time, supposed to be the final ICH meeting" (D'Arcy and Harron eds. 1996: 424). Naito recalled what he really thought at that moment: "As a rapporteur of the E5 EWG, I was ready to accept if no agreement was achieved."

Bringing Science into Politics: Making a Guideline Workable

At this point, all scientific attempts had proved to be failures. The MHW had ceased studies on external factors, and the EU had already stopped earlier. However, the research on these factors at least clarified the standpoint of each regulator and was written into the third draft of the guideline. The MHW would accept PK data with restrictions and promoted simultaneous phase II and phase III clinical trials based on Japanese, black, and Caucasian populations. Focusing on administrative integration, the EU tried to limit these factors to a manageable amount. The FDA, which seemed to be an arbitrator than an appealer, always focused on the quality of clinical trials but not geographic variations. How could they get the dialogue going? The old framework of negotiation that had torn the clinical trials to pieces seemed not to work anymore.

On the other hand, although the JPMA's attitude toward the acceptance of foreign data was ambiguous,[33] the global drug companies became impatient. Most of them were really not interested in a scientific understanding of racial differences; they just wanted to have a predictable guideline for their application processes. For example, the U.S. ICH Steering Committee Chairman Alex Giaquinto suggested an administrative solution of a "regulatory floor," an explicit statement of the minimum requirements for interregional approvals. The PhRMA also prepared for a situation in which not all drugs would be

[33] One senior expert told me that they did not really care about the domestic market, but neither did they hope it would be easily penetrated. For a typical response from Japan, see Koyama's comment in the ICH3 in D'Arcy and Harron eds. 1996: 452.

granted waivers for clinical trails. It commented, "We are left to deal with the paradox that some, but not all, compounds may prove to have clinically significant inter-ethnic differences" (D'Arcy and Harron eds. 1996: 434).

This concession inspired the EWG to search for new negotiation frames based on the above table of factors concerning racial difference. Two transitional proposals were subsequently submitted. The first strategy, as Uwoi Tohru recalled, was a decision-making tree. It could be described as a final attempt to save the old framework by rearranging the external and intrinsic factors into a flow chart by which decisions could be made. It was to be used to judge which part of a clinical trial was racially sensitive and therefore when additional trials were required. Starting with PK testing, crucial factors were singled out, such as the PK curve (linear versus non-linear), metabolic pathway (ethnically sensitive or not), the effective range (wide versus narrow), and so on. However, as might be expected, the chart grew into an enormous tree as the discussion continued and became too complicated to manage.[34]

The second and better-known strategy was "triage." It first appeared in the second draft in October 1994 and lasted until ICH3. Unlike the decision-making tree, which still tried to waive some trials for each drug, the "triage" strategy tried to "save" some drugs from repeated local trials by evaluating their characteristics. If the NCE was concerned about racial effects, additional clinical trials could be required when drugs were marketed in other places. The table concerning racial difference functioned here as a map that could locate those drugs that would be subject to additional clinical trials. The determining characteristics were summarized by Naito as follows: 1) the characteristics and usage of the drug and modality of therapy (long-term or short-term use; administered orally or by intravenous injection); 2) the dose response in different populations; 3) the developmental status or stage of the drug; and 4) the intended population to be exposed to the drug (D'Arcy and Harron eds. 1996: 425). Although this strategy was practical in that it minimized the number of drugs that would need more clinical trials (or maximized the number of drugs that needed no further trials), it met with difficulties. From a technical point of view, since the characteristics were different from one product to another, it would be impractical to list all possible conditions in a guideline.

On the surface, it seemed that no scientific guideline could be made. However, these strategies should remind us of the political nature of guidelines. It is not necessary that a guideline describes the truth; it must merely address the way people create a social consensus called "truth." Up to this point, the EWG had wished for an explicit guideline

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[34] Some of these judging points are listed as shown in the appendix D of the E5 guideline.

on racial difference because they expected that it could be operationalized precisely. However, it was unrealistic to try to come up with such a rule among people who were conceptually divided.

It was Roger L. Williams of the Center for Drug Evaluation and Research (CDER), FDA, who saved this negotiation by bringing up the concept of bridging studies. This successfully released the tension caused by the cultural differences over race. Naito recalled, "Yes, I remember clearly the day when I was asked about the concept of bridging study by the FDA, I told myself that it was just what we pursued." Of course, at that time the EWG faced huge pressure from the Steering Committee, which needed to take over the job if no progress was seen (Uwoi 1998a). However, this did not mean that EWG members finally found the ultimate answer to the problem of racial difference. On the contrary, the bridging study was the event that ended this hopeless scientific pursuit.

The notion of the bridging study was first mentioned in the fourth draft of the guideline, where it was conceived "as a study to generate the necessary information to permit the extrapolation of the phase III efficacy data to the region's population" (D'Arcy and Harron eds. 1996: 425). At first glance, it was an improved version of the "triage" strategy—when local agencies suspected that a drug might have racially specific effects, they could require the producer to provide additional data using local subjects. In reality, however, this was a political compromise that satisfied the cultural imagination of race on all sides. Unlike the triage concept, where the criteria for additional trials were predetermined, in the bridging study scheme local agencies reserved the right to order them. While industry appreciated this strategy, assuming that no more clinical trials would be required if their applicant drugs showed no racially specific effects, the MHW accepted it for different reasons. Having failed to secure a requirement for local clinical trials for every drug, it considered the bridging study a "redemption" whereby small-scale trials specifically for the Japanese could be requested (ICH-Japan study group 1995: 137). Philosophically speaking, considering the cultural division over conceptions of race and state, the bridging study carefully marked the territory where the ICH could regulate the matter of racial difference by turning it from a problem to be solved into a manageable question.

Some struggles were seen at ICH3; some representatives wished facilitation of the triage strategy and others argued that there would be intentional barriers set by regulators. Even so, the concept of bridging studies basically began to prevail. One pharmaceutical representative commented to me cynically that the bridging study compromise was just a new form of the Japanese-style clinical trial (i.e., keeping some clinical trials done in

university hospitals in Japan under the supervision of senior physicians), but the Japanese felt hurt as well. For example, Uwoi Tohru complained to me that it was not until the advent of the bridging study that the global pharmaceutical companies correctly used the word "extrapolation." "Before then, all the so-called strategies were only applied for waivers," he added. He was right. People were not satisfied with the bridging study concept, but it was the best they could get.

Table 4.6 Definition of Extrinsic and Intrinsic Factors of Racial Difference

Factor	Definition	Example
Extrinsic racial factors	Factors associated with the environment and culture in which a person resides. Extrinsic factors tend to be less genetically and more culturally and behaviourally determined.	Includes social and cultural aspects in the region such as medical practice, diet, socioeconomic status, and particularly important to the reliance on studies from different regions, practices in clinical trial design and conduct.
Intrinsic racial factors	Factors that help define and identify a subpopulation and may influence the ability to extrapolate clinical data between regions.	Includes genetic polymorphism, age, gender, height, weight, body composition and organ dysfunction.

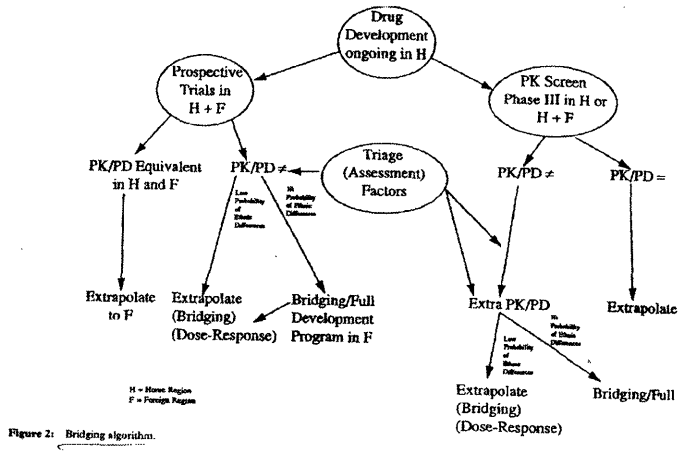
Source: Adopted from the ICH E5 guideline.

All previous strategies were wrapped up in this new scheme; the bridging study was thus described as if it was the product of a coherent, scientific narrative. We witness the bridging study's birth at the ICH3 proceedings. The categories of "extrinsic" and "intrinsic" factors of racial difference remained as the first criteria by which to judge whether a product was racially sensitive (table 4.6). Following the first evaluation (mainly PK and PD information), questions were asked to confirm which trials had to be repeated in phase II and III stages. Here the concept of a decision-making tree and triage were preserved, as shown in fig. 4.2. The bridging study was used when no waivers could be applied. Where requested, smaller trials would be arranged (Koyama 1999: 59).

The drafting of the guideline proceeded smoothly (a list of EWG meetings held after ICH3 is shown in table 4.7). The sixth and seventh drafts, which almost reached Step 2, were criticized for being confusing and unclear (D'Arcy and Harron eds. 1996:

431 and Naito et. al. 1996), but it was soon realized these drafts were as clear as could be conceived. Much bargaining took place on this point. Japan argued that bridging study should apply to tests in phase I and phase II. Furthermore, in some cases it required a larger sample size for bridging studies. On the other side, the FDA did not want to accept Japanese data because its quality did not meet their "comfort level." In addition, PhRMA asked Japan to limit the number of bridging studies to only one per product (for the "ceiling policy"; see Naito 1999: 6-7).

Fig. 4.2 Bridging Algorithm Model



Source: D'Arcy and Harron eds. 1996:439.

These conflicts, although painful, reinforced the necessity of the bridging study approach.[35] When the idea of a clinical data package appeared in the tenth draft as the criterion for determining when a bridging study was required, the triage concept became history (Naito et al. 1997).[36] Step 2 was finally signed off in March 1997, and the final draft was announced at the ICH4 that November. As these drafts clearly state, the guideline "is not intended to alter the data requirements in the new region; it does seek to define when these data requirements may be satisfied with foreign data" (D'Arcy and Harron eds. 1996: 431).

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[35] The conflicts were also related to the discussion over good clinical practice (GCP, E6 guideline) in Japan; however, since this requires more discussion, I choose to leave these for a future study.

[36] The term "clinical data package" here refers to the clinical data on test drugs required for the evaluation of whether they have racial effects. Yet the idea that it should be "complete" aroused heated discussion at the birth of the E5 guideline. The Japanese thought it would imply that no bridging study could be required if this data was claimed to be "complete."

Table 4.7 Timeline of the Discussions on the E5 Guideline, 1995-1998

Time	Event	Achievements
November 1995	ICH3 in Yokohama	Draft 7 formed; bridging study approach confirmed
January 1996		Draft 8 circulated (full side phase III was asked by the MHW)
April 1996		Two corrected versions (draft 9 and draft 10) derived from draft 8. Complete clinical data package proposed
May 1996	EWG meeting in Virginia	Draft 11 and draft 12 formed (triage concept dropped)
July 1996		Draft 13 and draft 14 circulated (bridging study limited to one per product)
September 1996		Draft 15 circulated
November 1996	EWG meeting in London	Draft 16 circulated (bridging study related to safety required)
March 1997	EWG meeting in Narita	Draft 17 circulated; the step two reached. Draft 19 formed
November 1997	ICH4 in Brussels	Draft of the E5 guideline announced
February 1998	EWG meeting in Washington, D.C.	Draft 20 formed; step four reached
August 1998		E5 guideline implemented (draft 21, the final version)

Source: adopted from Koyama 1999:58, Table 1, and Naito et al. 1997.

The final implementation of the E5 guideline in August 1998 marked the temporary end of the long journey of racial difference back and forth between the realm of science and politics. Of course, the ICH is a rather a scientific, technology-oriented forum and not really a politically driven one like the trade-oriented MOSS talks. But this does not mean that all cultural controversies and prejudices could be properly settled. On the one hand, the E5 guideline favors industry: as pharmacologist Helene Dumitriu pointed out, the guideline should just be called "acceptability of foreign clinical data," since "it aims to overcome obstacles to using foreign clinical data (whether they represent genetic differences or differences in medical culture)" (Dumitru 1998: 142). On the other hand,

however, we see resistance from local authorities: as Uwoi mentioned, it was helpful that the members of the E5 EWG realized that "[the bridging study] required the accumulation of administrative experience among regulators" (Uwoi 1999: 48). So after all, what had been divided was still divided.

The E5 guideline, as a product of political bargaining, hides all quarrels under a superficial harmony. It provided Europe and United States with feasible ways to make "extrapolatable" racial data that travel across different regions; meanwhile, it satisfied the MHW's nationalistic agenda by giving it administrative privileges to decide whether Japan would like to join the global. From this perspective, the guideline should not have worked for each side given this self-conflicted aspect of its nature, but this was not quite true. This is the theme of another chapter, in which Taiwan's encounter with the global is addressed.

CONCLUDING REMARKS: RACE, DRUGS, AND THE INSTITUTIONAL VOICE OF THE NATION-STATE

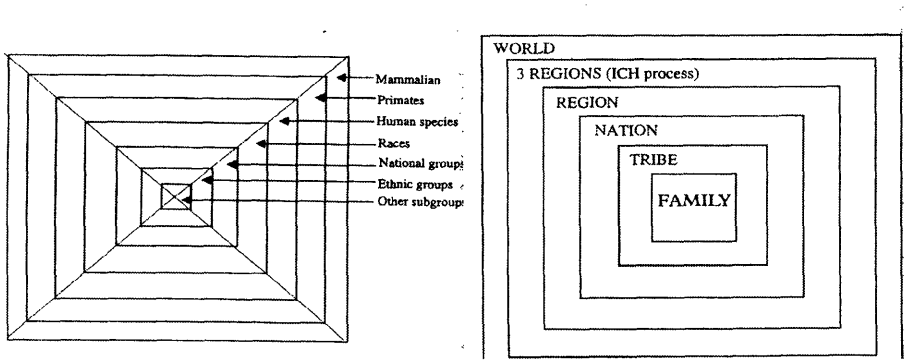
In ending the story about the birth of the E5 guideline, perhaps we should ask, What can we learn from it? I summarize the three lessons we can learn from this selective ethnography of Japan and globalization. First, providing a concrete study case deepens our understanding of the cultural scheme of a world organized around the notion of "population." Second, focusing on the case of pharmaceuticals, the story of the E5 guideline defines two distinctive modes by which Japan encountered the bio-global. Only through the observations of a "slow motion" narrative can we catch the real-time responses of the local as it faces globalization. The third lesson is that ethnography offers a practical way of appreciating the voices appearing in this narrative. It tries to describe their characteristics as something other than a collection of individual voices, or as fictitious voices forged by the ethnographer, an issue I will discuss at the end.

Regarding the first lesson, let us return to the beginning of this journey, where I cited Donna Haraway's creative sketch of the three techno-scientific configurations of the world (mainly the United States) in the twentieth century. As a salient example of the mechanisms by which this world operates, this ethnography supplements Haraway's observation of the replacement of a configuration from the first part of the century based on an essentialist notion of "race" with a "scientific" configuration based on population that she links to the period from the 1940s to the 1970s. Having not yet moved on to Haraway's next paradigm, based on the hot concept of genome, the world of proprietary

drugs operated under a conception of population that utilized scientific tools, such as statistics and the frequency of genetic expression, to measure a population and define its behavior (Haraway 1997: 219-229). There seems to be an interesting "lag" between the formation of cultural norms and how these norms are practiced in reality, but I would assert for now that this is because of the technological nature of the biological/social units that construct the world of drug research, marketing and regulation.[37]

However, unlike Haraway, who turns to a study of the cultural norm of families as the basic unit of this socio-biological mess, this thesis takes a different approach, trying to understand the topologies of the biological/social units that construct this world. I have argued elsewhere that population is not merely a biological category; in some historical situations it can function as the foundation of a political entity (Kuo 2002). The discussion of racial difference at the ICH provides us with a good example whereby we can explore different topologies in the realms of biology and society and explain the fundamental divisions in concepts of race and society.

Fig. 4.3. Biological Classification of Populations (left) and Societal Classification of the World (right).



Source: D'Arcy and Harron eds. 1996:444 and 450.

Let me take for example Etienne Labbe's ICH3 presentation on ethnic difference and the harmonization of regulations. He listed two distinct and "arbitrary" classifications, one biological and the other societal, by which race and state can be defined (fig. 4.3). In the biological classification (left), race was located between the level of the nation and the human species. Thus, biologically speaking, race is a larger category focused merely

[37] In fact, as we will read later in chapter 6, there are uneven developments, even distinct routes though which each state moves from one configuration to another in terms of biology and society. Using the ICH as an example, the originality of this ethnography partially resides in its attempt to reveal the complicated nexus where these routes cross at the global level, creating cultural and ethical conflicts that are neither essentialist nor constructionist.

on biological characteristics. In the E5 discussion on "racial" as compared to "ethnic" difference, Labbe stated that "'ethnic' may be more adequate since it covers genetic and cultural aspects, defining a more homogenous sub-population than 'race' does" (D'Arcy and Harron eds. 1996: 443). As we know from the previous discussion, this interpretation fits with the FDA's approach to the consideration of racial difference in clinical trials.

However, when moving to the societal classification of the world, which showed the harmonization the ICH hoped to achieve, we see contradictions. The goal of the ICH, according to this diagram (right), was to seek administrative integration between the level of region and that of the world. It made perfect sense for Europe, since at beginning the EC [EU] used this approach to harmonize regulations among its member states. After the United States and Japan joined this discussion and formed a global platform for the discussion of racial differences, it still worked, for race could be interpreted as a larger unit beyond the state. It just added some more states into discussion (for the purposes of the harmonization talks, the U.S could be considered a region consisting of many states and Japan a state). However, when EWG members decided to work out ethnic factors, they met with problems. They had to take local factors into account, thus making the state not just an administrative unit, but a carrier of biological characteristics (as referred to by the category of "nation" in the biological topology). All this made a mockery of the pursuit of a scientific guideline and administrative integration.

On the other hand, Japan held to only one topology, both biological and social. Borrowing Labbe's classifications on the biological side, the MHW fused ethnicity, nation and race into a single unit, "the Japanese," and on the sociological side it collapsed the level of tribe into that of the state, which was represented as a "region" in the ICH. The two classifications could thus be interchanged within the unit of the nation-state, which comprised both an administrative organization and a collective population sharing the same biological characteristics.

From this perspective, the differences between Japan and the West may be as subtle as those concerning the conceptual scales by which conceive the state and race in relation to each other. However, while Labbe tried in vain to persuade his colleagues of his views, the problem of the scales resided in conflicts arising from the fact that, as suggested by anthropologist Marilyn Strathern, "what appears in one society as a focus of significance, a key artifact, in another can be 'an accessory activity'" (1991: 74). These conflicts are also seen in the MHW's appeals to the West. While the MHW hoped to deal with the state and race together, the other parties drove the discussion in the opposite direction. Perhaps we need not follow Strathern's philosophical discussion about which epistemology anthropologists should stand by in their works; however, we should keep in mind the

practical problem she reminds us of. She writes, "The anthropologist's contexts and levels of analysis are themselves often at once both part and yet not part of the phenomenon s/he hopes to organize with them. Because of the cross-cutting nature of the perspective they set, one can always be swallowed by another" (75). Conventional interpretations of the making of the E5 guideline fall into this exact trap. Like Marcel de Serres in the nineteen century, the ICH attempted to operationalize the primary unity of human races by imposing its viewpoint (or context) on local agencies. When this strategy failed, as shown in this chapter, the practical approach of bridging studies eventually arose. With this result, however, European and U.S. experts accused Japan of playing politics. However, if these misunderstandings stem from a conceptual division over definitions of race and the state, how can we judge whether one side is more scientific than the other?

At this point, this ethnography tries to give a "symmetrical" or "fair" interpretation to Japan's behavior, which is the second lesson we can learn from these events. Although this chapter does not differ much from previous studies of the Japanese, utilizing concepts such as the dialectics of difference that tends to split the Japanese from the rest of the world, it does reject non-anthropological and Western-centric accounts that portray the Japanese as conservative, closed off, and always rejecting globalization, or as selfish economic animals that pay no respect to the rules of the free market. Using the case of pharmaceuticals, this chapter carefully traces the process of Japan's encounter with the global, presenting a totally different scenario from conventional discourses, which only blame Japan's protectionism.

This chapter identifies two modes of this encounter, one bilateral and the other global. The dynamics of the encounter moves from strictly business to science and cultural values. The bilateral mode started with the needs of the global drug industry, as described in Chapter 2, to exploit as much market as possible before the patents on their products expire. Drug companies attempted this through the United States, the world superpower. For this reason pharmaceuticals were listed in the MOSS talks, the most important event in 1980s U.S.-Japan relations. Obviously, MOSS was a difficult channel for dialog. In addition to the trade friction reviewed in Chapter 3, this chapter points out that the polarized imagination of the differences between Japan and America does not belong to Japan exclusively. All these prejudices confirmed policy analysts' expectations about the difficulties these negotiations would face. However, negotiations over pharmaceuticals presented an exception; because of the participation of the "non-political" MHW, the negotiations were quickly settled. From their perspective,

drugs were not a business for profit, and there was no responsibility to promote or protect industry.

The MHW went further and helped form the ICH, a true global stage that gave Japan a chance to move away from its normal relationship with the United States. Compared to the MOSS talks, the ICH was less political because it avoided the direct involvement of governments. The MHW had enough reasons to join the ICH; the "harmonization" of the title echoed well Japan's cultural values and in practice it fitted well with what Japan was seeking from globalization when its economy peaked in the postwar era. Only through this can we understand why Doi dared to make the issue of racial difference a topic for discussion. Even so, the ICH did not guarantee that science could build a standard acceptable to both Japan and the West. The second part of this chapter identifies the limitations of science. The point is, whose science should be chosen in judging racial difference? At first, polarization seemed to return, but this time due not a political prejudice but to a cultural division, with Europe and the FDA on one side and Japan on the other. It was this division that resulted in a failure to make a purely scientific guideline. In the end, superficial harmony was achieved at the cost of clarity.

Of course, the Western experts and industry people I have talked to blamed the MHW's ambiguous standpoint for this failure. Just as I have read in many books about Japanese mentality, these individuals said that the MHW was hypocritical in its negotiations. In their opinion, the Japanese attitude toward racial difference at the meetings was always changeable and uncertain. Basically, I do not agree with this account. I know that the Japanese seldom express their true feelings to foreigners, and there is a distinction between "principle" or "standard" (*tatemae*) and "real intention" (*honne*) in their social practices. Even so, I do not think it is appropriate to make an easy link and reach a subjective conclusion that cooperation at the ICH was Japan's *tatemae* and closing its market to the world was its *honne*.

I agree that at the ICH the MHW did not insist on some issues, such as the category where racial difference belonged. As discussed in Chapter 3, the Japanese wanted to include it in the category of safety but not in efficacy, but representative Naito did not insist. He said, "E5 later developed into a complex topic independent from others in that category. As it went, which category it belongs to meant less and less for us." But, except for these minor issues, the MHW's standpoint on racial difference was firm and consistent: as the nation-state of Japan, Japanese people should be considered separately from other races. The bottom line for harmonization, as seen, was PK testing, and the MHW accepted this long before the formation of ICH. If there is a problem of communication, it might have resided not in whether Japan was willing to speak its need,

but in whether its voice was clearly heard.

The significance of the institutional voice, as I have reviewed in Chapter 1, is the third and last lesson this ethnography hopes to offer. Here I shall define three formations of voice that can be heard in this ethnography. First, on the dialogic level, Japan did have a clear voice, if we listen carefully. Before getting involved in this field, I could only hear interpretations from one side. However, my fieldwork enabled me to hear voices from the other side as well. In fact, despite the industry people blaming the MHW for being obscure in its opinions, the MHW's standpoint was clearly stated in local material. Although this does not mean that fieldwork can help us to approximate reality, it does help me to know better the context in which these voices argue against each other. As shown in table 4.9, each side had its own interpretations of the issue and the way it was settled; in such a case, these opinions and strategies should be considered as institutional voices.

Secondly, as stated in Chapter 1, a conference is a structured conversation, and this was especially so of the ICH. The second part of this chapter nicely demonstrates this characteristic. After the Steering Committee accepted racial difference as a topic for discussion, it was moved to the EWG meeting, where all subsequent debates took place. In addition, the process of discussion in EWG, as mentioned previously, had to follow the ICH procedural rules. Thus, as we can see in this chapter, each round of discussion covers several meetings and the change of topics can be easily traced through the drafts. In other words, the different institutionally voiced opinions as can be heard through archival studies of these meetings and interviews based on these documents.

However, the above characteristics are not specific to Japan. They can also be applied Europe or the United States. What is specific to Japan's institutional voice is the way its opinion on racial difference was presented. As seen in this chapter, I did collect some individual voices to support my observation, but basically these voices are as coherent as if they were spoken directly by the institutions the speakers represented. Of course, cultural consensus played a big part in this phenomenon, but there are still structural factors worth considering. First, in the case of E5, there were in fact fewer people involved than we might think. The MHW organized teams for the ICH topics that consisted of experts (*senmonka*), usually professors from the national institutes and teaching hospitals, supported by the MHW and led by a high-level administrator (*jimukan*). In the case of efficacy topics, Naito Chikayuki led the invited experts; the *yakkeigikan* involved were Kurokawa Tatsuo and later Tominaga Toshiyoshi. Although Doi Osamu was the official leader of the MHW delegation, the delegation itself was

highly fragmented—basically, each team worked independently. In a parallel with Sheila Jasanoff's keen analysis of the role of science advisors in U.S. policy making (Jasanoff 1990) in Japan senior physicians enjoy absolute power in determining medical policies. A JPMA scientist told me that in the case of E5, Dr. Naito's opinion was the opinion of the MHW.

In addition, the E5 team had *yakkeigikan* as its members. As mentioned before, *yakkeigikan* are a new species in the government, but their origin should be understood in the larger context of Japan's bureaucratic culture. Japan is a country run by a remarkable bureaucratic body that determines almost all its policies. Thus for those elites who want to work for the government, being and working as a bureaucrat is a life-long training process. *Yakkeigikan* belong to this group. In addition to the usual training received as bureaucrats, they are sent to short-term programs to update their knowledge of specific areas. They are capable of coping with the system and the knowledge that is discussed. In short, they are small, homogeneous group. As Kitakawa and Kainuma observe (1985), they were self-controlled and disciplined, repressing their individuality in order to promote their national values (167-170). As globalization came, they gained the power through the mechanisms of *bachigai* and *gaiatsu* pointed out by Sharon Traweek (Traweek 1996).[38] Like high-energy physicists, these technocrats used the *gaiatsu* of the ICH in the name of internationalization (*kokusaika*) to gain the power to issue drug regulations. They worked at the margins of two empires: the global conference dominated by the FDA and the PhRMA, and the Japanese bureaucracy led by physicians and medical officials. All these factors created in this group of people a unified reformist voice; the absolute safety of drug used and the health of Japanese nationals was what these technocrats defended.

Though I am not sure whether he knows it, I see all these institutional characteristics in Tominaga Toshiyoshi, who became Director of the Fundamental Research Promotion Division, R&D Promotion Department, OPSR. It was a mid-summer evening in 2003; I was just about to wrap up one of the longest interviews I had done in Tokyo with him, and it had been pleasant. He talked with confidence about how the *yakkeigikan* had improved the primitive good clinical practice (GCP) regulations, the policy to promote the contracted research organization (CRO) industry, and the ICH. However, when I asked about the E5 issue, he was reluctant and not as confident as before. He seemed to be deciding what he should tell me. Finally, he spoke: "It is a sensitive issue, really. Many people were involved and we fought very hard, some from

[38] The original meaning of *bachigai* in Japanese is the situation of feeling improper or out of place. Here it indicates the difficulty of categorizing some individuals in Japan due to their overseas experience.

inside and others from outside. We were independent and followed science always," he tried to assure me.

"But, what was your opinion?" I asked. "How did you figure out your existence as an individual alongside this bureaucracy?" I emphasized the word "individual."

Tominaga seemed not to expect this question. He looked at me for a while, and replied: "It is the MHW's responsibility to protect people's health even when they are not aware of the danger. People live in trust of the government."

Although this statement was well-spoken, it was not the answer to my question, and I knew it. "It's getting late. Perhaps we can talk over this topic next time. Thank you so much," I concluded. Yet Tominaga did not reply. With his back to the setting sun, he sat in front of the window and his shadow covered me. A voice came slowly from the dark: "Do you really think that a technocrat cannot have his individuality?" I was stunned. As a foreigner, I had not thought of this either. "I have no idea." I repeated, "I do not know, really."

Chapter 5
Countermelody in a Fugato Called "Bridging": Taiwan Catches up with the ICH

> What clearly is left out of this un-historical historiography is *the politics of the people*. ... This was an *autonomous* domain, for it neither orientated from elite politics nor did its existence depend on the latter. ... The ideology operative in this domain, taken as a whole, reflected the diversity of its social composition.... However, in spite of such diversity one of its invariant features was a notion of resistance to elite domination.
>
> Ranajit Guha[1]
>
> I have to voice, for only my own voice can prove my existence.... It must be me [who would vanish] otherwise. I would be blown by a burst of squalls, like a match [flame], from any direction. Just that easy.... My voice proves my existence, therefore I keep voicing, continuously.
>
> Ji Xian[2]

PART I
LIVING PEOPLE, MUTED STATE: TAWIAN AND THE WORLD

The Politics of Voice in the Modern World

In Chapter 4 we witnessed a "dissonance" between Japan and the other ICH participants on the issue of racial difference. Although, like other dissonant notes, this discussion requires a "resolution" (a harmonic chord) according to classical music theory, my study has shown the failed approaches that attempted to reach it by simply eliminating other voices (i.e., making a unison of notes). This, as we now know, did not work with Japan and contributed to an unresolved situation—even the guideline that was made was vague. However, the story did not end there as some policy analyst of U.S-Japan relationship might suggest. As we will see, when Taiwan joined the debate it turned the situation into a fugato, a more complicated musical form in which every melody is independent in its content yet combined with the others forms a common theme. This chapter is thus an ethnographic effort to find this lost melody that will refresh our understanding of the fugato called "bridging."

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[1] In Ranajit Guha 1982, "On Some Aspects of the Historiography of Colonial India," pp. 840-41.

[2] "Wo de shenyin yu wo de cunzai" (My voice and my existence) from *Sansi Chienji* [my first thirty years: a collection of poems], 1945.

But first we have to know how Taiwan can express itself, given its difficult political situation described in Chapter 3. It is not a fortuity for an anthropologist to read subaltern studies if she or he is keen to understand the politics of people's voices and how they are treated in historical narratives. This field is well articulated in the manifesto of Guha, the key founder of subaltern studies, which I quote above. As we know, subaltern studies is an academic discourse as well as a cultural formation that originated in the rejection of conventional interpretations about the independence of India and its political consequences. The histories projected by these interpretations, which Guha criticizes, were based on conceptions of colonialism and nationalism that were dominated by colonists and elites. In order to resist this domination, the project of subaltern studies set its course by calling attention to the peasants whose voices were missing from these narratives.

The early works of this school of thought provided convincing evidence of the role of these people, though the way they were represented became an issue in later works. According to this emerging presence, the subaltern can be understood as a kind of collective individual, conscious of itself, an author, an actor—in short, the classical subject. This allows the subaltern studies movement to differentiate between the subaltern itself and the representation of it by imperialism, and thus calls attention to the blank spaces in previous discourses. Anthropologists can learn more from these studies. As the quote above indicates, Guha had no intention of making the subaltern either a "supplement" or a "counter-discourse" to existing historical interpretations. It is instead an agency that creates an *autonomous* discourse of politics in its own right. In this way, subaltern studies deviated from the banal approach of Marxism and "history from below," and the anthropological term "voice" is thus appropriate as a description of its intentions.

Inspired by subaltern studies, this chapter is an evocation of some of the missing voices in the discourses on science and politics concerning the ICH and globalization. Unlike Guha's resistance to nationalist and colonialist interpretations, my ethnographic motivation is an echo of Stephen Tyler's criticism of scientific discourse (or, if I may, "scientific centrism") that has preoccupied the modern world (Tyler 1986). "In the totalizing rhetoric of its mythology," he writes: "science purported to be its own justification within its own discourse, and the more it controlled its discourse by subjecting it to the criterion of proof, the more uncontrollable its discourse became" (123). We have witnessed, in the making of the E5 guideline described in Chapter 4, how the endeavor to make a universal standard for all human races succumbed to the various interests of politics and business. Since this is a tale of the modern world (or the postmodern world, in Tyler's terms) "allowing for certain intentional interpretative

liberties" (125), this chapter devotes itself to an ethnography of the scientific narratives that attempted in vain to make this guideline work.

Also, instead of dealing with a general category of people, as subaltern studies does, this thesis chooses Taiwan as its main character. It is of specific importance because, at the level of discourse, the voice of the Taiwanese people is definitely different from that of the state. As will be shown in this chapter, it is easy to access Taiwanese people's individual voices or various collective voices, and these are lively and undeniable. However, as a state, Taiwan resembles the last book in Ray Bradbury's fictional world of *Fahrenheit 451*; its existence is only recognized when the world tries to erase it from all discourses as if it never previously existed.

The most recent example can be seen in a World Health Organization (WHO) conference held in Phuket, Thailand, on May 3, 2005, about the reconstruction of South East Asia after the huge tsunami disaster in December 2004. As a state nearby, Taiwan did what it could to help the affected countries: it sent rescue teams and donated $55.72 million, the eighth largest such sum in the world. Even so, Taiwan was not allowed to participate in any of the conferences concerning the tsunami, and this is not exceptional. According to local sources (*Lianhe Xinwenwang* [UDN News], May 7, 2005), the WHO agreed that experts from Taiwan should join the post-tsunami discussion; however, after the Taiwanese delegation arrived, they realized this meant only their personal opinions and not their appearance *as a group*. They were like air—no name tags, no introductions when joining the discussion, no communication with WHO officials, and no record of their participation. If global conferences are a discursive stage for states, "The WHO ignored the existence of Taiwan; ... it did not even want to leave any trace about its participation," the newspaper commented.

The above situation is nicely illustrated by Ji Xian's poem quoted at the beginning of this chapter. Ji, recognized one of the influential poets in post-war Taiwan, wrote this existential poem as a thoughtful response to political uncertainties, and it was brought up again sixty years later by President Chen Shui-bian immediately after the People's Republic of China (PRC)'s announcement of its threat to absorb Taiwan by any means, including non-peaceful ones.[3] Borrowing this poem, Chen indicated the cultural aspect of the problem of Taiwan's statehood; Taiwan is already an independent state; what is problematic is its legal existence as such in global society. Taiwan is an "illegal resident"; the PRC has been attempting to make this so by every means. Erasing Taiwan's voice is the first step, Chen emphasized; those who are repressed and treated unfairly and unjustly

[3] Chen addressed this poem in the opening ceremony of World Poem Festival held in Kaohsiung on March 25, 2005.

should make their own voices heard, firmly and steadily, for keeping silent and remaining passive helps the repressors justify their deeds.

As a Taiwanese who grew up and was educated on this island, I know from personal experience its absence from the political map of the world; however, it is an accident that relates its silent voice to the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). In other words, from the initiation of my investigation of Taiwan's involvement, its problem has been to be treated as an *autonomous* domain; Taiwan is not a necessary part to the accomplishment of the ICH's project, nor does it hope to change its situation through the ICH. Its "intrusion" into the discourse on the ICH and E5 guideline, I can see retrospectively, is rather an unwitting start on an odyssey to discover a writerly agency that has been long disregarded and to find the missing meaning of ethnographer whose craft is to make ethnographic text a "process-entity" or means for cultural critique. The rest of this section explains this journey.

In the midst of my fieldwork, I arrived in Taiwan in November 2002 and began lecturing at National Yang-Ming University (hereafter YMU). Not having intentionally chosen where or for how long I would stay, I found YMU to be a small yet interesting school. It is a research complex located in Shihpai, a suburban town north of Taipei, and it consists of about thirty institutes. Despite its short history, thanks to the take-off of Taiwan's economy and the government's decision to allocate more resources to medical care and research, this school possesses three characteristics that set it apart from the others in Taiwan: an intensive involvement in medical policy making at the national level, a huge investment in life sciences research, and a strong interest in pharmaceutical development and biotechnology.[4]

After spending several years away, Taipei was new to me. However, at the time I was not very interested in exploring the city because it was only a brief resting place on my academic journey. In a few months I would either return to Tokyo, my field site, or to Boston, where my intellectual home is located. After completing my duties at school, I spent a lot of time in the dormitory, reading field notes and writing paragraphs on my observations on Japan's health care and business. The first semester finished, but I was still in Taiwan; the time passed so slowly, as if it could stop forever. Like Hans Castorp in *Magic Mountain*, I started finding that I might not be able to return to Tokyo in the near future. I decided to attend two courses on medical policy and the biopharmaceutical industry. I said to myself, since I was in Taiwan now, why not make the best use of the

[4] For a discussion of the importance of the National Yang-Ming University in the context of the history of modern medicine in Taiwan, see Kuo 1995.

place?

During the next term, I attended Professor Huang Weng-Foung's research seminar on pharamcoeconomics and health policy and a series of lectures on current trends in biopharmaceutical development organized by Professor Tien Weichen. Both seminars were policy-oriented and distinct in their formats. As the former Director General of the Bureau of Pharmaceutical Affairs (BPA), Huang strong-headedly and powerfully led discussions. In contrast, Tien, who had long served as the president of the Development Center for Biotechnology, showed his good connections with industry. Many CEOs were invited to give lectures, making this seminar a must for people who wanted to know the latest about biotechnology and its possibilities in Taiwan. Basically, I participated in Huang's reading seminars frequently and went to Tien's from time to time, depending on the topic. They spoke, and I listened.

I had not expected the information and reflections that these seminars gained me. Concerning the core of ethnography, Stephen Tyler points out the function of the interaction between speakers and hearers:

> Every act of saying is a momentary intersection of the "said" and the "unsaid." Because it is surrounded by an aureola of the unsaid, an utterance speaks more than it says, mediates between past and future, transcends the speaker's conscious thought, passes beyond his manipulative control, and creates in the mind of the hearer worlds unanticipated. From within the infinity of the "unsaid," the speaker and the hearer, by a joint act of will, bring into being what was "said." (459)

This was not the case for my fieldwork in Taiwan at the time, since I was a passive listener at the beginning. However, as this chapter shows, the more I listened, the more I found that was interesting to know. From this ambiguous situation of saying and listening, my ethnographic journey departed.

Outside of the Global: Huang Weng-Foung, a Veteran Technocrat

In a seminar room at the Institute of Health and Welfare Policy, Huang Weng-Foung opened his lecture on international health policy by sharing his long dream of working with the WHO, where his mentor Hsu Tsi-chou served at the Office for the Western Pacific Region from 1970 to 1979.[5] As one of the Ph.D. bureaucrats appointed and

[5] Hsu Tsi-chou (1920-1986) is one of the key persons who established Taiwan's public health system. His life and career also reflect many aspects of the ways Taiwanese intellectuals cope with their self-identities. He was born in Tainan. Like many Taiwanese elite under Japanese occupation, Hsu went to Japan and studied medicine at the Imperial University of Kyoto. After graduation he moved to China, working at a Japanese hospital during the Sino-Japanese War. When the war ended he was enrolled in the

promoted by that veteran of international health, Huang presents the typical image of an elite technocrat hugely influenced by the maverick Hsu Tzi-chou. Before moving to this school, he had worked for the DoH for over fifteen years.

"This is the way I start a day," Huang said. "I get in the office and go to my desk, on which the computer is central. I turn it on and click the icon, and out pops Explorer, where the homepage has been set to http://www.who.int—you know, the website of the WHO." Like a stock analyst does with the *Wall Street Journal*, Huang browses the latest news at the WHO everyday, even more than once a day sometimes: what are the ongoing projects in the Western Pacific Region, who will take charge of them, where is a disease epidemic breaking out, etcetera. Huang sighs and worries with the WTO; he rejoices at what they achieve and comments on what goes wrong, as if he is the person in charge. "Just like watching shows," Huang stated. It seemed to be an odd opening for a lecture about international health. Instead of sketching the scope by which the international health should be defined and the issues covered, Huang started with a self-confession, something trivial and common enough that people would not normally think about it. "Does this have something to do with finding a job at the WHO? Does it have anything to do with international health?" I asked the student on my right.

Later I learned that it was a thoughtful opening with pedagogical goals. In fact, Huang has used this anecdote on many occasions when speaking about Taiwan's participation in world health. The fact is, for the Taiwanese people, it is just not possible to access global organizations such as the WHO, and Huang knows this well. In fact, Taiwan has been completely cut off from this organization, as one of eighteen U.N.-associated organizations, since 1971. As a medical student, Huang witnessed all the consequences of this, the first and most immediate of which was the halt of all formal contacts and cooperative projects, including training programs. Then, except for the current working members, no new recruiting of Taiwanese to the WHO took place. Some Taiwanese kept personal connections with the WHO, but these ties faded and eventually

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Peking Union Medical School, where he received six months of training on disease control. Since Hsu can speak fluent Taiwanese, Mandarin and Japanese, he was soon selected to serve in the government when it moved to Taiwan with the defeated KMT. He was also selected as one of the first group of Taiwanese to study in the U.S., where he earned a master's degree in public health at Pittsburgh University. He served in different places after returning, and because of the international fame he earned for his role in Taiwan's family planning project in the 1960s, he was invited to the WHO Regional office two years before Taiwan was expelled from the organization. During his nine years of service at the WHO, Hsu helped to spread the "Taiwan experience" to countries suffering from overpopulation and poor rural health. Even so, he was forced to step down from the position, and he returned to Taiwan when the PRC opened its door to the world. His was appointed as the first Minster of the Department of Health with high expectations, and he successfully trained the group of technocrats who became Taiwan's public health policy makers. Hsu died of liver cancer in 1986.

disappeared in the early 1980s.[6]

As a result, information about Taiwan was dropped from all global health figures. Although the government kept updating all the statistical data and made them the same as those used in other WHO member states, these data are just "missing" from all WHO statistics and the subsequent circulation of knowledge. I really mean missing, because the information on Taiwan is not absorbed or incorporated into the information on the PRC. The PRC is unable to obtain the latest data for practical reasons—to do so would entail recognizing Taiwan as an independent political entity. Taiwan became a state that had been erased from the information maps of the world, such as the annual *The World Health Report*.[7] Nobody knows how large it is, where it is located or what its population is. On the other hand, the world is "ignored" by Taiwan, a self-satisfied state. No complete information on any WHO member country, including the PRC of course, is available in any library on this island.

In addition to the cruel isolation, which can be seen in other fields as well, Haung's ironic lament had implications closely connected to the historical context. This is not simply the complaint of a zealous fan of the WHO who, like a Red Sox diehard, continues to support her beloved team even though she moved to Geneva from Boston ten years ago. Huang's behavior can be more accurately explained as that of a Taiwanese nationalist suffering from "phantom limb syndrome." Originally called "hallucinated limb," phantom limb syndrome became widely known to physicians when about 6,000 amputees returned from World War I. Research suggests that 70 percent of amputees continue to experience sensation as if they still had the lost arm or leg. Some amputees even believe their lost limb is still intact.

It is almost the same in the case of Taiwan's relationship with the WHO. Under the name Republic of China (ROC), it was one of the countries that founded this organization, and by the 1970s it had received substantial assistance with the development of public health. I have argued elsewhere that the result of the process was the reconstruction of a modern medical institution upon the Japanese legacy from before wartime further

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[6] According to Huang Pei-Yu's study (1996), 29 experts were employed on global projects for the eradication of malaria and other parasitic diseases, public health policy, family planning and nursing, mental health, and women's and children's health. These Taiwanese experts were not forced to resign or change their nationality after membership was taken over by the PRC. The reason for this, according to an expert, is because the PRC would not have been able to fill the jobs if all the Taiwanese experts had left. Also, the WHO hoped to retain a certain amount of experts who were familiar with China (112-114).

[7] To take Taiwan's population control as an example, although the U.S. Population Crisis Committee has twice rated Taiwan's program the best of all developing countries', Taiwan is shut out of *The World Fertility Survey*, *The Demographic Health Survey*, and other related medical data-gathering and analysis efforts under the auspices of the WHO. In addition, according to a Taiwanese expert who used to work at the WHO, the WHO destroyed all data on Taiwan from before 1971. See Huang 1996: 117.

strengthened by the international aid for problem-solving projects, such as the eradication on malaria and the population control program (Kuo forthcoming). As I have described in the Chapter 3, the "golden age" of public health in Taiwan had an obvious international component; in turn, the world considered Taiwan a good example of what was achievable in a developing country. At a personal level, these projects changed Taiwanese experts' vision about their role in the world. Starting with Hsu Tzi-chou, many technocrats trained post-war received scholarships to study abroad, mostly in the United States. Upon returning, they formed a group that shared a common vision.[8] From their training in the United States they realized the problems and knew the importance of cooperation with American experts; the success of these projects and the international fame provided the proof they needed.

However, all this has gone, and gone so soon that only a few people were even aware of its influence. Before the global outbreak of severe acute respiratory syndrome (SARS) in 2003, the WHO denied Taiwan's existence, trying to repress it into history. Having been isolated for so long, Taiwan seems to have forgotten how to link the WHO, the "lost limb" that once carried it out into the world, in order to return to the global. Huang portrays himself as a member of a generation whose careers had been changed by this loss. He admitted, "It is unlikely I will serve at the WHO, at least in the position I would like to serve in." He added when showing a photo of the current Director General of the WHO, Lee Jong-wook, "Lee was born in 1945, and is just a few years older than me. He started his career in the WHO in 1983, around the same time I had been involved in some governmental projects and was appointed as Director General of the BPA. After nearly twenty years of working experience in different global programs and regional offices, this enabled Lee to be elected as the leader of this big institution. Meanwhile, my work limited me almost completely to the domestic. I have lost the chance and am too old to catch up with him now."

Aiming at the highest position in the WHO, Huang is indeed ambitious and is proud of his abilities. Like other Taiwanese elites, Huang was born into a family of physicians and was well educated, earning a degree in pharmacology at National Taiwan University (NTU) Medical School a Ph.D. in hospital management at the University of Minnesota.

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[8] According to the WHO report (WHO 1988), since its establishment it has provided fellowships to physicians and public health workers in developing countries to study a specific topic in public health, such as epidemic control, health education, or health management. The budget increased by three times during the second decade of the WHO's existence (1958-1968) and achieved great progress by helping the receiving countries to train their own health personnel. For example, in 1960 there were almost no doctors in Congo, yet after sending 140 medical assistants to study overseas, by 1967 all positions in its health system were filled by locals.

His plan to head a hospital run by his family changed in 1978, when he was invited by Hsu Tzi-chou to return to Taiwan to fill a post at the DoH; at 29, Huang became the youngest section leader there. He soon built up a reputation in the field of good manufacturing practice (GMP) and drug pricing. Naturally, he was one of the government negotiators dealing with PhRMA. He found his true interest in policy and made the best of it. "Asia has increasing influence on the world other than [through the] economy. In the 1990s the WHO elected a Japanese Director General, Nakajima, and now a Korean. I believe I could do a better job than they have done, if I had a chance," he commented.

I started to understand what he was saying. The key concept Huang emphasized was chance. He admitted, "I never cover up the fact that Taiwan is not a *de jure* part of world health. We know it has been isolated for more than thirty years." Huang stared around the room and continued, "We do not want anything outrageous; we just hope to return the global and be treated like others." As I listened I looked around the classroom; the students felt the emotion yet did not seem to be persuaded. Apparently it was difficult for them to conceive of the vision their teacher was trying to create. The damage has been done. These students lacked contact with foreigners and the chance to work with them. But Huang continued, "That is why we need international health taught here." "I want to be international. The Taiwanese have to be international. Unlike other states, Taiwan's right to join international activities [*guoji kungjian*] is not taken for granted. We have to earn it with blood and sweat. Thus it is not only my hobby but also my duty to follow the WHO news as close as possible. Through the news I try to *live with* the global. In the following one hundred minutes I will show you the way by the world operates, and this will prepare you for the time [when] we prevail. I cannot tell you when or how, but I believe that it must come."

I doubted whether the global vision could be taught this way, but I have to say it was the most touching opening of any international health lecture I had ever attended. As Taiwan belongs neither to the category of the developed world, nor to that of the developing world, its public health problems should be considered in the context of global politics. The country is too rich to cry for help, yet it is not advanced enough to offer the services others can't. What Taiwan needs is just a position in world health of reciprocity; what it once possessed it wants returned. Thus a national movement to return to the global has arisen. Along with its democratization, Taiwan's campaign to rejoin the WHO has continued since 1997. This chorus expands year by year, attracting the public, scholars, and lately the government. It becomes a ritual-like movement for all Taiwanese that take place every year during the World Health Assembly, including lobbying events, protests, and bilateral negotiations with possible supporters.

Even so, the welcome Taiwan has earned is still thin. The outbreak of SARS illustrates well the problems that Taiwan has experienced in its efforts to join the global.[9] Taiwan has found a loophole-like entry into the global health network. During the SARS outbreak, Taiwan was excluded from the WHO's Global Outbreak Alert and Response Network and only received second-hand information from Center of Disease Control (CDC). Only after serious breaks in the disease control network caused by a large-scale nosocomial outbreak in April did the WHO reluctantly respond to Taiwan's requests and took the initiative to send specialists to offer guidance. Taiwan's experts were able to take part in a SARS-related meeting hosted by the WHO for the first time in the mid-May; all were designated "as permitted" by the PRC government as a "courtesy."

The PRC's failure in containing the epidemic has weakened its voice in the WHA when it opposes Taiwan's participation. The time of return seemed to have come. There was a mutual need to include Taiwan in the global. The consequences of the failures of SARS control in the era of globalization tarnished the WHO's image:

> The globalization of infectious diseases is such that an outbreak in one country is potentially a threat to the whole world. The need for international cooperation on epidemic alert and response is greater today than ever before due to increased population movements, growth in international trade and biological products, changes in methods of food processing, social and environmental changes. (Government Information Office ROC 2004)

SARS showed how serious it was for the WHO to overlook Taiwan: this country is a busy center for international trade and hosts more than 300 thousand people from South East Asia. Thus, because "*any loophole in this global health network presents a danger for the global community*" (emphasis original), Taiwan cannot be excluded from the WHO.

While waiting for judgment day, Taiwanese people felt excited and frustrated. The U.S. first showed positive support for Taiwan's wish, yet the PRC's disgraceful performance disappointed all who had eagerly hoped. Wu Yi, the PRC's Minister of Health, made a forceful speech that was considered insulting and cheating to the Taiwanese at the General Committee of the WHA. She pointed out that the PRC government had promptly responded to the outbreak in Taiwan and had provided all necessary information. Thus Taiwan's plea to join the WHO was a "political ploy" and part of "separatist" activities. Wu scornfully asserted, "Their true motive is not to develop health undertakings in Taiwan but to create 'two Chinas' or 'one China, one Taiwan' in the international community.... The political attempts of the Taiwan authorities have all

[9] For related information on this outbreak in Taiwan, see CDC-Taiwan 2003.

met with failure in the past six years. This year will see the same result." With intensive lobbying, the PRC's allies did not vote for Taiwan, successfully blocking its WHA bid.

While Taiwanese officials expressed their regret at this result, what tore harshly at the Taiwanese people's heart was a scene that followed. When asked why Taiwan's need to join the WHA was ignored, Sha Zukang, the PRC's representative to the U.N. in Geneva, replied impatiently, "Already declined! Haven't you heard the decision of the assembly? Who cares about *you* (Taiwanese)? [*shei li nimen*]" (emphasis original, fig. 5.1).

Fig.5-2 Taiwan's Campaign Team Cheered Up by Banners Reading "WHO ISOLATES TAIWAN?" in five languages (left) and Sha Zukang's rude response to Taiwan's plea (right).

Source: Video clips from *Taishi Xinwen* [TTV News], May 19 2003.

The same scenario was repeated in 2004. Although that year Japan joined the "pro" group, under the PRC's political pressure the assembly decided to leave Taiwan's request pending. In a speech about Taiwan's efforts to join to the WHO, the President of the Taiwan International Medical Alliance, Deng Jou-fang, admitted that SARS had proven that even a serious global epidemic or pandemic could not overcome political repression (Deng 2003). "We do not need any emergent issue in order to join the WHO. SARS is a signal strong enough to make the world acknowledge the political situation we experience." There seems to be a long way ahead for Taiwan on its way to the global.

Resisting Capitalism: Hu Oliver Yoa-Pu, an "ROC" Nationalist

It was not easy to meet Professor Hu Oliver Yoa-Pu. In his early fifties, Hu had been a senior faculty member of the Pharmaceutical Research Institute, National Defense Medical Center (NDMC), Taiwan's oldest military medical school. I was introduced to Hu by one of my university colleagues who worked under the direction of Hu at the

Taiwan Product Quality Research Institute, a non-profit organization devoted to the inspection of GMP and related research. Hu continued carry out his ideas by founding this institute after he returned from the BPA, where he served as the Director General. "He is very knowable on drug polices. If you want to know more about the Asian market, you should visit him," my colleague encouraged me.

Of course, I knew this well. Hu was a typical elite produced by the NDMC. After earning his Ph.D. in clinical pharmacokinetics, he was appointed as a member of the Advisory Committee on Pharmaceuticals (ACP) in the DoH, on which he continues to serve. Hu is quick, smart, and full of energy. As the Dean of Research, Development and Continuing Education at the NDMC, he is always busy. When I asked him when would be a good time to have an interview, since he looked busy, Hu only replied, "Let's do it now or never. I cannot give you a block of time; I am fully occupied by work."

I originally expected to find out his thoughts on the state of Taiwan's drug regulations before the government took note of the ICH and the relationships between regulation and the Taiwanese drug industry. The regulations, as discussed in Chapter 3, were known to be somewhat loose. Because Taiwan's amended patent law could not grant market exclusivity protection to products that had been registered before 1986 but had failed to make it on market before the amendment, the global pharmaceutical industry tried to compensate for this loss by forcing Taiwan to set high technical bars. They knew that drug quality was the key to separating their originals from local "me-too" copies. Although the Taiwanese government introduced the GMP system in 1982 and completed implementation in 1988, the local manufacturers' quality was still questionable; local firms were not good enough to produce qualified generic drugs.

Clinical trials were another technical bar that widened this gap. Previously, most clinical trials were done in different Taiwanese hospitals for the purposes of formulary listing. They were an administrative process and the standards were so low as to be meaningless. Thus when competition with local companies heated up, global firms felt "extorted" by these unnecessary clinical trials, which slowed down their sales and increased their marketing costs. Thus the global drug industry wanted the government to require a single trial for all of Taiwan, but one that was good (and costly) enough to block local competitors. Since 1986, PhRMA has pressured the Taiwanese government through the USTR in U.S.-Taiwan trade negotiations. One of the results was an agreement to require 24-subject trials for bio-equivalence (with half the participants designated as a control group) in 1989. These studies, at an estimated cost of 1.2 million NTD each, were difficult for the producers of generic drugs to conduct. Before the introduction of the ICH, the bar was further elevated, requiring trials recruiting at least forty subjects for every

product that sought registration beginning in 1993. In addition, the modified law included a seven-year safety monitoring system for generic drugs that entered the market.[10] This was the so-called "July 7 announcement" (notification number: 08246232). As far as is known, this amendment was related to the 1992 trade negotiations in which Taiwan was listed as "priority foreign country" in an annual Section 301 report (see Chapter 3).

Like a movie director reviewing his work, Professor Hu recited the above story for me with his commentary. While listening to his views about this scenario, I was impressed by his enthusiasm and outspokenness. Unlike the people I met in Japan, Hu was fluent in English and did not mind anyone quoting his words. He looked powerful, as if he worked for the U.S. Food and Drug Administration (FDA) and not the government of a small country. "Everybody likes to work with Oliver, because they know that I always lead the team that never loses," Hu said. His interpretation goes as follows. Taiwan's negotiation with the United States was a continuous fight against unequal treaties that could be traced back to the opium war of 1842. For Hu, the modification of the patent law or the amendment of the law of pharmaceutical affairs was not the point. The point was the unending desire of global companies to conquer Asia. Hu described the various ways PhRMA pushed Taiwan to surrender. "These guys always believe in the top-down approach but not that [of] communication among professionals. They go directly to our Minister of Economic Affairs, our Premier, even our President, through the American Institute in Taiwan.[11] They can always find a way to accuse you of malpractice. What they want is to enjoy a barrier-free market. Even so, I just do not buy it."

Hu believed that the government should be the only apparatus to resist such a political invasion, and he thought he did a great job. He reminded me that although the United States forced Taiwan to require clinical trials for retrospective pipeline production protection, Taiwan did not sign this treaty until 1993, when almost all new chemical entities patented before 1986 had developed into products in market. Hu stated, "I totally understood the situation of Huang Weng-Foung and Hsiao Mei-Ling, my predecessors [as] the Director General of the BPA. We are old friends from the ACP and are a team." He remembered the scene when Taiwan and the U.S. negotiated in Washington in 1991. "It

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[10] In fact, the United States considered it a retrospective protection for the products patented by 1986 but marketed after then. Originally in the U.S.-Taiwan business negotiation meeting, held March 7-9, 1993, the USTR strongly insisted that protection extend longer than eight years, while Taiwan thought seven years of protection was enough. The negotiation resulted in a compromise: for the first five years, the companies producing a generic drug had to submit the results of a local clinical trial on the same scale as the original. For the sixth and seventh years a bioequivalence study had to be conducted at validated laboratories.

[11] The American Institute in Taiwan is the informal embassy of the United States to Taiwan that has been in operation since the end of diplomatic relations in 1978.

was in winter. Huang was there on behalf of Hsiao. I was there, too, as a visiting fellow at Johns Hopkins [University]. Huang called me one day before the negotiation. I shared with him my thoughts that contributed the success of this negotiation." The deal Hu referred to was the 40-subject clinical trial agreement. Taiwan promised that in order to replace all meaningless duplicate listing trials, the DoH would ask for one "good local clinical trial" for each product that sought a market in Taiwan. In Hu's opinion, it was not a trade-off, because Taiwan needed to build up its experience in clinical trials. "Huang is a good technocrat, and I know science. That is why we can work together well."[12] Aware of the changing role of clinical trials in boosting the biotechnology industry, Taiwan welcomed this amendment and used it as a "payoff" to trade for a certain moment of peace from these hungry capitalists.

The evidence, Hu pointed out, was that PhRMA asked Taiwan to remove the clinical trials requirement after 1994, because they found that they did not need it anymore. PhRMA claimed that the 40-subject trials were not "scientific" enough and thus were an "inappropriate non-tariff barrier." But this time Taiwan could not return to the dark ages. Hu taught me that the rule for medical regulations is that only a higher standard can replace an existing one. But PhRMA did not care. It made other complaints about Taiwan's reviewing practices—that the DoH's review process was too long, that the facility for clinical trials was not sufficient, and so on—which according to Hu were nothing but childish tricks to undermine the Taiwanese government's drug regulation credibility. For him, in the field of pharmaceuticals there should be mutual understanding among all countries, and the authority of such an understanding should be respected. Hu was strong and did not like to see his country looked down upon. He said during the interview, "Leave this to Oliver and it will be done. All companies know this." Indeed, for Hu, Taiwan seemed not lose any battle against these companies. His memory is a series of victories. He teased, criticized, and made fun of PhRMA for its ignorance of science, lack of local knowledge, and poor imagination. He explained, "Being a bureaucrat in Taiwan, you have to be smarter than your rivals. You have to penetrate their conventional thinking and provide an agenda for them. You must not follow their rules of game and you must lead them to follow your vision."

Hu's ideals are so high that he still insisted on calling Taiwan the "Republic of China," a term that almost nobody knows outside of this island. Let me introduce the background of this complicated fact. Firstly, Taiwan does have formal diplomatic relationships, which can be seen in table 5.1, in which all fourteen organizations it holds

[12] This view was confirmed by Huang Weng-Foung; he said that these negotiations started a new era of clinical trial policy in Taiwan.

membership in are listed. It is clear from this list that most of these organizations were established before Taiwan was expelled from the U.N. They are organizations for agriculture research, an old agenda for boosting the economies of developing countries. These organizations are legacies of global aid to Taiwan. Although Taiwan's economy has transformed from agriculture to industry, some of these organizations still function well—with little or no political influence.[13] Meanwhile, Taiwan continues to participate in some economic organizations, such as the Inter-American Development Bank and the Central American Bank for Economic Integration. Although Taiwan is active in these organizations, they are too small and regional to have any impact on the world economy. More questionable is Taiwan's role in them. It serves as a major donor; it gives other member countries financial support in order to win their political loyalty. Terms like "money diplomacy" or "money bullet diplomacy" are used to describe this dilemma.

Table 5.1 International organizations in which Taiwan holds membership as a state, 1995

Name of Organization	Founding Date	Headquarters Location	Year Joined	Status
Asian Development Bank	8. 22. 1966	Manila, Philippines	1966	Member
International Cotton Advisory Committee	9.5.1939	Washington, D.C., USA	1946	Member
International Office of Epizootics	1.25.1924	Paris, France	1954	Member
Asian Productivity Organization	5.11.1961	Tokyo, Japan	1961	Member
Afro-Asian Rural Reconstruction Organization	3.31.1962	New Delhi, India	1968	Member
Food and Fertilizer Technology Center for the Asian and Pacific Region	4.24.1970	Taipei, ROC	1970	Founding member, host state
Central American Bank for Economic Integration	5.31.1961	Tegucigalpa, Republic of Honduras	1992	Member

[13] For example, the Asian Vegetable Research and Development Center, a non-profit international research institute, is active and has a global reputation; its approximately twenty internationally recruited professional staff and 210 locally recruited researchers are based in Shanhua, a small town in southern Taiwan.

South-East Asia Central Banks	1966	Kuala Lumpur, Malaysia	1992	Member
International Seed Testing Association	1921	Zurich, Switzerland	1962	Member
Asian Vegetable Research and Development Center	5.22.1971	Shanhua, Taiwan	1971	Founding member, host state
Association for Science Cooperation in Asia	1972	Manila, Philippines	1972	Member
World Trade Organization (WTO, formerly GATT)	1.1.1995	Geneva, Switzerland	1995	Observer (became Member in 2002)
International Commission for the Conservation of Atlantic Tuna	3.21.1969	Madrid, Spain	1972	Observer
Inter-American Development Bank	4.8.1959	Washington, D.C., USA	1991	Observer

Source: Ministry of Foreign Affairs, *Junhua minguo waijiao nienjian* 1995:798-803.

Putting aside the minor organizations in which it can hold membership under the formal name ROC, Taiwan remains a member of some larger international organizations in which it is impossible for it to appear under its proper name. Indeed, since 1971, the problem of how to name the country has been an issue in its international relations. Its competitor, of course, is the PRC, who took over Taiwan's seat at the U.N. Even so, Taiwan's attitude changed with global politics. In the beginning, Taiwan was trying to maintain its membership (under the name ROC) in any international organization it could while resisting the PRC's various applications for membership. This rationale for this policy was know by the phrase "gentlemen won't stand together with thieves" (*hanze bu lianli*), meaning that the KMT (the ROC) would not coexist with the Communists (the PRC). However, after the PRC's open-door policy in the late 1970s, it became harder and harder to maintain this stance. This was especially so when the PRC used the same policy in their efforts to establish diplomatic relations, asking Taiwan to leave or to "downgrade" its status to that of a part of the PRC. In order to maintain its visibility, Taiwan had change its attitude toward the PRC from a rigid "no talks, no contact" to the

more flexible "no avoidance, no stepping down."[14] The insistence on a proper name, in this instance, became less important.

Fig.5.2 Chinese Taipei Olympic flag (upper left) and Taiwan's National Flag (lower left). The sad fact that Taiwan cannot present its national flag in any global situation, including the non-political Olympic Games, made Chen Shih-Hsin, the first ever Taiwanese gold medallist, cry at the medal presentation ceremony (center and right).

Source: Public Source (left, upper and lower) and Illustrate Bank *Muzi* at http://gallery.muzi.com (center and right).

Some compromises were made to maintain Taiwan's memberships in the face of the PRC's interventions, of which the most well known was the "Olympic committee formula." In 1975 the PRC tried to join the International Olympic Committee (IOC) on the condition that the ROC Olympic Committee be ousted. The IOC, however, did not accept Beijing's U.N. formula. It decided instead to let the PRC join as the "Chinese Olympic Committee, Peking [Beijing]" and call its Taiwan counterpart the "Chinese Olympic Committee, Taipei." The decision was soon readjusted to reflect the political reality, with the official names changed to "Chinese Olympic Committee" and "Chinese Taipei Olympic Committee," respectively, For Taiwan, Olympic athletes represent their Olympic committee, not their country. A concomitant change was that the Chinese Taipei Olympic Committee was not allowed to fly the national flag of the ROC at the Olympic competition; the flag could not be hoisted and the country's national anthem could not be played when its athletes won medals (see fig.5.2). Despite Taiwan's protests, this arrangement was formalized and used as the reference for Taiwan's membership in

[14] According to Kao Lang's study (1994), since the 1980s, Taiwan's diplomatic policy can be summarized in the following four principles: 1) to enhance the relationship with those states that already had formal relations with Taiwan through more cooperation on agriculture and industry; 2) to form relations with states that Taiwan did not yet have formal relations with by establishing representative offices; 3) to win diplomatic recognition of newly founded countries; 4) to actively participate in global organizations.

almost all important regional and international organizations, such as the Asian Development Bank and the Asia Pacific Economic Cooperation (APEC), and later the World Trade Organization (WTO).

I noticed that Hu consistently used the name "ROC" to refer to Taiwan. It seemed as if to him this title was the way he showed his commitment to his country. "Don't doubt. I am an ROC nationalist. I will never change the name of my nationality at any global conference," Hu told me when I asked him about this. He explained his battles with the PRC to me with the following analogy: "Just like in a community, we live across the street from the PRC. We have a good garden, where beautiful flower blossoms, but the PRC's garden is only a weedy sward. They know that our garden is good; that is fine. But how dare they change their door plate to ours and claim that it is their garden!" In fact, Hu's standard Mandarin reveals his ethnicity and he does not hide it; however, as a mainlander, he had no intention of heaping pity on the PRC.[15] "I do not hate these people, though they are near-sighted and their behavior is foul. I fight only because they treated us too unfairly. They stomp on my dignity and push me into a corner." Professor Hu's nationality might be confusing, but his standpoint is clear. He has a strong commitment to the country in which he is living, whether it is named Taiwan or ROC. What he worries about is that this country he loves so much is too weak to keep out global capitalism. When I asked him how to improve our pharmaceutical industry, Hu just said, "You tell me!" It was the first time he admitted his limit as a government officer, and the interview ended with it.

The Road to Excellence: FMPAT, the Medical Nationalists

I visited the Federation of Medical Professional Alliance in Taiwan (FMPAT) on a sunny afternoon just before its twenty-sixth training course on clinical trials. The FMPAT is located in downtown Taipei across the road from the NTU Medical School, Taiwan's oldest medical school, founded when the island had just been handed over to Japan. Like its campus, which juxtaposes old colonial-style buildings and minimalist modern ones, this school always reminds one of its long history of incubating the Taiwanese intellectuals who treat people's bodies and minds on the one hand and pursue excellence in medical research on the other.

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[15] "Mainlander" here refers to a category in Taiwan's domestic politics. Taiwanese mainlanders are the descendants of soldiers and refugees who moved to Taiwan with the defeated KMT. The political preference of such people is usually presumed to be pro-KMT and pro-unification with the PRC. I will return to this point in Chapter 8.

The FMPAT has remained in the place where it was founded. Among those engaged in social movements advocating for Taiwan's liberalization and democratization, the FMPAT was praised as "the conscience of our society" (FMPAT 2002: 3). Founded by a group of medical professionals who were mainly graduates from the NTU led by professor Lee Chen-Yuan (1915-2001), an internationally renowned scholar on snake venom research and the successor of Tu Tsung-ming (1893-1986), the first Taiwanese to obtain a doctoral degree in Japan, the FMPAT states that its goal is the revival of the spirit of the many Taiwanese physicians who devoted their careers and lives to social reforms under Japan's rule.[16] Demanding immediate reform to end the KMT's one-party rule, the FMPAT instigated and participated in several demonstrations in its early years for this purpose, on issues such as the direct election of the president and the self-determination of Taiwan's future. Because these activities were famous and influential, for the public the FMPAT was seen as political, a group working for nationalism rather than for medical reform. When I began some archival studies on Taiwan's regulatory drug environment, I encountered the FMPAT, for it was the first group to realize the importance of clinical trials, and it organized courses and seminars on this topic. This interesting finding led me to decide to visit the FMPAT; I was curious about the reasons they had started this effort, and why it became the only issue directly related to medical science that they worked on.

"We started this project with a very simple idea; we wanted to do something to improve our medical standards up to the world level," said Wu Shuh-min, the President of the FMPAT and one of key founders of this association. The son of Wu San-Lein—a Taiwanese intellectual, politician, and businessman—Wu Shuh-min continued his father's career as a strong sponsor of many social movements. However, besides his busy political life, Wu was also a well-established physician specializing in the respiratory system. He graduated from Kaohsiung Medical College, the school founded by Tu Tsung-Ming, and had practiced in the United States for over twenty years before returning to Taiwan. According to Wu, it was not originally his idea to introduce modern clinical trials. However, when K.C. Chen, the founder of the International Research-Based Pharmaceutical Manufacturers Association (IRPMA) in Taiwan and one of the founders of the FMPAT, suggested the idea to him, Wu gave his full support. Although pharmacology was a remote discipline in Taiwan's clinical practice (see Chapter 3), Wu's

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[16] In fact, the FMPAT's birth was the product of a famous demonstration in 1991 against, among other things, laws that badly violated freedom of speech. That demonstration was held in front of the NTU Medical School, and in March 1992, Lee formed an association—the FMPAT—to continue the social reform efforts the Taiwan Cultural Association, one of the most influential opposition groups during Japanese colonization, started in the 1920s and he immediately obtained support from his former student physicians.

foreign experience had proven to him the importance of clinical trials in medical science. In addition, Lee Chen-Yuan's opinion was important. As an M.D.- Ph.D., Lee always thought that the FMPAT should give more emphasis to issues of public health and medical policy, and his knowledge of pharmacology made him appreciate the role of clinical trials in the advancement of pharmaceuticals. He made the final decision on this project, and Wu and Chen took charge of it.

K.C. Chen revealed more of the origins of this project. I interviewed him at Maywufa Biopharmaceutical Enterprise Group, where he was serving as CEO when it became the first Taiwanese research-based drug company to go public. "Working at that time for Bristol-MyersSquibb, I was one of the few members from the pharmacological area," Chen explained. Even so, having worked in industry for over thirty years, Chen had different concerns. "I knew well that clinical trials were the key to this industry and to the competitiveness of Taiwan's biotechnology. But I needed physicians' help." Thus, Chen has preached this idea since the FMPAT's founding and obtained Wu Shuh-min's support. The ICH was one of most important events triggering this project. "We the industry knew well the ICH since its beginning. However, without any foundation, how can Taiwan talk about the ICH? In fact, at the beginning, only Wu and I worked on this project," Chen remembered.

The project Chen was referring to was the establishment of training courses. From 1992 to 1994, the FMPAT organized a series of introductory lectures titled "A Conference on Clinical Trials." As expected, at beginning not many people paid attention to this activity because of its newness; others knew of its importance but were hesitant to come for political reasons. "You know, the FMPAT was regarded as NTU-centric and politics-driven," Wu Shuh-min further explained. Wu and Chen in fact arranged meetings with hospital officials who thought participation in these lectures could lead to "improper" political interpretations, clarifying the lack of political agenda and the beneficial character of the conferences. "Good physicians can tell the difference," Wu said. "For instance, we visited a famous physician in cardiovascular disease. We told him the reason for these lectures and promised him a special seminar on cardiovascular drugs to be held soon; he understood and agreed to come."

Another problem was the content of conferences and speakers. Clinical trials are an advanced interdisciplinary science. Looking at the titles of these lectures—"The FDA and its Role in Clinical Trials," for example—we can see that they were neither specific nor well organized. As K.C. Chen admitted, he did not know much about what should be taught in these lectures and who should be invited, and he called upon his old friend Shaw T. Chen, then the medical group leader of the FDA. K.C. Chen recalled, "In fact, it

was Shaw Chen who urged [me to consider] the idea of modern clinical trials when I was at Squibb. So it was natural to think of him when this project started."

Shaw T. Chen had a different approach to clinical trials. Unlike other Taiwanese doctors, Chen earned his master's and Ph.D. degrees in chemistry at Johns Hopkins University before pursuing a medical degree, and he had a chance to work at the FDA, where he received rigorous training in the conduct of clinical trials. Chen had a clear goal when he went into the study of clinical trials. In fact, he grew with the expansion of the FDA (see Chapter 2). "Perhaps it was not a bad thing to stay in the United States," he said. "Although I did not know exactly what was going on in Taiwan, I know the best in the world." Despite K.C. Chen's recommendation, Shaw's participation in the FMPAT's project was minimal at first. For this, Shaw has his own interpretation. "I was watching," he recalled. Considering Taiwan's drug development environment, Chen was thinking of what would be the most efficient way to introduce the most advanced ideas on clinical trials.

Apparently, Shaw Chen's concerns touched the most fundamental question about these lectures: what were their educational goals and target audience? Clinical trials are not just a concept or a method. They are closely linked to existing regulations and require cases to practice on. Since clinical trials are such a broad field, there needed to be a clear idea of who the audience was and which topics were suitable. Unfortunately, this was simply difficult for Taiwan. Some initiatives, such as the state-sponsored Taiwan Cooperation Oncology Group, focused on scholarly research in clinical trials, but the FMPAT refused this approach, for its impact was slight. Even so, the FMPAT's "public" approach was problematic as well. The industrial base in Taiwan was so weak that it was unable to provide enough practice cases or incentives for physicians to participate in clinical trials; this effort was destined to have limited influence.

So what, then, was the FMPAT's goal? Returning to Wu's comment at the beginning of this section, these lectures were considered to be a social reform. There was no relationship with the development of industry; the underlying reason for these lectures was to fulfill an elite ideology that Taiwanese physicians should pursue excellence in knowledge and practice. Their excellence and superiority, as demonstrated historically, was believed to be a force that would lead to more social movements. It was another kind of Taiwanese nationalism aimed at reaching the global standard. This is what tied these people together, as Wu Shuh-min indicated when I asked how he knew Shaw Chen: "I did not know him before. But we shared the same ideology." Wu explained that he and Chen were members of the North America Taiwanese Professors' Association, an oversea Taiwanese group that argued for Taiwanese self-determination.

Although I wondered how far this project could go, I appreciated Wu, K.C., and Shaw's ideas. There must have been something more than rational calculation that made them do this. I suddenly remembered a poster hanging in K.C. Chen's office that showed an eagle hovering over a canyon. At the bottom was written a verse from Isaiah in Japanese, English, Chinese, and Taiwanese.[17] I went over the words of this passage in my mind: "But those who hope in the Lord will renew their strength. They will soar on wings like eagles, they will run and not grow weary. They will walk and not be faint" (40:31). With a strong belief in the righteousness of its actions, the FMPAT walked on its way to excellence in clinical trials.

PART II
THE BIO-GLOBAL CONNECTION: FORMING AN INSTITUTIONAL VOICE IN THE ICH

Setting the Channel: The E5 Guideline as a Way in

In the Part I, I described three groups or individuals who presented three perspectives concerning Taiwan and the global. As a medical technocrat, Professor Huang focused on Taiwan's isolation and the education of a new generation who can bring Taiwan back to world stage by recalling the "golden age" of Taiwanese public health. Hu, an "ROC" nationalist, gave Taiwan's existence a new meaning by focusing on its strategies of resistance to global capitalism and political threats. This vision had formed a firm standpoint, somewhat like that of the MHW officials, and Hu considered the United States to be the main, if not only, source of global capitalism and the PRC the source of repression. It is thus necessary to remain "independent" from these powers in order to preserve Taiwan's dignity. In the same direction as Hu, the FMPAT worked on a way to make Taiwan more competitive in the era of biotechnology. These medical elites believed that Taiwan's statehood could be ensured only by its economic power and medical excellence.

Although these people vividly constructed their visions about Taiwan and about how it should present itself in the world, they could not be said to constitute the "pre-ICH" mode of Taiwan's international presence, because, as I have noted repeatedly, Taiwan could not make use of statehood to generate its institutional voice. Stephen Tyler has shown us how difficult it was to create speech, to make it meaningful and capable of

[17] The Taiwanese translation of this quote is written in the romanized form introduced by Western missionaries in the nineteenth century.

generating more meanings by interacting with other speech (Tyler 1978). His observation can be used to help understand state agencies. At the global level, the above voices are too fragmented, too vague, and too "meaningless" to be recognized as speech articulated by a state agency. However, in writing ethnography, my job is neither to lament Taiwan's current situation nor to advocate the necessity of giving Taiwan a proper status. It is also not my job to "forge" a voice for Taiwan or use this voice to justify Taiwan's de facto existence. Far from this, in this section I will take note of the dynamics of how an institutional state voice for Taiwan was formed and how it was recognized by the global.

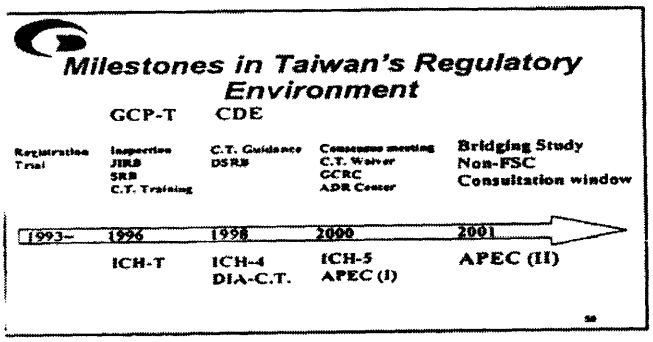
I hope to show two intertwined pathways by which this was achieved. The first can be roughly understood as the trial of "translation" as described by Bruno Latour (1993). I will show the process by which some individual voices were magnified, synthesized and institutionalized. These "Archimedean points" formed a trial of strength that produced a voice that was recognizable to the global. The second trial was the formation of a rhetorical agency, as described by Stephen Tyler (1978: 141-149). Echoing Tyler's analysis of intersubjectivity and its necessity in sustaining communications, my argument is a somewhat a reversed agenda in which Taiwan's "ICH mode" made itself a rhetorical subject by maintaining its voice in its ICH communications. These communications, I will argue, construct a dynamic field about the ICH that always refers to Taiwan's interdicted statehood. A final attempt to realize agency will be discussed at the end of this chapter.

I did not witness the birth of Taiwan's institutional voice on the ICH, nor did I find out about it intentionally. I came across this voice in a lecture at YMU before the outbreak of SARS. The speaker was Chu Mong-Ling, the executive director of the Center for Drug Evaluation (CDE), and the title of lecture was "The Role of Regulatory Science in the Pharmaceutical Industry." Before attending his lecture I knew nothing about this person and the institution he headed. I was only there because his speech belonged to a lecture series called "Introduction to Biotechnology and Its Management" in which I regularly participated. The speech title looked interesting, but I did not expect that it would have much to say about Taiwan. Having examined Japan's experience in encountering the ICH for a while, I was not sure whether Taiwan played any role in this affair as well.

The lecture went as I thought. In the first part Chu reviewed the origin of regulatory science in the nineteenth century, the establishment and development of the FDA, and its involvement in drug development. In the middle of the talk he moved to the initiation of the ICH and the need to establish global technical standards for new drugs (for more details, see Chapter 2). Up to that point, nothing went beyond my expectations. However, when his talk turned to a slide of "Taiwan Formosa," my attention was caught. It showed

Taiwan's drug regulation development in parallel with the evolution of the ICH (fig. 5.3). Chu traced the origin of Taiwan's development to the "July 7 announcement" in 1993, which founded an ad-hoc committee called "ICH-Taiwan," improved the country's clinical trial environment, and later established the CDE, the largest organization for in-house drug review in Asia outside of Japan, in 1998. As a counterpart to the ICH, the CDE provided a wide range of services and was actively involved in many reform initiatives, such as reviews of clinical trial protocols, inspections of trial sites, the establishment of a pharmaco-vigilance system, and the implementation of GMP. In addition, it had organized a series of international conferences on the ICH, the third of which was scheduled for November 2003.

Fig. 5.3 Evolution of Taiwan's Regulatory Environment.



Source: Chu Mong-Ling's Slide Presentation, March 4, 2003.

While listening to Chu, I could not help but wonder how much I could rely on his accounts. My political sense told me that Taiwan would not be able to attend any global organization, even the "non-political" WHO. In addition, the ICH, as described in Chapter 2, is an exclusive club for states that have the most advanced pharmaceutical industries. Taiwan did not belong to it. I asked myself how the CDE could achieve what Chu had described. If Taiwan could be allowed to join the ICH, it would be interesting to compare it with Japan, which always seemed to resist globalization. However, it was likely that Chu was just exaggerating Taiwan's contributions to the world in a way that I had heard on many occasions of this kind. I was obliged to clarify these problems.

After the lecture, I caught up with Professor Chu. I told him about myself and asked if I could make an appointment for interview. To my surprise, as soon as he knew my intentions, Chu said, "Why don't I drive you downtown so that we can talk on my way back to the office?" I got in his car. During the ride, Chu explained to me that Taiwan had in fact seized upon an issue by which it could cut through to the ICH: bridging studies.

Bridging studies! It was just what I was concerned most about in Japan's frustrations with the ICH and vice versa (Chapter 4). I felt that there must be some relationship to my previous fieldwork, but Chu stopped the conversation there. He referred me to Chern Herng-Der, his Deputy Director. "If you are interested in bridging studies, you should talk to Dr. Chern. He is a clinical pharmacologist and has been involved in the E5 guideline since 1995."

When we arrived at the CDE, Chu introduced me to Chern and we made an appointment. I wanted to know why and how the E5 guideline was an issue for Taiwan at the ICH. Chern and I talked in a meeting room at lunchtime. In contrast to Chu's heroic portrait of Taiwan's involvement in the ICH, Chern revealed that this relationship had modest origins, rather like the impression he gave of himself, a typical physician from Southern Taiwan.[18] He was not the first Taiwanese to attend the ICH, Chern clarified. Taiwan had sent people there since its beginning. The person who had attended ICH1 worked for FMPAT, but she did not even take any notes. Also attending were a specialist from the BPA and two section managers; they also attended ICH2. Although they were government people, their voices were only background noise at the ICH. Chern explained, "In almost all global conferences, we were total outsiders. Our presence did not mean anything. Not because of being isolated and excluded; we just failed to find a way in. No ideas were exchanged; no information was shared. Most importantly, without these channels, no experience was accumulated."

Chern admitted that he did not know anything about this conference before he attended ICH3. One day Chern saw a poster about the ICH conference on the activity board at the NTU hospital, where he was the newly appointed chief of clinical pharmacology, and he found it interesting. He then called Hsiao Mei-Ling, the Director General of BPA at the time, asking her to send him to the conference. Hsiao, one of the disciples of Hsu Tsi-chou and the successor of Huang Weng-Foung, led the ACP, where Chern was a junior member. "We are both alumni of the NTU and have known each other since I was abroad." Chern finally obtained a chance to attend ICH3.

Chern's eyes were wide open at the ICH, even though he was still foreign to it. As an expert long involved in the GCP, Chern soon found that it was not necessary for Taiwan to draft its own guideline, since the ICH would replace it all anyway. "The task now is how to follow these activities in a timely fashion," he wrote in his journal. Chern

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[18] Like many Taiwanese physicians of his generation, Chern was born into a physician family in Chiayi and graduated from the medical school at NTU. According to an article about his career, when he was asked why he wanted to study medicine when he applied to the NTU Hospital, one of the best in Taiwan, he answered, "For me, it is not an ideal or a wish; rather, it is natural choice after appreciating my father's life and career over the years."

was curious about every issue discussed but had no idea which was the most important. "It was a drug company that told me about bridging studies," Chern recalled. As an outsider, Chern did not have a chance to talk to people except those who were also from Taiwan. He learned about the controversial concept while having breakfast with a representative of a foreign company. "My intuition told me it was the chance we needed to catch!" Chern looked excited when he showed me his journal entry about his decision to attend the section meeting on the E5 guideline, which had just reached Step 2, and he learned a lot:

> The analysis of the ethnic factors is just what [concerns me] most. The categorization of these factors (as corresponding to the categories of Asian, Black, and Caucasian) can be a new concept worth being introduced to Taiwan. This requires more thought to tackle the [right] problems, such as bridging study, triage, and regulatory floor. (Chern's personal journal, November 3, 1995)

Also, Chern was aware of Japan's "awkward" insistence on racial difference, although he did not clearly understand it. In the same journal he wrote that the Japanese lacked creativity and rationality, with a footnote indicating what he meant by that: "Their [scientific] logic sounds unclear, and the explanation is not satisfactory."

It seemed to Chern that Taiwan might be able to differentiate itself from Japan if it followed the rules set up by the ICH, as he wrote in a personal report immediately after ICH3 (1995): "I can see three issues that will have an immediate impact on Taiwan.... How to accept 'foreign data' is the most controversial but a very important step toward harmonization. I see, though not clearly, the tendency in the future towards three major races in the world, Caucasians, Blacks, and Asians, which will be incorporated into early clinical trials and replace all local requirements.... It is arguable that the Japanese data can represent all Asians needs for scientific evidence. Yet, on the other hand, Taiwan cannot close itself [off] and reject all foreign data (like Japan does) if it wants to join the global market."

I let Chern clarify further by asking whether he felt that the racial difference did not really exist. He corrected my use of the term "feel." "I am a pharmacologist, and, for your reference, my dissertation is on pharmacological genetics," Chern answered. He knew well the most extreme cases cited by the Japanese on the different metabolic rates in Asians and Caucasians. However, he did not think that those differences were large in general. "Japan's response was not consistent with my clinical knowledge that only a few people need readjustment of the dose." I asked how he felt if no Taiwanese clinical data were to be used before a certain product was imported. Chern insisted again that we should separate the standard issues from those of racial difference. "Indeed, Taiwan's

standard was primitive; yet this was not the reason that we did not care about possible racial differences or requested more trials with local subjects. We recognize these differences and would like to [address them with] clinical data that meets scientific standards," he replied. Apparently, Chern was taking the same approach as the FDA on racial difference.

But beyond the above considerations, Chern was keen to Taiwan's political status. Taiwan needed to build an instrument to articulate its voice, and hosting global conferences was the only way to sustain such a voice. He wrote in his journal, "The last day of the conference gives me a feeling of attending a historical event and want to rush back to start a big project or mission, that kind of thing. Great conference; I did learn much about the art of managing such an event." As soon as he returned he began to act. He wrote a report for Hsaio and proposed a three-year project for the FMPAT, persuading them to establish a committee to follow the ICH. In this proposal, he argued that this committee should follow the ICH closely. For the ICH, it demonstrates how it was very much in Taiwan's interests to implement the guidelines and express the country's wish to host conferences. He concluded, "The following three years will be crucial in deciding whether Taiwan will be a center for clinical trials in Asia." Chern explained to me his reasons to choosing the FMPAT to conduct this project: first, the members of the FMPAT were mainly NTU alumni whom Chern was acquainted with. Its leader, Lee Chen-Yuan, was a renowned pharmacologist who had been one of Chern's teachers. Second and most importantly, Chern knew that the FMPAT had previously organized training courses on clinical trials; he could not think of a better group than the FMPAT to be in charge of clinical trial regulations.

A few months later, a committee was founded under the sponsorship of the DoH. It was established in the spring of 1996 as the "ICH in Taiwan" committee (hereafter ICH-Taiwan). Chern's individual seed of thought had a place to grow.

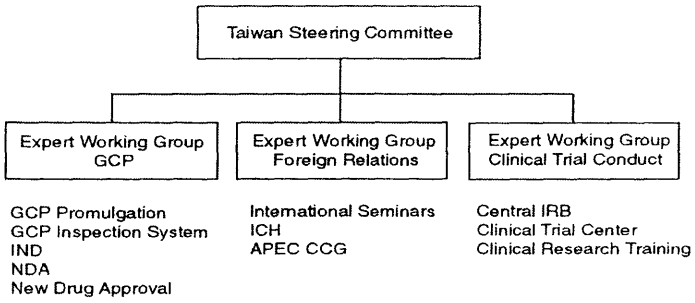
Intrumentalizing Taiwan's Voice: From Local ICH-Taiwan to Global CDE

ICH-Taiwan did not obtain its financial support solely to follow bridging studies or GCP; globalization and business strategy were also key factors. In a review article on the formation of the ICH-Taiwan, K.C. Chen, its Secretary General, explained why the DoH decided to fund this committee (Chen 1998). He mentioned that the APEC general meeting, held in October 1995, had resolved to establish a Cooperation Center for Good Clinical Practice in Singapore (CC-GCP, later called APEC CCG). This resolution brought pressure to bear on Taiwan's hope to serve as a center for clinical trials in Asia.

Yet, it also provided the impetus for academia, industry and government to work together to form an organization that could extend the country's efforts into global activities such as the ICH.

Like the ICH itself, the main body of ICH-Taiwan was the Steering Committee, which was chaired by Wu Shuh-min of the FMPAT. Under this committee were three expert working groups. These groups are not intended to deal with single guidelines; rather, they are oriented toward solving problems that arise during the implementation of ICH guidelines. As shown in fig. 5.4, these groups are concerned with one global and two domestic tasks. The GCP working group finished the Taiwanese edition of the GCP guideline, which was later revised to catch up with the E6 guideline, in November 1996. In addition, it introduced the GCP inspection system.

Fig. 5.4 Structure of ICH-Taiwan



Source: Chen 1998, Fig.1.

The working group in clinical trial conduct established a joint institutional review board (JIRB) to accelerate the protocol review process. With the help of the FMPAT and Chern, the JIRB successfully expended its coverage to include five medical centers, including the long-competitive NTU hospital and VGH Taipei, three quasi-medical centers, and nine regional hospitals by June 1998. The length of the review process was reduced to two to three months. The clinical research training courses continued. With the help of Shaw T. Chen of the FDA, from 1996 onward this working group initiated a new series of workshops. These workshops were held regularly three times a year, and for each one three U.S. speakers from academia, industry and regulatory agencies were invited. By 1998, 1,779 medical professionals had attended these workshops.

The most interesting expert working group, in my opinion, was the one on foreign relations. Headed by K.C. Chen, this group was devoted to maintaining close relations with the regional CC-GCP. Meanwhile, it kept watch on the ICH, hoping to make

connections with it and host international conferences, though at that time only few people though this was possible. The ICH-Taiwan identified itself as a follower of the ICH, and it was far behind. For example, in order to update information from the ICH, ICH-Taiwan published a bi-annual newsletter starting in July 1997. This 30-page thick newsletter did not in fact contain much information, a reflection of the cruel fact that at that time Taiwan did not have much exchange with the global.

Even so, an organization had at least been formed. In order to make itself visible, Taiwan had to have a focus instead of just passively receiving information. The issue of bridging studies came up again at ICH4, where Taiwan's first organized, substantial delegation, consisting of 36 representatives from the DoH, academia, FMPAT, and IRPMA, was in attendance.[19] Led by Lai Mei-Shu, then the Vice Director of the DoH and a colleague of Chang Hong-Jen, ICH-Taiwan conducted a collective, systemic observation of the ICH at this meeting. Unlike at ICH3, this time the Taiwanese delegates were prepared and knew what to pay attention to.

Chern raised several points in his report to ICH-Taiwan (Chern 1997). First, up until the fourth conference, the ICH had proposed 45 guidelines, 36 of which had been completely implemented. The main task for the future of the ICH member countries was not to create new guidelines but to put them into practice domestically and in non-ICH states (for an analysis of these guidelines, see Chapter 2, Part III). It was an opportunity for Taiwan. Second, as it still remained in Step 2, the E5 guideline had become an obvious obstacle to harmonization. The main point of debate, as described in Chapter 4, resided in the possible repetition of clinical trials using local (Japanese) subjects. Thus, Chern predicted, the E5 guideline would be an issue even after its implementation.

Third and most importantly, the Taiwanese delegates clearly apprehended Japan's attitude toward racial difference. In fact, it was this controversy that allowed Chern, as a clinical pharmacologist, to approach ICH members. Chern spoke to Tominaga Toshiyoshi of the Ministry of Health and Welfare (MHW) and learned that Japan did not allow products that had not been subjected to a clinical trial in Japan to be imported, even if their phase I data showed no significant differences in effect based on racial difference. Chern also asked Naito Chikayuki, the MHW expert on the E5 guideline, about Japan's attitude and learned that although Japan would not be pleased with the guideline to come, it would have to implement it. Chern raised this issue with the EU, and Jean-Marc

[19] The size of this delegation was indeed eye-catching. Among Asian countries other than Japan, which sent thirty-five people to the conference, Taiwan had the biggest delegation, compared to Korea's twenty and the PRC's 14. In fact, it was the also the biggest delegation in the history of Taiwan's participation in the ICH.

Husson of the European Federation of Pharmaceutical Industries and Associations (EFPIA) replied that they assumed Japan had a baseline for the acceptance of foreign data and had carefully examined the coming guideline. All this helped Chern understand the situation. He concluded that if Taiwan could seize the opportunity to be the first non-ICH state to follow the ICH guideline, it would be a great leap toward the country becoming a center for clinical trials in Asia.

Still, Taiwan needed a chance to prove itself to the global. For this, hosting a Drug Information Association (DIA) meeting was a turning point that came at just the right time. Founded in 1964, the DIA is a non-profit, scientific, member-driven association with over 27,000 members (DIA 2001). Every year it organizes over thirty meetings, workshops and symposia around the world, most of which are held in the United States; but some are also held in Europe, Canada and, starting the 1990s, Asia. The DIA's plan to hold an international symposium in Taipei titled "Recent Developments in Clinical Trials in Asian Pacific Region" gave Taiwan the necessary opportunity to promote itself at ICH4. Thousands of brochures advertising the symposium were distributed, along with booklets on Taiwan's GCP reform. Taiwan's dream seemed to be nearing reality.

Nonetheless, I wondered why Taiwan was chosen. Why had the DIA given Taiwan the chance it needed? Chern told me a story of contingency: the DIA did not intentionally choose Taiwan for this symposium, and he never thought of making it such a big event. Again, personal networking had proved important. In July 1996 Chern attended a DIA workshop on GCP in Tokyo. It was a small conference organized by Tsutani Kiichiro, then a professor at Tokyo Medical and Dental University. It was held in a lecture room at the university and only ten foreigners were invited, each from a different country. After the conference Professor Tsutani invited all the guests to dinner and asked whether there was any country that could host the next meeting. "I volunteered," Chern said. "I did not consider the DIA much; I thought that it was not a big deal."

Chern did not know the amount of important publicity attached to this conference. When he reported the idea of hosting it to ICH-Taiwan, all the members were excited. They immediately decided that this symposium had to be large and global. This plan was reported to the DoH, which decided to link it with the government's ongoing biotechnology development policy.[20] The most immediate influence it had on the

[20] In September 1995 the Taiwanese government organized an inter-ministerial committee on the enhancement of the biotechnology industry. A few months later it established a committee on the pharmaceutical industry under the Ministry of Economic Affairs, streamlining the administrative requirements for transfers of technology. For a brief introduction in English to Taiwan's biotechnology policy before the 1990s, see Yuan 1990. For recent developments, see *Asia-Pacific Biotech* 20, a special issue on biotechnology in Taiwan.

government was seen in April 1997 at the meeting of the Science and Technology Advisory Group, where the advisors recommended strengthening the legal dimensions of the drug regulation system. The DoH, echoing this decision, proposed the establishment of a professional, semi-governmental organization. According to its proposal, this institute, which later became the CDE, was formed to help make Taiwan a center for manufacturing and production. The forces of business and globalization made brought about the realization of the "global" CDE.

The 1998 DIA symposium acted as a catalyst for all these actions. Held only a few months after the birth of CDE, it was a festival to celebrate its bright future. For this first ever event, the most crucial was on foreign speakers. Tustani helped to invite those who had attended the previous DIA meeting, and the DIA supplied the FDA officers Taiwan most needed to have in attendance. For example, among the speakers were ICH coordinators Roger Williams, then Deputy Center Director for Pharmaceutical Sciences, and Robert Temple, the Director of Office of Drug Evaluation. More importantly, Taiwan set the focus, ethnic factors, for the conference. It arranged a half-day session on this topic, and Williams and Temple, who had been involved in the E5 Expert Working Group (Williams is the person who suggested the idea of bridging studies; see Chapter 4), shared their experiences. From a retrospective viewpoint, it was the most successful part of this conference.

Yet Chern did not stop there. He knew well how to promote a conference and how to promote Taiwan itself. Before the conference, he negotiated with the DIA to publish the proceedings in its *DIA Journal* (vol. 32, supplementary issue, November 1998). Chern felt at that time that the journal would be one of the few to cover this issue in Asia; besides, the DIA needed more members in Asia due to the rising proprietary drugs market there. On the other hand, as a guest editor, Chern knew how to "force" presenters, most of whom were extremely busy, to contribute papers for this issue. "We sponsored their flight tickets only when they submitted papers. No paper, no ticket," Chern said. He finally selected thirty papers, half of which were either written by Taiwanese authors or about Taiwan. This was not a direct promotion of Taiwan, but it ensured that information about the symposium and about Taiwan would continue to be disseminated after the event.

Furthermore, in catching hold of this precious chance, Taiwan was attempting to establish a global network to maintain its national voice. The formation of the Asia-Pacific Clinical Research Alliance (APCRA) was proposed at the end of the meeting. Ten countries whose representatives were present joined, and Chern served as chief

correspondent.[21] Chern explained, "I simply did not want this be a single event. A network can help its effect last longer." He carefully explained this network in a memorandum (Chern 1998): the APCRA would be identified as an informal network of experts interested in drug regulatory science, and would have no political affiliation. Like the ICH, it would have a steering committee working primarily on bridging studies; it would also deal with the implementation of other guidelines and other cooperative initiatives. Joint training courses and regional conferences would be arranged by the committee and experts from the FDA and Japan would be invited. If everything went well, "We can prepare a regional conference in May 1999 and invited them as consultants," Chern claimed.

It seemed like everyone had seen a light ahead for Taiwan. After attending the annual meeting of the DIA in Boston in 1998 with Hu Oliver Yoa-Pu, Chern felt a new era might be coming soon. He wrote in *ICH-Taiwan Bulletin*, "I believe the DIA would be a starting point for Taiwan to be the center of clinical trials in Asia. In the 'post-DIA' era, more challenges would come, and we should step forward and welcome them."

Creating Its Own Stage: APEC as an Economic/Political Arena

"What was your next step in the so-called 'post-DIA' era?" I then asked Chern Herng-Der about ICH-Taiwan and the CDE. Although the DIA is a global association and had allowed Taiwan to host an international meeting, it seemed to me that this was just an event, an occasion. Its impact on the global was small. Of course, Chern had made the most of this conference by editing an issue of the *DIA Journal* in which Taiwan was the main character; however, the country could not bring up issues or start follow-up discussions if there was just one gathering. Subsequent conferences would wash out the memory left by earlier ones; big, global conferences would cover discussions that had taken place at small, regional ones. That is the rule of conferences, or better, of information in the modern world (for more discussion on this point, see Chapter 1). The CDE, despite its pioneering position among Asian states, would be soon marginalized and surpassed by other regional powers. Although it proposed the formation of the APCRA, it was not attractive enough to develop a whole series. Taiwan, after all, is not the center of Asia.

My argument goes as follows: there are so many conferences held around the world,

[21] They were Kiichiro Tsutani of Japan, Shin Sang-Goo of Korea, Ellick Wong of Singapore, S. L. Lin of the Philippines, Iwan Darmansjah of Indonesia, Muhammad Aabdul Malek of Bangladesh, Vichai Chokervivian of Thailand, Chim Choy Lang of Malaysia, and Su Ling of the PRC.

not only in big cities like New York or Washington, but also in lesser-known places. Yes, many big figures came to the DIA meeting in Taipei, but they would soon forget it. They were not movie stars or pop singers. They had no obligation to remember where they had visited and whom they had met at a single conference. Chern agreed on this point. "That is why we planned to set up a regional network on pharmaceuticals and clinical trials. We did know the fact that we must step out of Taiwan, but the political reality was really harsh." Indeed, although the CDE was encouraged to attend the CC-GCP dominated by Singapore, Taiwan could not share leadership with this competitor.

So Taiwan aimed its efforts at recognition to the "non-political" forum of APEC. Founded in 1989, this regional network gradually developed into an active forum around the Pacific basin. Its main goals are economic and trade-oriented, with members engaging with one another as economic entities. The key to achieving this vision are the "Bogor Goals," set at an APEC summit in Bogor, Indonesia in 1994, of free and open trade and investment in the Asia-Pacific region. Unlike the WTO or other multilateral trade bodies, APEC members have no treaty obligations. The organization operates on the basis of non-binding commitments, open dialogue and equal respect for the views of all participants.

In addition to the economic benefits it brings, APEC membership has political significance for Taiwan because it is the only forum in which Taiwan and the United States can meet formally. Both Taiwan and the PRC noted this when both countries applied for APEC membership in 1991. With the help of Korea, an agreement was made between Taiwan and the PRC. Taiwan's presence in APEC was allowed on condition that it used the name "Chinese Taipei" and that its Minster of Foreign Affairs could not be part of its delegation. The tension between Taiwan and the PRC did not disappear, though. When Taiwan tried to make connections during meetings, the PRC attempted to block all possibilities.[22] In view of its history of blocking Taiwan from a Free Trade Treaty with Japan and the U.S. and later with Association of South-East Asia Nations (ASEAN), it is doubtless that the PRC is the one and only obstacle to Taiwan's hope of global recognition, and the two countries' relationship in APEC is no exception.

The project to establish a network on pharmaceutical regulatory science focusing on bridging studies was submitted by Taiwan and discussed at the sixteenth Industrial and Scientific Technology Working Group (ISTWG) meeting in March 1999. As expected,

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[22] One silly but possibly true example of this tension has to do with the fact that at AEPC banquets, Taiwan's seat is usually next to the United States, as the seats are arranged in alphabetical order. One year, however, the rumor spread that the PRC pressured the host country to move Taiwan's seat to another place, for it did not want to see too many formal contacts between Taiwan and this superpower.

the CDE and FMPAT were the main advocates. However, Chern admitted that at the beginning he did not know if APEC could serve this purpose. "I should put it this way: a chance came and I caught it. That is all," Chern remembered. The call for proposals was first sent to Taiwan's Ministry of Economic Affairs (MOEA), and the Vice Minister passed a copy on to the DoH, asking it whether it had anything to contribute. Hsiao Mei-Ling, then the Specialist General of the DoH, made a call to Chern.

When talking with Hsiao, Chern got the feeling that the proposal for establishing a pharmaceutical regulatory science network would fit the needs of the ISTWG. "As you know, seeing that bridging studies would be an important issue for Asian countries, we had the idea to form an Asian network for the ICH regulations. It was the way we thought through which Taiwan could become the center for clinical trials in Asia," Chen said. "And APEC offered us a better stage than the APCRA. Since drug regulation is an economic issue concerning industry and science, it would be better if this network was set up based on an existing one."[23] Therefore, with the help of Yang Shih-chien, then Minister of State in charge of the affairs of science and technology and an APEC veteran, the CDE and FMPAT drafted the proposal "APEC Network of Pharmaceutical Regulatory Science-APEC Joint Research Project on Bridging Studies" (proposal number:16.B.6.07), which was sent to the ISTWG along with the other seven proposals.

The project looked attractive. The overall objective was to establish a platform for solving common problems and better mutual understanding on issues on drug regulation. It would contribute to APEC's priority activities by enhancing policy dialogue and review via networking and joint research projects. It would harmonize drug regulations in the region with global pharmaceutical research and development activity, which in turn would raise the level of standards in clinical research, drug development and regulation in APEC countries. Even so, Taiwan realized the difficulties that this plan would involve and tried its best to prevent possible political obstacles. The proposal had to be endorsed by two member states in order to be sent the general meeting, so Director General of BPA Hu Oliver Yoa-Pu wrote to the directors of pharmaceutical affairs seeking their support. On the non-governmental side, Chern Herng-Der persuaded his colleagues at the newly established APCRA of the importance of this network. Shortly before the opening of the meeting, two groups of Taiwanese delegates were sent to gain more support: MOEA officials went to Hong Kong, where the ISTWG meeting, the main battlefield for this issue, was being held. Hu, Chern, Wu Shuh-min, and K.C. Chern of FMPAT, joined by Shaw T. Chen, rushed to Singapore and Malaysia, trying to advocate their standpoint on

[23] Another concern was that the APCRA included some South Asian countries, which were unlikely to participate in activities on a regular basis.

the topic.[24]

Let us move on to the meeting of the ISTWG in Hong Kong.[25] Taiwan's project went smoothly. Following Taiwan's extensive communication with other member states, the CDE's proposal earned sponsorship from Singapore, Philippines, Mexico, Malaysia, and Australia. However, the attitude of the PRC could not be predicted. Since every project required all member states' commitment, the atmosphere of uncertainty lasted late into night as under-the-table talks and political negotiations went on. Chern expressed his anxiety on that day. "As a scientist, it is really far beyond my head. The only thing I have learned is that the negotiations met deadlock. The PRC held a strong attitude that no proposal from Taiwan could be passed. When I talked to the PRC delegates, they confirmed this. One even told me that he did not see any problem in this project, but he could not betray his government's decision."

Later I learned the reason behind the PRC's refusal. It was purely political and contingent; it had nothing to do with pharmaceuticals. In February 1999, the U.S. Department of Defense issued a report on Security in the Taiwan Strait, mentioning the increasing missile threat by the PRC. In order to achieve effective control, this report introduced the Theater Missile Defense (TMD) system that would include Japan, South Korea, and possibly Taiwan (later Taiwan was "formally" excluded by the U.S. but "informally" included by Japan). This single explosive issue had an immediate impact on U.S. Secretary of State Madeline Albright's visit to the PRC in early March as well as the discussions at the ISTWG meeting. Apparently, science had done its best, but politics made the final decision.

Chern recalled, "We worked till the last minute and learned that the PRC was going to boycott all the proposals brought up by us. Thus we could do nothing but do the same to their proposals."[26] In so doing, the Taiwanese delegation explained again that it had no intention of blocking any projects for political reasons, and that it wished other countries could do the same in the interest of friendship and cooperation. Facing this situation, the ISTWG resolved that these projects could be conducted if the conflicts between Taiwan

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[24] According to K. C. Chen, the visit was a rare success. "Though they are officials, Hu and Chern are professors and scholars. Wu is a senior physician and his long experience in the United States helped us to explain the need for harmonization. As for me, I had just been inaugurated as president of the Federation of Asian Pharmaceutical Associations, the biggest organization of this kind in Asia. Thus, it was me who provided the channel needed to reach the top of each country. Fortunately, we obtained all we planned."

[25] The following reconstruction on the sixteenth ISTWG meeting is based on a report published in *The ICH-Taiwan Newsletter* 6, and on the reports of informants who attended it.

[26] In that meeting Taiwan proposed eight projects (three for Group A, one for Group B, and four for Group C), compared to the PRC's one (Group B). Except for Taiwan's "political" objection, the PRC proposal was criticized as unqualified by other members and re-submission was requested.

and the PRC could be solved.

As the political clashes between the United States and the PRC on the TMD system waned, there was no reason for the PRC to impede an economic project like the proposed pharmaceutical regulatory network. With the help of the United States, the next ISTWG meeting, held in Seattle in August 1999, approved the proposal for the APEC Joint Research Project on Bridging Studies.[27] Its minutes briefly summarize the approval:

> With respect to 17.B.6.06 proposed by Chinese Taipei (and held over from the 16th ISTWG meeting pending consensus), the group endorsed the proposal with support from Australia, Philippines, Mexico and Malaysia.

After waiting for two yeas, Taiwan was finally granted a chance to build a stage for global conversation, a series of conference of its own.

Making the Power of Voice: Searching "Scientific Evidence" for Bridging

The CDE soon prepared the first network meeting, held in Taipei on May 7 and 8, 2000. Eight countries—the United States, Japan, Korea, Singapore, Malaysia, Thailand, Indonesia, Australia, and France—sent representatives, and various regional directors from leading companies also attended. It was the issue of bridging studies that brought these people here. More importantly, it enabled Taiwan to lead a global conference on its own, and allowed Taiwanese officials to sit with key persons from around the world.

This network followed existing political relations within the APEC, which I will briefly sketch here. APEC is a big organization consisting of 21 member countries,[28] but in realty it is divided into regional groups. Excluding the North American Free Trade Agreement (NAFTA) member states and remote Australia, in Asia there are three groups outside of Japan: the ASEAN, the newly industrializing economics (NIEs), namely Taiwan, Korea, Hong Kong and Singapore, and the rising PRC. Since the United States, Canada, and Japan were already formal members of the ICH they would not be actively participating in this meeting. Some ASEAN counties and the PRC, despite their huge populations, had relatively weak drug-buying power. In addition, because of political concerns they were hesitant to attend any conference hosted by Taiwan. This left only the NIEs as possible candidates for leading this network. Except for Hong Kong, which was

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[27] According to K. C. Chen, Shaw T. Chen was asked to express Taiwan's wish to host this network, thus the United States later supported this proposal.

[28] The APEC member stats include, in alphabetical order, Australia, Brunei Darussalam, Canada, Chile, People's Republic of China Hong Kong, China, Indonesia, Japan, Korea, Malaysia, Mexico, New Zealand, Papua New Guinea, Peru, Philippines, Russia, Singapore, Chinese Taipei (Taiwan), Thailand, United States, and Vietnam.

taken by the PRC in 1997 and was thus unlikely to actively join in the meeting, Singapore and Korea were the most advanced countries, but they were not well prepared to conduct bridging studies. Thus Taiwan knew that it was the only country qualified.

For first APEC meeting, the CDE prepared three themes for discussion: ethnic factors, implementation methodology, and regulatory perspectives. The first theme worked on intrinsic and extrinsic factors that were of concern in Asian populations. The second was about bio-statistical methods to be used in applying the concept of bridging studies. The third was experience sharing on current practice of the E5 guideline. The entire meeting tried to carry out a systematic review of ethnic factors and their estimates impacts on drug regulations rather than drawing any conclusions.[29] Industry representatives, who expressed uncertainty about how bridging studies would affect approval processes, questioned Japan directly in this new forum, asking how the E5 guideline could be practiced without any "political" considerations. However, Taiwan's main expectation for this meeting was not just to provide a stage for these groups. It had to have its contribution, its distinct voice, in this debate.

To achieve this purpose the CDE could not avoid a confusing but basic question that had greatly concerned the E5 EWG all the way through the making of the guideline. That is, how should an "Asian race" be defined? Once Taiwan decided to consider racial difference in its reviewing process, it had to provide an explanation of its policy. Although the CDE's claim was attractive and accepted basically all Asian data, it looked like a political strategy lacking any scientific foundation. Chern Herng-Der admitted this problem: "In fact, when we set up our bridging study policy we did not have any scientific evidence. We just followed what the ICH suggested. The 2000 (APEC) meeting made us clear up the differences in our policy from those of OPSR (Organization for Pharmaceutical Safety and Research), but we still did not have evidence."[30]

Indeed, race was the key question that the CDE could not avoid. Following the "Western" logic that divided the world into three different racial groups—Caucasians, Blacks, and Asians—the CDE was not interested in proving the differences between Asians and Caucasians. Instead what it sought was a scientific study that demonstrated how "close" East Asian people were to each other biologically; this would show that

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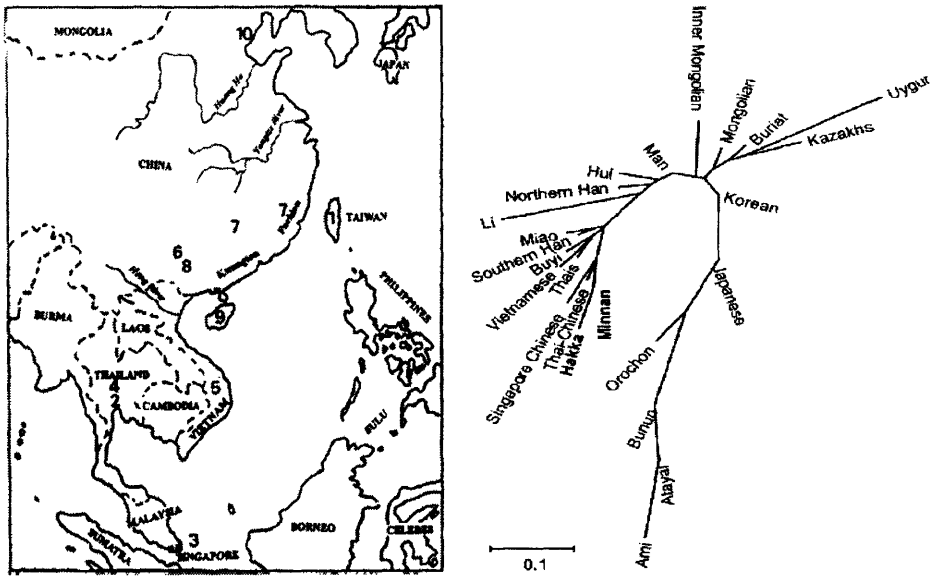
[29] Some suggestions were made at this meeting, such as various statistical models to solve the problem of the extrapolation of existing data (for details, see Chapter 7, part II). Moreover, transparency and efficiency would be stressed in all bridging study consultations. For example, it was suggested that a checklist should be used to consider whether the applicant drug was racially sensitive.

[30] In fact, internal documents show that the CDE did not have any idea of the extent to which racial difference among Asian races should be taken into account after the 2001APEC meeting. See the meeting minutes of the 20th Government-Industry Joint Meeting on Clinical Trials, June 1, 2001.

bridging studies were necessary and that a single bridging study for all East Asians would be adequate.

Fig. 5.5. East Asian populations and their genetic relationships by HLA mapping



Note: Left: East Asian populations analyzed in Lin Marie's study: 1. Minnan and Hakka ("Taiwanese"); 2. Thai-Chinese; 3. Singapore Chinese; 4. Thais; 5. Vietnamese; 6. Buyi; 7. Southern Han; 8. Miao; 9. Li; and 10. Northern Han.

Right: Neighbor-joining tree of 24 populations in Asia (Nei's standard genetic distance).

Source: Lin et al. 2001:Fig.1 (left) and Fig.2 (right).

However, such a study was not easy to find until Chern saw a paper published in *Tissue Antigens* in 2001 (Lin et. al. 2001). In the rest of this section I will do a brief ethnography of this paper, tracing how this scientific study was produced and interpreted according to political concerns. However, when it traveled to the ICH, it served as the scientific basis for the CDE's discourse on racial difference. The issue the paper dealt with was the sensitive matter of the racial origin of the Minnan (Holonese) and Hakka, the so-called "Taiwanese."[31] Conventional accounts say that the ancestors of these people originated from the Central Plains of North China and migrated to southeast

[31] It is a term that contrasts them with "mainlanders" (*waishenren*), as mentioned earlier in this chapter.

coastal area during the invasion of northern pastoral nomads. Hence these people represent the descendants of "pure" northern Han Chinese belonging to the great tradition of Han (*huaxia*). Arguing against this assumption, Lin Marie and colleagues analyzed the human leukocyte antigens (HLA) haplotype frequencies from samples collected from East Asian races, as shown in the left of fig. 5.5, and they constructed a phylogenetic tree by measuring the genetic distances between these samples (using Nei's standard). The authors wanted to show the genetic affinities among these races.

The result of this study is interesting. The tree shows that Taiwanese people have a close relationship with southern Asian populations such as the Vietnamese, Buyi, Southern Han, and Miao. According to Lin, this corresponds with another historical account that says that the Taiwanese are the descendants of a southeast coastal indigenous population, the Yueh, and not northern Han Chinese. The relations among Asian races can be better illustrated by neighbor-joining tree shown on the right in fig. 5.5. As we can see, in this genetic map the Minnan and Hakka (in boldfaced type) merge first with Thai-Chinese and Singapore Chinese, and together cluster with the other southeast races, except for the independent Li. The body of this tree loosely encircles the races from the north, including northern Han, Hui, Man, Buriat, Uygur, Kazakhs, Inner Mongolian, Japanese, and Korean. Thus, this study concludes that the traditional account of the origin of the Taiwanese is not scientific. HLA mapping tells us the truth: that the Taiwanese, along with southern Han and other Asian races from the south, belong to a historical tribe, the Yueh that is distinct from the northern Han. Furthermore, it maintains a split between the populations in Taiwan and those in southeast coastal provinces of the PRC by calculating blood type frequencies of these populations. Although the Taiwanese migrated from the southeast part of the Chinese mainland, Lin et al. suggest that they might be genetically distinct.

Although this is a scientific paper, those familiar with Taiwan's politics can sense the political motivation behind the study and its implications. Taiwan has long been troubled by the question of how to identify itself as a political entity separate from the PRC. I cannot review in detail here all attempts to make such a distinction, but briefly, because its global visibility is illegally repressed by the PRC, Taiwan has to reject by any means anything related to this superpower, including culture and race. According to Ding Xueliang, a Chinese political activist (Ding 2000), Taiwan's "anti-*zhonghua*"[32]

[32] *Zhonghua* is a troublesome term hard to translate into English. As a vague term for the Chinese race, conventionally it means everything that is "Chinese" or has Chinese characteristics. Even so, when it is used for a political purpose, such as in Ding Xueliang's article, the term can be narrowly read as "China," as its political representation the PRC, or as everything related to that country. In order to preserve the vagueness necessary in Taiwan's case, I chose to keep the term way it is written in Chinese. For more

movement works in four different yet related fields. In politics, the Taiwanese reject joining the Communist authoritarian regime. In worldview, they assert their separate status from Mainland China. In culture, Taiwan is anxious to build its own interpretation of its past and its own verbal expression (the "Taiwanese" language). In biological terms, it hopes to cut its racial ties to the Han Chinese, which provide the PRC a priori justification for taking over the island. From this viewpoint, Lin at al.'s paper can be categorized as a refutation of both cultural and racial connections with the Chinese. As the authors claim, "We hope to clarify the *truth* about the origin of 'Taiwanese'" (193, emphasis added).

This paper quickly aroused attention when it was published, since it was the only scientific literature that dared to address this sensitive topic, and because it confirmed the difference between the Taiwanese race and Han Chinese.[33] Therefore, after it was introduced in a newspaper, it was soon translated into Chinese and was widely circulated (as a full article, an abridged version, and a brief summary). Lin was later invited by the Taiwanese community in the United States to speak about the study, and her speech was transcribed and disseminated as a popular non-scientific article. Alongside these documents, an enormous quantity of secondary materials is available on internet BBSs and discussion boards, and in newspapers, criticisms, discussions, citations, and explanations; and they continue to spread and circulate. The PRC, as expected, did not like this research. Its academia openly attacked Lin with harsh criticisms. For example, on August 19, 2002, the newspaper *Haixia Shibao* [Strait Times] reported that scientists at the Chinese Academy of Science criticized Lin's study as "absurd, disgraceful, and of no scientific merit." One famous geneticist even said, "The attempt to apply [the result] to fulfill any political goal is also a shame. [There is no doubt that] the people in Mainland China and the Taiwanese share the same blood and come from the same ancestor." Though it was a scientific document, Lin et al.'s study was brought into the political discourse of state and race.

However, in the context of ICH, this paper moved in the opposite direction, which I call the "displacement" of politics in science. It was Chern Herng-Der who found another use for this paper. He said, "One day I read a column about harsh criticisms on Lin's

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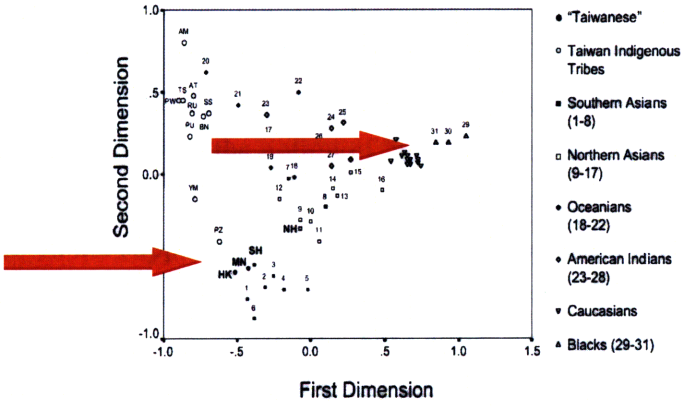
discussion on Taiwanese people's understanding of their identity in terms of political status and cultural affinity, see Chapter 8, part III.

[33] Before Lin's paper, others had tried to clarify the origin of the Taiwanese through the analysis of immunoglobulin, G6PD deficiency, a-thalassemia and b-thalassemia, and other biological markers such as a 9-bp deletion. For details, see Chu 2000. Regarding the study's political sensitivity, in fact, it was reported that when Lin submitted this paper to *Tissue Antigens*, one editor member from the PRC strongly requested that the board reject it, but this attempt did not succeed.

motivation for this study. Before then I had no idea about this study, but I was grabbed when reading this news. I immediately checked the reference and found this paper. Strangely, I had a feeling that it might be what I want, and it really is." Chern surprised me. I wondered how he could interpret this paper, if not politically. He showed me a figure from Lin's paper, the one I have used above (fig. 5.5, right), and explained, "You see, Holo and Hakka belong to the group of the southern Han. But, we should remember that Taiwan also has mainlanders, the northern Han if you want to say. To put it another way, we have both. If the northern Han are close to the Japanese and Korean, we can say that Taiwan is perhaps the only state that has both kinds of Asians subjects. That is, we are the best place to conduct clinical trials."

Fig. 5.6 Correspondence analysis of "Taiwanese" with other racial groups. Red arrows indicate the distance between the Taiwanese (MN and HK) and Caucasians and Blacks.



Source: Lin et.al. 2001, Fig. 3.

Chern introduced another figure in Lin's paper that shows the two-dimensional image of the distances between the ethnic groups of the world (fig. 5.6). Its description reads, "Minnan and Hakka are closely related to the southern Han, and are clustered with other southern Asian populations. Northern Han are separated from the southern Asian cluster, and form a cluster with other northern Asian populations." However, Chern read this figure in a different way. Instead of reiterating the difference between the north and the south, he pointed out to me how close they are in comparison to Caucasians and Blacks. "Lin's study nicely echoes to my understanding on racial differences: Asians should be considered a group compared to Caucasians and Blacks." Chern even told me that Lin would soon publish another paper on the relations of the Asian races by tracing their P450 genes. "I think its result will give more support to my theory," Chern said

firmly.

Chern's interpretation was powerful, and for me, a shock. He gave me a sense of a gestalt of scientific and political perspectives; many observers could only follow popular perspectives. While in the original context, people saw only the separation, the break between Taiwan and the PRC, Chern saw continuity, the sameness among all Asian races, including Han Chinese.[34] Presuming that Chern knew the conventional interpretation of the study, I asked him whether he realize this "misreading." I did not know Chern's political beliefs, but I assumed that the interpretive switch he was making would encounter resistance and be difficult to promote. Surprisingly, however, Chern's succinct reply did not even address this topic. "It just felt right," he said. Looking at my puzzled face, he added, "Of course, I know my reading is different from many others. In fact, I have consulted Dr. Lin to make sure that my interpretation is acceptable, and she agreed with me." Chern then revealed his relation with Lin: both belong to the Taiwanese Presbyterian Church, a religious group that has long been involved in social reform and the self-determination movement during the period of KMT control. "We were not acquainted with each other before. However, because of that paper, we got to know more about each other. In fact, we share the same ideas," Chern concluded.

I was truly fascinated by the notion of "the same ideas." What was that? Chern did read this paper differently. If he did not follow the scenario of "conversion," or even "enlightenment" in the support of Taiwanese nationalism, what did he mean by saying this? I suddenly realized that the Kuhnian metaphor of scientific revolution did not fit this discussion (Kuhn 1962: Chapter 10), and that I might have made an incorrect assumption about whether Chern's interpretation was convincing. Arguing whether the Taiwanese race is related to the PRC in this scientific paper did not represent revolution in the linear sense. Chern's reading could rather be considered a "displacement" of knowledge accomplished by detaching it from the original reading and context and putting it into a new network. Race was not at stake in this paper—the state was. Chern's reading revealed a deeply embedded implication in Lin's "racist" discourse that secured the integrity of the Taiwanese state. Lin did not insist on a nation-state like Japanese scientists did for their country; she just wanted to reject a racial account that might justify the PRC's desire to intervene in Taiwan.

In other words, Lin's paper is a political declaration of a break from the imaginary

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[34] In fact, the interpretation should be taken further based on this figure. Blacks and Europeans are much closer to one another than Northern and Southern Chinese. However, the genes used here may not be truly representative of the genes involved in drug effects. Mitochondrial sequence, Y chromosome sequence, SNIPS, etc. could be used instead.

unified Chinese race of the PRC. Chern's interpretation of Lin's paper, though it looks like a "betrayal" of Lin, complements her argument. His reading does not reject links to Mainland China, but it also constructs more links for Taiwan to the world. It is thus a declaration that puts Taiwan back on the world map as a state and skips the PRC in the process. The concept of bridging studies, in this sense, is a political statement: it does not overplay Taiwan's racial uniqueness (or the uniqueness of Han Chinese), which would pose the danger of giving the PRC a reason to "unify" with Taiwan. Instead, it just silently replaced a racist slogan "Chinese are all over the world" (so that they deserve clinical trials on their subjects) with the nationalist/global one, "We are all Asians creating world harmony." Only by the above interpretation can we understand why nobody argued against Chern's "misuse" of this paper. When I asked Wu Shuh-min about the paper, he replied that he did not feel there was anything wrong. Again, he seemed to have "the same ideas" as Chern.

With this scientific work, the discourse of CDE's bridging study policy was complete. This paper later appeared in every subsequent discussion of the E5 guideline. For example, one paper by Wang and Chern stated that "in general, Taiwan accepts all Asian data. A study by Lin et al. in 2001 found that the so-called 'Taiwanese', accounting for 91% of the total population in Taiwan, are comprised of Minnan and Hakka people who are closely related to the southern Han, and are clustered with other southern Asian populations in terms of HLA typing. … As the Taiwanese regulatory authority acknowledges the trial data conducted in Taiwan regardless of the ethnic origin of the subjects, it will acknowledge all Asian data as well" (2002: 40). "Now no one can beat me at bridging, since I have gone through all scientific problems," Chern claimed, like a confident child who knew he would get the best possible score on whatever test was given. For me, only one problem was left: how to advertise this idea to the world?

Sustaining the Voice: Reaching Out to the World, Looking Back to Asia

While organizing meetings and facilitating the implementation of the bridging policy, the CDE was eager to reach out to the annex of the ICH, the Global Cooperation Group (GCG). As described in Chapter 2, the GCG is a tool to fulfill the capitalist desire to achieve a single global market. It disseminated information about the ICH to "outsiders" in an effort to avoid unnecessary requirements for drug registration in these countries. Although the GCG could never bring about any change in the ICH's structure or operations, it was the only place where the voice of non-ICH countries could be heard. For the ambitious CDE, it was perhaps the only available channel by which Taiwan's

voice would be able to reach the core of the ICH.

To achieve this end the CDE needed a proper identity. This is because the GCG only worked with organizations, and therefore APEC was Taiwan's ticket on board. It is hard to locate the point at which the CDE initiated its appeal for participation in GCG activities, but we can see some hints at the 2000 APEC meeting, where Bertram A. Spiker, the PhRMA representative of the ICH Steering Meeting and the co-chair of GCG, was invited to make the closing remarks. At this meeting, Spiker was impressed by the CDE's bridging policy, and the effect was immediate. Knowing that the PhRMA would host a half-day satellite session before ICH5, to be held in San Diego in November 2000, the CDE asked to present its policy on bridging studies and PhRMA soon agreed.

It was an occasion that benefited both PhRMA and Taiwan. From a capitalist point of view, PhRMA did not want any "extra" trials—that is, trials required by regions other than the United States, Europe, or Japan. This was especially so in the case of the E5 guideline; nobody knew how to make it work and how to prevent the same kinds of requests from being made by non-ICH counties. At this point, Taiwan was a good example. It is rich to buy advanced drugs. Its regulatory authority followed the ICH and faithfully adopted them into their regulations. Although following the E5 guideline does allow the possibility of requesting local trials, the CDE's policy seemed to allow trial requirements for almost all applications that had no racial sensitivity to be waived. It could be a model for non-ICH countries, and thus it should be widely advertised.

On the other side, Taiwan appreciated this opportunity. The CDE knew that it was bridging studies that made this appearance possible. Unlike large developing countries such as Brazil and India, whose huge markets made them a topic at ICH5 as potential invitees to the ICH, Taiwan had to find a way to catch up with the global. APEC was the first stage of crafting a sustained voice, a voice that Taiwan could now continue to sustain by its appearance at the ICH. Taiwan seemed to have returned to the "golden age" of the 1960s, when it was a shining star of public health in the Western Pacific region. At that time, Taiwan was a recipient of aid and the Western countries were the aid donors. Thirty years had passed. Finally, at the dawn of the new century, Taiwan returned to the global stage, this time as an invited partner.

The time for ICH5 came. On the morning of November 8, two hundred people from regulatory authorities around the world attended a meeting hosted by GCG co-chair Elaine Esber. In the first part of program Chern briefly, for perhaps ten minutes, explained the CDE's work on bridging studies with presentations by GCG members. The most creative arrangement was yet to come. In a panel discussion, Chern suggested Chang Hong-Jen, then Taiwan's deputy director of the DoH, present Taiwan's efforts to

catch up with the ICH on behalf of ICH-Taiwan. Chang was the first high-level government official who was able to make an appearance on such an occasion. Of course, as I described in Chapter 3, Chang had had abundant government experience, including in pharmaceutical affairs. However, what made Chang's presence meaningful was his position: he was a Taiwanese official seated with the top representatives at an international summit.

Table 5.2. Presenters from the ICH Steering Committee

ICH member	Name	Affiliation and position
U.S.	Elaine Esber	Founder of ICH, former FDA representative to ICH steering committee and co-chair of GCG
	Robert O'Neill*	Office Of Biostatistics, FDA, E5 EWG member
	Robert Temple*	Director, Office of Medical Policy, CDER, FDA
	Bertram Spilker	Senior Vice President of Scientific and Regulatory Affairs, PhRMA, co-chair of GCG
E.U.	Yves Juillet	EFPIA, ICH Steering Committee member
Japan	Uwoi Tohru	JPMA, ICH Steering Committee member, E5 EWG member
	Mori Kazuhiko	Director, Consultation Division 1, OPSR
	Sato Daisaku	Deputy Director, Evaluation and Licensing Division, MHLW, ICH coordinator

* teleconference presenters.

Source: adopted from 2001 APEC website. http://www.cde.org.tw/ documents/ activities/download/active_apec2.htm.

Of course, this satellite meeting was small. However, it enhanced the CDE's connection with the ICH. Looking at the list of 30 presenters at the second APEC symposium on the APEC Network of Pharmaceutical Regulatory Science-APEC Joint Project on Bridging Studies (hereafter the 2001 APEC symposium), it is clear that Taiwan was able to host a real global festival. About four hundred people from Asia, Europe and the United States attended. Five topics surrounding bridging studies were discussed: 1) implementation of ICH guidelines in the APEC region; 2) regional bridging strategies for industries; 3) pharmaceutical regulatory science; 4) regulation and consultation processes for bridging study requirements; and 5) statistical models for bridging studies. Obviously,

bridging studies were the theme that Taiwan wanted to sell, and it said what its audience wanted to hear.

On the other hand, symposium participants brought global visibility to Taiwan. Big figures from the ICH occupied center stage at the meeting (for their names and affiliations, see table 5.2). As the CDE recalled, "It was a milestone in Taiwan's endeavor at the ICH, because it was the first time it had chance to interact with the ICH steering meeting members, including those in the GCG." These people were a powerful magnet that attracted Asian participation. The inner circle was comprised of officials from the regulatory authorities. According to the APEC website, Malaysia, Singapore, Australia, Thailand, and Korea sent representatives. As presenters, they had a chance to talk to the ICH officials and exchange ideas. In fact, many of them returned to Taipei for the 2003 APEC meeting. The CDE reported, "This meeting was phenomenal; it opened up Taiwan to a new era of the diplomacy through medical affairs" (*ICH-Taiwan Bulletin*, no.9). Indeed, the 2001 APEC meeting was a victory for Taiwan, scientifically and politically. Although this meeting presumed an "ICH central, Asia peripheral" view, this did not bother Taiwan much, for this scene suggested a return to the "golden age" of public health that its medical elites had long dreamt of.

But the CDE did not hold to this conference tightly. APEC decided to move the next meeting to Tokyo and return to Taipei in 2003.[35] Then it moved to Seoul for the 2004 meeting and is to return to Taipei in November 2005. "Why couldn't we keep this series in Taiwan, as it was so successful? Did we fail to keep it with us?" I asked Chern Herng-Der. "No," he answered. "We could keep it as long as we wished, since we are the principal sponsor of this network." Chern explained the problems behind the illusion of glory. For example, industrial people did not show up in great enough numbers. Lacking international experience, few local people took the chance to speak to the global. However, the most critical problem was politics. Taiwan could not win participation from ASEAN members, Hong Kong, and the PRC. Chern said, "We have tried our best, but you know the PRC, a place where politics is superior to everything. Besides, ASEAN goes with it."

Chern knew clearly that any conference about East Asia that failed to have the PRC's presence would fail. "Given such a difficult situation, if Taiwan hopes to be a real leader of Asia-Pacific region, it has to give this meeting some freedom to travel around. We will be much rewarded when it returns," he reminded me. In the interest of

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[35] Although people consider these conferences serial, in fact there are two kinds of conferences held by the APEC network. The 2000 and 2002 meetings were workshops and not open to general public, and the 2001 and 2003 meetings were symposiums that allow public participation.

broadening international participation, Chern asked Sato Daisaku if Japan could host the next meeting, so the 2002 meeting was held in Tokyo. "You see, the PRC came, as well as Singapore," Chern said. As for the 2004 meeting, Chern used his personal connections with Shin Sang-Goo at National Seoul University, whom he had been acquainted with since the DIA meeting in 1997. A convention was formed: the meetings would be held in Taiwan one year and elsewhere in Asia the next. As with Taiwan's strategy on bridging studies, the APEC meeting could not just be a meeting for Taiwan and Taiwan alone. It had to link to somewhere else to ensure its continued existence. "This is the only way it can survive and live well," Chern concluded.

Chern was right. The 2003 APEC meeting had the broad theme of "Regulatory Communication," and the speakers were even more enticing than in 2001. In addition to those present at the 2001 meeting, two key persons from the U.S. and EU drug authorities, Murry M. Lumpkin, Principle Associate Commissioner of the FDA, and Thomas Lonngren, Executive Director of the European Agency for the Evaluation of Medicinal Products (EMEA), joined the show as part of the main cast. Of course, they would not fly halfway around the world just for this conference, but since ICH6 was held in Osaka, Japan, that year, the APEC meeting was intentionally arranged to directly follow it. When I chatted with Elaine Esber during the meeting, she told me that this was her idea. As a founder of the ICH who had served the organization for over ten years, Esber was expressive about Chern. "This meeting would never have a chance to invite you without Chern's effort," I said to her, and she agreed. Responding to my comment on his aggressiveness in promoting Taiwan to the world, she smiled with understanding and looked at me with her dark eyes. "Yet he is always polite, isn't he?" she said.

CONCLUDING REMARKS: WEN-HUA KUO AS THE AUTHOR AND ACTOR OF TAIWAN'S INSTUTIONAL VOICE

In the afternoon of July 11 2003, I stood at the corner of the alley leading from my home in Taipei, waiting for a limousine sent by the CDE to take me to the airport. I was to attend the ICH GCG meeting as an APEC expert. The car arrived on time. I opened the door and saw Chern Herng-Der sitting inside. He told me that he had just found out that my home was only few blocks away from his. "It is amazing that we live so close," Chern greeted me. We had always met at the CDE or at conferences; this was the first time we were alone in a non-public place. In the four short months since I had attended Chu Mong-Ling's lecture "The Role of Regulatory Science in the Pharmaceutical Industry," I had become an "expert" and "consultant" on the E5 issue, and I was to go with Chern to

this conference. This had come so quickly for me, and when I tried to find words to describe my feelings, I couldn't.

I remembered Chern's invitation the other day. He asked me if I could attend an ICH business meeting with him, not as an observer, but as a participant. "You said you are studying the E5 guideline and the ICH, thus you must see in person how it operates, although it is a short meeting," Chern explained. "But, my understanding on globalization is: do not work local viewpoints. Talk to the top and meet real key persons; they will save you a lot of time. The door is open, but you do not need to reply now." This was too good a chance to pass up, so I responded immediately that it would truly be my pleasure to go. However, after hanging up, I stated thinking what this conference would mean to me, and what I meant to Taiwan in this narrative. I did want to have access to the "inside" of this conference, but I had never considered in what identity I would do this. I also had an ethical concern based on my increasing knowledge of Taiwan's strategy of making itself increasingly visible in the world—I would have to go and check whether what I had heard and written was not exaggerated or distorted.

Let us summarize what we have learned up to here. This chapter consists of two parts, or, retrospectively, two "modes." The first part deals with the "silent" mode. The review of the pre-ICH experiences of Taiwan shows how a group of Taiwanese defined in various ways as medical elites and technocrats tried to form an identity for their country in response to the onset of globalization. Various strategies were identified; some resisted the invasion of global capitalism while others welcomed the advanced science that clinical trials brought. Some pointed out Taiwan's isolation and looked forward to the future, while some hoped to return to the good old days of the country's former public health achievements. Although these were vivid expressions, they were not the institutional voices addressing the global.

In contrast to the "silent" mode, the second part of this chapter is a description of the formation of Taiwan's institutional voice through the metaphor of bridging, which has a manifold meaning. First, it bridging is the key concept of the E5 guideline that was made to deal with the consideration of racial difference in accepting foreign clinical data. But it had a different use in the case of Japan and Taiwan. While the West was trying to use bridging as a means to make data from Caucasian trial subjects extrapolatable to the Japanese, Japan considered it a way to separate itself from the rest of the world (so that a "bridge" was required). That is the origin of all the confusion. Taiwan recognized racial difference and welcomed bridging, because it granted Taiwan a weapon with which to resist the pressure from PhRMA. More importantly, Taiwan took this deadlock as a chance to get the attention from the global. As an Asian state, Taiwan claimed it could do

what Japan could not. Second, bridging was the strategy by which Taiwan formed its voice. As indicated in this section, the two processes went hand in hand all the way to the formation of the CDE, the institute for the ICH. Taiwan hoped to be a center of biotechnology and clinical trials, and this was the reason to form such an institute. The formal process, as can be seen, resembles a regular policy-making process, or a "trail of strength," as Bruno Latour would suggest (1993b). However, this ethnography shows the process underlying the formal decisions, which provided the motivation needed to give rise to Taiwan's voice. The personal connections among these medical elites, serving as bridges linking them to one another, constituted a path-dependent trial by which the formation of the institute could be worked out. Third and the last, Taiwan's institutional voice did not exist independently. It must be made sense of in the context in which it was situated. In this sense, what is at stake is not how loud this voice was when it was heard by the world, but the "bridges" that it created as it communicated with others.

As this story came to an end, Chern's seductive invitation pushed me into a dilemma about my role in it. At the beginning, I believed I was an ethnographer of the ICH and a passive listener to Taiwan's story. However, I could not remain that way; my nationality, social and cultural background, previous training, and research in Taiwan have always pulled me into the expanding network that worked to produce Taiwan's voice. I felt that I was working at the boundary between observation and the observed, along the bridge of ICH GCG. Where should I go? This dilemma had two aspects. First, who was I in this narrative? Could I still pretend to have "objectivity" from my standpoint of observation, claiming that I could separate myself into Wen-Hua Kuo, the MIT-trained STS researcher, and Kuo Wen-Hua, a medical graduate who studies the ICH and the E5 issue? Second, what would I do in this narrative? The traditional notion of "disinterested" anthropologist was troubling, since I had moved far away from that position. In order to achieve the best understanding on this topic, I traveled and exchanged my knowledge with my expert informants. We traded information based on the assumptions that I was a Taiwanese medical doctor and policy researcher from the United States, while they were local scientists and policy makers. The more I learned, the more I could trade for this knowledge. During this process, "the anthropologist" was never my identity.

This dilemma is not new. Arthur Kleinman has mentioned his difficult position as both a psychiatrist and an anthropologist in *Writing at the Margin* (Kleinman 1997). But regarding my concerns about ethnographic voice, the CDE clearly intended to have me involved, thus making this problem more difficult. Taiwan's project of voicing would not be complete if no written material was generated. When Professor Chu invited me into

his car, the interaction began and the CDE appeared in my network of knowledge, just as I did in theirs. In *Science in Action*, Bruno Latour (1988) points out the way so-called "scientific facts" are created by a lively process about how scientist "wrap up" ("black box" in Latour's term) their work by means of narratives. In the case of bridging studies, the CDE were the first people working on this topic, and I was the person who would complete it. Of course, the CDE had not fabricating any scientific truth. Its desire, so to speak, was always to "voice" itself. But just to voice is not enough—a voice needs a witness, in the form of an academic study or a journalistic report, to turn it into a lasting form of writing. The CDE was just trying to preserve this beautiful moment and make it last forever. The *DIA Journal* mentioned earlier in this chapter is the interim product, and this chapter is another one.

In any case, I decided to go to the meeting. Let me explain first why Taiwan was invited at all. Through the Steering Committee meeting held in Tokyo in May 2001, it knew that the E5 guideline would be discussed first within the ICH member states and regions, and then a questionnaire would be distributed to non-ICH countries. Furthermore, considering the good results achieved in the satellite meeting before ICH5, the GCG decided to extend its meeting into a one-day conference held before ICH6, and it invited four regional groups, including APEC, to join its preparatory meetings. The CDE would definitely not miss this chance. The minutes of one CDE internal meeting read, "APEC will recommend one representative to join the satellite session as either speaker or a member of the preparatory committee. Taiwan will use its project [on bridging studies] to earn this representativeship. We hope the result will single out Taiwan's leading position in this region" (CDE 2002). Taiwan was awarded the position, and had two representatives join the preparatory committee on behalf of APEC.

The meeting I attended was the second preparatory meeting. Because the other invited organizations invited did not show enough interest in this issue, in the first meeting the CDE had successfully bargained for two sessions at the ICH6 meeting about the APEC Network of Pharmaceutical Regulatory Science and Taiwan's policy on bridging studies. Chern even asked to attend the Implementation Working Party, which was organized to solve the difficulties created by the E5 guideline (for details, see Chapter 6, concluding remarks), as an observer. My participation thus gave me a chance to witness these achievements.

However, what surprised me more were Chern's connections; they were too real to deny. When we had breakfast with Rashmi Shah, an MHRA officer and a clinical pharmacologist, Chern introduced me as an independent researcher on the ICH, and discussed with Shah whether he could hold a training course at the CDE. During our

conversation, Chern greeted people he knew that passed by, including Eric Abadie, the EU representative and co-chair of the GCG, who later came and joined us. It seemed to be a normal scene of the sort that occurred at all international conferences. People meet, eat, drink, talk and catch up on what has happened since last meeting. Yet it had great ethnographic significance. At the beginning of this chapter, I described Taiwan's failed attempt to participate in the WHO; now I was witnessing this "illegal citizen" finding its bridge to the world through Chern.

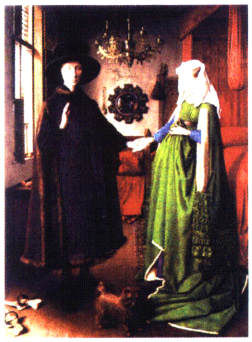
Taiwan was indeed smart and outstanding. Even in such a brief meeting, it grabbed hold of every chance to promote itself. In his presentation, Chern carefully reviewed every achievement Taiwan has made in drug regulation, rather like Chu's lectures I attended. The story was supplemented by evidence: submissions of clinical trial protocols increased after the foundation of the CDE, and its reviewing quality was good enough to be accepted by the very picky FDA. Chern's talk was so compelling that anyone listening would think Taiwan was the best place in Asia for clinical trials. This narrative was important for the GCG, because Taiwan's firm support of bridging set a good example about how this "politically" created guideline could be exercised "scientifically." Taiwan nicely caught the rhythms of the capitalist dance between the ICH members and the rest of the world. It was only in his last two slides that Chern even mentioned the APEC network, and then only to promote the 2003 meeting to be held in Taiwan. The GCG members, after listening, rewarded Chern's efforts by saying that they would suggest to the Steering Committee that they offer one or two non-ICH observerships for some working groups.[36]

When the meeting finished, I was deeply touched that I had been able to help represent Taiwan. Hayashi Yoshikazu of the MHLW caught me at the lobby before the dinner. He had been quiet at the meeting, but he wanted some information on Taiwan's recent policy on bridging studies. As I talked to him about my opinions, Javroongrit Yuppadee, the ASEAN representative, joined the conversation. She was interested in Taiwan's next step after bridging studies and its possible impacts on South East Asia. It was the first time Chern and I were not together, but these other officials seemed to have waited for this moment, hoping that I could fill in what Chern had not said in the meeting. Looking at their eager faces, I suddenly felt that I was no longer an outsider. They considered me a colleague of Chern, a Taiwanese official, and knew the CDE's tricks well. I had been placed in a position in their network of information, but they had no idea

[36] The ICH has invited experts from the non-ICH counties to working groups for some issues. For example, in the discussion on pharmacopoeias (Q4), the expert working group asked experts from India and the PRC to join in.

about their places in my network. Thus the information flow proceeded oddly. Although I explained my identity as a policy analyst and APEC representative, they still believed that I should know something about the CDE, which I did not quite understand. In turn, they did not understand my inquiries because they were not sure of their political implications. The dialogue was finally saved by the lobsters when we reached Les Crustaces, the restaurant where the evening meal was being served.

Fig. 5.7 *Left*: Some GCG meeting participants at the restaurant. *Right*: Portrait of Giovanni Arnolfini and His Wife (Arnolfini portrait), by Jan van Eyck (1434).

Note: the Back Row: Caroline Loew of the PhRMA (left), Uwoi Tohru of the JPMA (third to left), and Mike Ward of the Health Canada (fourth to left). The Front Row: Hayashi Yoshikazu of the MHLW (left), Eric Abadie of the EU (third to left), and Sabine Kopp-Kubel of the WHO (fourth to left).

Source: Wen-Hua Kuo (photographer, left) and National Gallery of London website, http://www.nationalgallery.org.uk (right).

Food changed the mood. Everyone seemed to forget their identities as government officials for a moment. They chatted about cultural and racial differences while discussing the menu like friends. Alex Giaquinto and Eric Abadie, the co-chairs of the GCG, were to resign after ICH6. "I am a scientist. I am so glad that I will not be bothered by these politics," Abadie told me. The Japanese representatives, Uwoi Tohru of the Japan Pharmaceutical Manufacturers Association and Hayashi Yoshikazu, were to leave the committee as well. Seeing this, I suggested that we have a group picture to celebrate the achievements that GCG had made, and I took the photo (fig. 5.7, left). Until that moment, I could not confirm my position. I would be leaving this field, too, and would no longer consider myself part of this group. Thus I took up the camera, choosing to watch

from a distance. Because of my position, I was allowed to take the picture. If this chapter is the narrative I made, one could say that I was carefully hidden behind the lines. Even so, in this section I emerged, just as I appeared as a reflection hidden behind the flash in this photograph. Like reflection in the concave mirror in van Eyck's Arnolfini portrait (fig. 5.7, right), my narrative and my photograph revealed the presence of the ethnographer who narrates the story.

This also marks the narrative end of this chapter. Let me summarize three points concerning the meaning of voice in ethnography. First, when globalization came, Japan and Taiwan responded differently in crafting the means by which they voiced themselves. In the case of Japan, although we read of some individuals, such as Doi Osamu, who insisted on racial difference as a topic for discussion at the ICH, in general, individual voices were repressed and hidden behind institutions. The MHLW was always the mouthpiece for Japan's opinion, and its voice was consistent. It was the strength of the institution, not an individual, that maintained this consistency; the person in a certain position might change from time to time, but the voice was the same.

However, in Taiwan I found a totally different mechanism of voicing. It is hard to tell which institution dominated the E5 policy in Taiwan, but individuals certainly played a critical role. Because of Taiwan's awkward political status, its voice could not be heard in any global scene for states. Therefore, even government officials had to alter their individual identities. As a result, Taiwan's voice could only be presented as in terms of personal politics; anyone who cared about Taiwan's statehood could stand for it. Even though, as described in Part II of this chapter, Taiwan started to establish an instrument to form an institutional voice, it was individuals who made this voice heard. The true instrument for voicing, in this sense, is not any particular institute, but a group of people who roughly shared the same idea. This chapter has named some figurers: Huang Weng-Foung, Hu Oliver Yoa-Pu, Wu Shuh-min, C.K. Chen, Shaw T. Chen, Chu Mong-Ling, Chern Herng-Der, Hisao Mei-Ling, Lin Marie, Chang Hong-Jen, and others. Their endeavors constructed a path by which Taiwan's bridging study policy was shaped and became known to the world.

Second, in the context of making an "objective" ethnography, this chapter shows a complicated situation far beyond the old notions like "being there" and "witnessing" from Bronislaw Malinowski, which assume the absence of the observer (or the observed) in the making of ethnography, or like "deep description" from Clifford Geertz, which assumes the conceptual division of an active observer and a passive observed. Concerning texts as a form of voice in a broad sense, both the CDE and I are the authors of this ethnography. In order to make a voice for Taiwan, the CDE used literary technology to create various

forms of text. On the other hand, guided by my research interests, I was fascinated by the information provided by the CDE (first lecture slides, and later notes, minutes, reports, and interviews) and wrote it up as an ethnography. The challenge of this task is not making the narrative "objective" by distinguishing my authorship from theirs, or making it "disinterested" by separating my interests from theirs. The ethnography I can achieve is what Stephen Tyler calls "the mutual, dialogical production of a discourse, of the story of sorts" (1986: 126). After a certain amount of communication between speaker and listener, recorder and informant, what emerges is a joint work of the ethnographer and his narrative partners. As Tyler writes, "The ethnographic text is not only not *an* object, it is not *the* object; it is instead a means, the meditative vehicle for a transcendence of time and place that is not just transcendental but a transcendental return to time and place" (129).

Third and last, concerning the representative power of voices, this chapter, which portrays Taiwan as a "countermelody" in the fugato called "bridging," agrees with Ranajit Guha that this text should be considered an *autonomous* domain. It neither accuses any historiography of lacking such a voice, nor argues for an ontological entity that makes such a voice. Instead, this chapter tries to depict rhetorical identities that make voices meaningful in this ethnographic text. For this reason, this chapter also agrees with Stephen Tyler's understanding of ethnography: that it should no longer be cursed with the task of representation, because "its meaning is not in it but in an understanding, of which it is only a consumed fragment" (129). Evocation, as Tyler insists, is the key concept for this understanding. This chapter, as the medium by which some voices are evoked, is useful in many ways, contingent upon the context in which it was written, and how it will be distributed and consumed.

I do not want to make this discussion too philosophical, but I would like to share an anecdote here as this chapter ends. I remembered that on our way to the ICH meeting, in a terminal lobby in the Vienna International Airport, Chern Herng-Der asked me to work for the government after I completed my degree. It was early morning; we were waiting for the connecting flight. He asked me persuasively, "Don't you think that it is exciting, to attend international conferences and meet important people in the world? We are physicians, and Taiwanese physicians should have a more broad vision. You see, I am an M.D.-Ph.D., and you will have yours soon. If you choose this track, you may be able to decide the future of our twenty-three million people like I do. Think of it: *you* can do it!" Chern emphasized again and waited for my answer. At that moment, I could see the figures mentioned in this chapter, their life stories, and Taiwan's political future; they were all within me. I was overwhelmed. "I do not know, really."

PART THREE
States Strike Back: Preserving National Values for the Future

On a summer afternoon in August 2004, I made an appointment with Professor M at Kitasato University.

Located in Shirokane, a quiet area in Tokyo, which is home to many embassies and parks, the university is also the historical site where Kitasato Shibasaburo (1852-1931), a physician and one of the founders of modern bacteriology in Japan, established his research institute that later became the archetype for this medical complex. Formerly one of the most esteemed students of German bacteriologist Robert Koch, Kitasato had a brilliant career inside and outside of Japan. Before returning to Japan from his studies in Germany, he built an international reputation on the basis of his work on tetanus and diphtheria bacilli; in 1894, almost simultaneously with French bacteriologist Alexandre Yersin, his team discovered the *Pasteurella pestis* bacillus in Hong Kong. Under Kitasato's leadership, the Institute formed a strong tradition in medical research that continues toady.

Even so, I did not see any old buildings when I arrived. This campus had just undergone a major renovation in 2001 and housed the University Hospital and School of Pharmaceutical Science. Professor M shared a floor of the research building with another faculty member. His secretary welcomed me when I knocked on the door of his laboratory; the previous appointments were delayed. "Our professor is always busy," she apologized. As I sat in the reception room, I had a chance to look at this laboratory. Unlike the traditional classroom or laboratory, which is always dark and mysterious, it was a bright, commodious room divided by several cubicles, each of which accommodated a researcher or secretary. Facing the campus, the professor's work area was at the end of this room. In another corner was a small library, with a good collection of the latest journals stored on wheeled bookshelves. Except for the secretary, everyone continued working after I arrived. My intrusion seemed not to bother them at all. If I had not been informed about the place, I would have believed that it was a commercial company.

After twenty minutes, Professor M's guest left and he came out to meet me. In his mid forties, Professor M was still young and energetic. We shook hands and exchanged cards, as one is taught in Japanese class, but following this we switched to an American style of interaction. Professor M apologized to me again about the delay and guided me to his office, which was decorated with his university photos, photos of graduate school, and school souvenirs, all from an American city I was familiar with. "I did not know your undergraduate degree was in the United States," I said. "Yes, my undergraduate and graduate school were in the same city, as you see, just across the river, before I worked for the FDA," he replied with a smile.

This was not the first time I have met Professor M. The first time I saw him was at a conference on bridging studies in Taipei, where he presented a technical paper on Japan's response to bridging studies. I introduced myself after the conference and we talked in the corridor before he went dinner with other speakers. Unlike other Japanese scholars, who are often shy with their English, Professor M is talkative and straightforward, with perfect English. His attitude is not typically Japanese either. He did not dodge any of the sensitive questions that I asked him. He explained his main points to me in understandable terms, which surprised me. I wondered whether his theory would work if Japan continued to insist on its racial uniqueness. He simply replied that he personally did not think it was right and that I should not feel that it could not change. Regarding the reason he had come to the conference, he just said, "Everyone knows that when talking about bridging studies, they talk Taiwan. Besides, I have many friends here; they asked me to come, so I did." I immediately begged him to allow me to visit his laboratory when I went to Tokyo. I found his ideas interesting and wanted to know more, so I came to this American-style laboratory oddly inserted into one of Japan's most traditional medical schools.

We had a long talk and I grew to know Professor M's thoughts more clearly. He was educated in the United States and had worked in United States for eight years. Like what I heard from Americans, Professor M first told me that, in his opinion, racial difference or the Japanese uniqueness was nothing but a temporary excuse used to protect Japan's domestic industry, and he believed that it would not last forever. He was so persuasive that I was almost convinced that the Japanese government would soon give up its insistence. "But," I wondered, "Why doesn't Japan just simply accept the ICH guideline or use the procedure suggested by Taiwan?" Pausing for a moment, Professor M said that this was because the MHLW could not allow unsafe products to be imported into Japan without any investigation. Then he started to explain to me about his project to deal with racial difference, global drug development, target population categorization, and extra studies for external factors on racial differences, all of which I had heard from other Japanese scientists. I could not help but interject, "Wait a minute. If this is what you think, what is different from your original plan? This is still based on the assumption that you are different from others."

At this time I could see the Japanese spirit beneath Professor M's American behavior. Whether he was aware of it or not, this racial assumption was so deeply rooted in his mentality that it would never change. To waive the protection time was one thing, but to subject Japanese bodily differences to a universal standard was quite another. What was different were his words, which were new terms for interpreting this difference, a

workable way of recognizing it, and a methodology for convincing others that it was necessary to partially repeat clinical trials. I know it is not fair for Japan to accept a U.S.-dominated standard, but Professor M knows better. He explained, "I have worked at the FDA, and I know the situation. Think of it. If you replace the FDA with the OPSR, what will they do? My experience tells me that the FDA would ask for more clinical trails using U.S. subjects. I do not see why Japan cannot do what the United States practices." It was at that point that I knew the reason he visited Taiwan. Facing the same pressure from the United States, he was curious about how Taiwan would deal with them using bridging studies.

Before ending the interview, I tested Professor M by asking him why he did not share his opinions about the bridging study policy with his Taiwanese colleagues. "Well, I discussed bridging studies with them. But we never talk about policy issues." He said. "Don't you think that it is not our business to tell other governments what they should do or what they should not do? We are scientists." When he said this, I saw his American side return.

Looking back at his mysterious hint, I decided to look into the ways both Japan and Taiwan wove their visions on racial difference in scientific language. This was another starting point for this journey.

Chapter 6
Sounding Genomics: Situating the Japanese Race in the Post-E5 Era

> Only until the implementation of the E5 and E6 guidelines did the Japanese have the self-awareness of being internationalized.
>
> Naito Chikayuki[1]

> If it is agreed that the human species is one and that it consists of a group of populations which, more or less, replace each other geographically or ecologically and of which the neighboring ones integrate or hybridize wherever they are in contact, or are potentially capable of doing so, then it should be obvious that the task of the student interested in the character of these populations must lie in the study of the frequency distribution of the genes which characterize them—and not in the study of entities which have no meaning.
>
> Ashley Montagu[2]

PART I
BACK TO THE ORIGIN: THE DEADLOCK OF BRIDGING STUDIES

Bridging into the New Era

In March 1998 the E5 guideline was approved by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Steering Committee with some corrections; it was then implemented by the E.U. in March and by the U.S. Food and Drug Administration (FDA) in September. As for Japan, the Ministry of Health and Welfare (MHW, later renamed the MHLW) implemented it in August of that year (Notification No. 672 and PMSB Notification No. 739). Not knowing exactly what was behind the making of this guideline, the public celebrated this achievement that would accomplish the dreamt-of bridge between Japan and the global. In *Yakujinippo* (the Pharmaceutical News) on October 5, 1998, for example, a number of articles addressed various concerns about implementation of this guideline and the impacts of the ICH. It seemed that the E5 guideline was the indicator of

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1 Senior Consultant of the Organization for Pharmaceutical Safety and Research (OPSR), in interview.
2 "The Concept of Race in the Human Species in the Light of Genetics," in *The Concept of Race* (Free Press, 1964).

whether Japan would accept the ICH, and the ICH was the indicator of whether Japan would accept globalization.

Of course, some worried about the possible impacts globalization would bring; but on the surface their responses seemed calm. I reviewed the conversation between Doi Osamu of the MHW and Dr. Muzishima Yutaka in Chapter 4, in which the ICH was described as the "black ship" of international drug regulation. In fact, this long conversation discussed other issues concerning the new Organization for Pharmaceutical Safety and Research (OPSR), the reform of clinical trials, and new strategies of drug development, all related to the ICH. Other articles described reactions to the introduction of E5 and the other guidelines. For example, in the column "Today's topic," an article entitled "Global approval: a dream expanding" recorded how difficult the passing of such a guideline was. "The longest outstanding problem," it said, "was finally reached.... It is expected that a great amount of foreign data will be introduced." Another article, however, reported that in the near future, a spontaneous acceptance of clinical data would be achieved among all ICH regions.

Some articles addressed the industry's immediate responses to the implementation. Pfizer Japan, as noted, had submitted Viagra (sildenafil citrate) to the OPSR for approval at the end of July 1998, at the same time as Eisai's Aricept (donepezil hydrochloride). One article specifically mentioned the influence of bridging studies. It first interpreted bridging studies as one requirement for reviewing products that contained clinical trial data conducted in foreign countries. Although no one knew what standard the OPSR would use in reviewing such cases, basically the article expressed a polite and cautious optimism. If no bridging studies were required, it predicted, manufacturers would save a lot of money and time.

All this sounded fine. Japan seemed to be moving smoothly into the era of bio-globalization. Readers may remember Donna Haraway's observation of the three configurations of bioscientific thinking, the categories of unities and differences that constituted the human species discussed in Chapter 4 (table 4.1 and Haraway 1997: 219-229). Regardless of how much conflict the making of the E5 guideline had entailed, its implementation completed the bioscientific configuration of discourses Haraway describes as centered on the concept of population. With the conceptual algorithm of bridging studies, populations, or as they say, gene frequencies, could be transformed and interchanged in the world of proprietary drugs. The harmony of the ICH, though illusory, seemed like it would be able to satisfy both the Japanese government and global industry by stabilizing the configuration of bioscientific knowledge. However, this did not turn out to be the case. Haraway describes the change of focus in the American scene from

population to genome beginning in 1975 and continuing into the time of her writing in the late 1990s, and in this thesis I will show that at the beginning of the twenty-first century, the E5 guideline also attempted to make this move into genomics. Of course, as Haraway points out, commercialization is one of the factors that can prompt such a move. However, in the context of the ICH, the necessity of this move was instead embedded in the cultural and conceptual assumptions about race as a collective category. In the rest of this section I will describe the practical problems that made the discourse on racial difference "incomplete" and why this move was necessary for Japan. The former subject will be elaborated in the first part of this chapter and the latter in the second part.

To understand the practical reasons that bridging studies failed, we have to consider the E6 guideline, which was implemented around the same time as the E5 guideline (PAB Notification No.430, MHW Ordinance No.28). Titled "Good Clinical Practice (GCP)," the E6 guideline was designed to clarify the responsibilities and expectations of all participants in the conduct of clinical trials, covering aspects of trial monitoring, reporting and archiving. Although this guideline seemed to be a simple requirement for clinical trials quality, for Japan it was one of the most difficult guidelines to put into practice.[3] As I mentioned in Chapter 3, prior to the ICH, Japan conducted "Japanese style" clinical trials with numerous sites, loose site management, and a hierarchal structure based not on experimental methodology but on trust among investigators. Therefore, after the implementation of the two guidelines, if Japan wanted to keep some clinical trials in Japan, it would have to change its practices to conform with the "Americanized" clinical trials mandated by the E6 guideline; if not, global industry could waive any trial requirements with the help of the E5 guideline. This is what E5 veteran Naito Chikayuki is referring to in the quotation at the beginning of this chapter. For Japan, the guidelines were two "big bangs" as described in many presentations regarding the ICH's impact on Japan (fig. 6.1).

The interrelationship of the E5 and E6 guidelines created dual dynamics—between clinical trials and racial differences, as well as between industry, the FDA and the OPSR. Let us consider the dynamic between the two guidelines first. Unlike the E5 guideline, the making of which was painful and the results of which were a mess, the drafting of the E6 guideline proceeded smoothly and without dispute. The problem was not how to interpret what was good clinical practice, but how to actually implement it.

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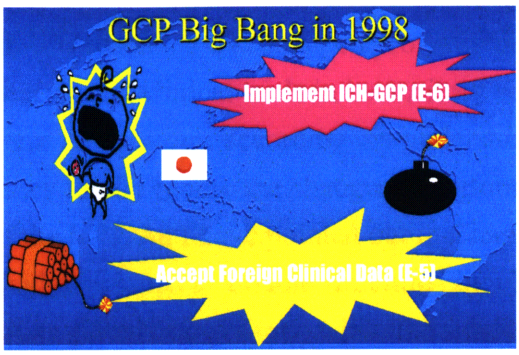
[3] GCP is a term I often heard from people that I interviewed in Japan. Apparently it is another issue that identified concerns about cultural conflicts between East and West in medical practices. Like the acceptance of foreign data, the issue about the quality of clinical trials can be traced back to 1985, when the MHW released regulations concerning good clinical practice. This issue deserves a study of its own and will not be dealt with here.

Fig. 6.1. Two "Big Bangs" For Clinical Trials in Japan: Acceptance of Foreign Data (bottom) and Implementation of GCP (top)



Source: Sato Takeyuki's slide presentation at the 2002APEC Meeting, Tokyo.

Leaving aside problems related to the hierarchy of the Japanese physicians who were key in conducting clinical trials, there were many social and cultural concerns that were difficult to resolve. For example, asking clinical trial participants for written and signed informed consent seriously violates the patient-physician relationship in Japan, where doctors are trained not to tell the diagnosis of a disease, if it is incurable, to the patient themselves. Also, it was difficult to use placebos in clinical trials in Japan. Previously, there had been only comparative studies, where the new compound was tested against an existing one. In Japan it is recognized as unethical to treat patients, no matter the purpose, with a substance that is known to be ineffective against their disease. Since clinical trial subjects must be recruited on a voluntary basis, it would be hard for anyone to carry out such trials in Japan until the social consensus was changed. As Etienne Labbe of the European Federation of Pharmaceutical Industries and Associations (EFPIA) concluded, "The quality of Japanese studies is very poor, not scientific, and does not [meet] our standards, particularly with regard to 'end-point' for assessment, and statistical approach. If I may say, the preclinical part of the Japanese dossier was of good quality, but the clinical part was at the stage of the middle ages." Thus, in practice, the dynamic between the E5 and E6 guidelines is ambiguous. It was likely that in order to retain some clinical trials, Japan would use its interpretation of bridging studies to force some trials to be done in Japan because of concerns about racial difference.

This ambiguity relates to the strategic dynamics between industry and the OPSR. The polarizing discourse of protectionism returned in industry's strategy to force the OPSR, the regulatory authority, to accept their agenda that assumes the primary unity of

human beings. On the one hand, multinational drug firms could continue the old accusation that Japan wanted to protect its pharmaceutical industry by delaying the importation of competing products. But upon the implementation of the E6 guideline, they could add the emerging industry of Contracted Research Organizations (CROs) to the list of guilty parties. In this extended discourse on protectionism, it was argued that Japan was attempting to keep more clinical trials in its territory so that it could establish its own CRO industry. These accusations, according my understanding, are narrow-sighted, because they totally ignore the changes that globalization had made during the introduction of the ICH. As I have pointed out in Chapter 3, Japan's pharmaceutical industry had developed a "double structure" in which the top ten companies behaved like their global competitors, while the small and medium-sized ones remained the same. These big companies did not really need protection to help them sell drugs overseas, and for the small and medium companies, the accusation of protectionism was probably not valid because they targeted to different market. The criticism of the CRO industry is possibly valid, but so far the Japanese government has not formed a concrete plan for building up its own CRO industry.[4] But no matter how problematic this discourse might be, it was powerful enough to make people recall the historical image of a protectionist Japan.

On the other hand, the OPSR did not feel that Japan was fairly treated. I heard some accusations that the FDA discriminated against Japanese data, as drug applications using these data failed to pass the excessively high GCP and Good Manufacturing Practice (GMP) bars. Japan might know that their clinical trials environment was not that "scientific"; however, the Japanese wanted to deal with these problems in their own way. To achieve ICH-qualified clinical trials, the OPSR has organized workshops and symposiums to explain this new system since 1997 and has conducted inspections of clinical sites inside Japan. It has repeatedly asserted that the FDA usually rejected the results of Japan's previous clinical trails based on their poor quality. However, under the international standard agreed to by the ICH, Japanese clinical trials should be considered qualified, no matter how they are done, but the FDA still accepts almost no Japanese data. No matter which side is right, these accusations reflect the embarrassing but true fact that the harmony of ICH rules did not bring peace to this situation. Instead, these guidelines recalled old tensions and created new dynamics that complicated the situation, all of which seemed to hinge on the basic concepts of human species and race. Apparently, the

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[4] Although this matter deserves further research, I hesitate to pursue it because of my deep concerns about whether health care should be recognized as a "business" that needs promotion by government.

bioscientific configuration based on population could not address these issues adequately in this context.

From the point of view of scientific progress, there was, as a result, an attempt to move to genomics at the ICH. However, STS research is concerned about the context in which this move was made: who was responsible for it and for what reasons? This will be the topic of the second part of this chapter. In order to achieve an understanding, I briefly review what I have discussed earlier about the making of the E5 guideline. In Chapter 4 I defined two modes of conversation about drugs and globalization. One was a bilateral mode, in which Japan had to deal directly with the United States regarding requirements for drug approval in the midst of trade frictions between the two countries. The other was the global mode of the ICH, in which the E.U. joined the negotiation and the discussion took place through the EWG, a body of experts and scientists. Obviously, Japan preferred the latter mode.

This was when racial difference was introduced into the discussion and a guideline needed to come out of it. During the discussion, the Japanese MHW was unable to keep Japanese racial identity an independent category (which would have implied that the Japanese should be dealt with separately), and it hesitantly agreed that all human beings are biologically similar. Even so, Japan did not accept that the idea of a universal standard by which all population differences could be accounted for by means of the proper algorithms. Bridging studies were a compromise agenda that preserved this assumption from attempts by European and American experts to "trivialize" the factors claimed to make up the difference among races. As the product of such a context, the guideline is both scientific and political. It does carry scientific meaning that should be the starting point for further negotiations. However, it is also a product of political compromise because it does not rule explicitly on how any racial sensitivities to drugs are to be considered. Although bridging studies using local subjects were required for those drugs for which racially distinct effects could not currently be estimated by algorithms, local regulatory authorities such as the OPSR have the freedom to require every applicant drug to undergo local clinical trials before being marketed.

From this description we can see the background for the genomic move at the ICH. Having accepted the E5 and E6 guidelines as the legal basis for the acceptability of foreign clinical trials, Japan and the United States could no longer refuse to use of foreign data without acceptable reasons. When tensions arose among industry, the FDA and the OPSR, the mode of conversation would switch back to the bilateral trade mode if no scientific reasons were given for administrative blockades. This mode, as I have mentioned in Chapter 4, did not favor Japan. Because of this, it was up to Japan to make

any move, and the strategy was clear: if the MHW wanted to have a certain number of Japanese subjects recruited into clinical trials, it had to return to the guideline and make revisions; in order to make such revisions, it had to have a scientifically justified reason

This is the reason I cited Ashley Montagu at the beginning of this chapter. As we know, Montagu work (1964) ended the bioscientific configuration of race by separating scientific biological diversity from cultural implications. Population genetics was the scientific tool of this new program, and it gave rise to the idea of population as the basis for an alternative configuration. This does not mean that there was a total break between the concepts of population and race, although many may see it as a paradigmatic shift. It might be so in theory, but this was not quite true in reality—most of the time people used these terms interchangeably. What was new was the idea of micro-changes in genetic information that took place at the borders of neighboring populations, making population a metamorphic collectivity rather than a fixed, unchangeable entity. Genomics should be considered the same way. Many might have expectations about the changes it would bring to the discussion of race, but this was not the case at the ICH. Genomics is a tool for showing the biological characteristics of individuals, but this does not mean that it would totally reject the collective unity of population. As Haraway observes (1997: 247), "The human to be represented, then, has a particular kind of totality, or species of being, as well as a specific kind of individuality. At whatever level of individuality or collectivity, from a single gene region extracted from one sample through the whole species genome, this human is itself an information structure." Scaling is not the point of this change; the point is the way this genetic information is presented. As I will show later in this chapter, in the context of racial difference, genomics was not introduced to dissolve the identity of the Japanese race but to reconfirm its existence in the era of globalization. This was achieved by providing the information needed to make race an independent category in global clinical trials.

Here is the plan for the rest of this chapter. The "slow motion" ethnography featured in Chapter 4 will be used in this chapter as well. The first part of the chapter is a sketch of the situation after the implementation of the E5 guideline. I will describe the gap between the ideal and the reality of the implementation of the E5 guideline. I will further analyze the dynamics of voicing among industry, the FDA and the MHW. When the failure to waive local clinical trials occurred, industry tried their best to push again through the channel of the U.S.-Japan Market-oriented, Sector-selected Discussion (MOSS) meeting, in which the U.S. government was dominant. While the FDA, which had made its own standard into the world standard, did not show any interest in either the ICH or MOSS, Japan also faced pressure from industry and the need to adjust this situation.

In the second part of the chapter I will analyze Japan's responses to this pressure from two perspectives with regard to voicing. First, the MHW attempted to formulate a new scientific framework for clinical trials in which the Japanese would be recognized as a separate category. As a more advanced science, genomics was called upon to serve this purpose. Meanwhile, the MHW tried to promote this program. It redirected the pressure from industry back to the global platform of the ICH, trying to revise the E5 guideline. Meanwhile, it formed a dedicated channel with the FDA so that it could deal with issues concerning this guideline without political intervention.

By the Guideline: The Ideal of Harmonization

Let us start with the scene when the E5 guideline was announced. Presented in the panel "Planning a Global Clinical Development" at ICH4, it was extensively discussed with high expectations; people thought that it would facilitate the global approval of drugs. A huge amount of costs and patients that had previously been required would be saved.[5] The guideline would not be complicated to implement according to ICH representatives' understanding. Etienne Labbe, for example, commented, "Surprisingly this paper [the E5 guideline] does not provide the pharmaceutical industry and the regulatory bodies with sophisticated procedures to extrapolate foreign clinical data to the population of a new region and to accept these data as supportive for the assessment of a new drug application" (D'Arcy and Harron eds. 1998:346).

Indeed, as stated in its introduction, the guideline provides "guidance with respect to regulatory and development strategies that will permit adequate evaluation of the influence of ethnic factors while minimizing duplication of clinical studies and supplying medicines expeditiously to patients for their benefit" (ICH 1998: 1). The flow chart shown in fig. 6.2 indicates how drug applications should be assessed. To initiate an application for registration using foreign data (question 1), a special data package is requested that includes "characterization of pharmacokinetics, pharmacodynamics, dose response, efficacy and safety in the population of the foreign region(s), and clinical trials establishing dose response, efficacy and safety" (2). It also required additional studies, so-called "studies for bridging," to meet new regions' regulatory requirements.[6]

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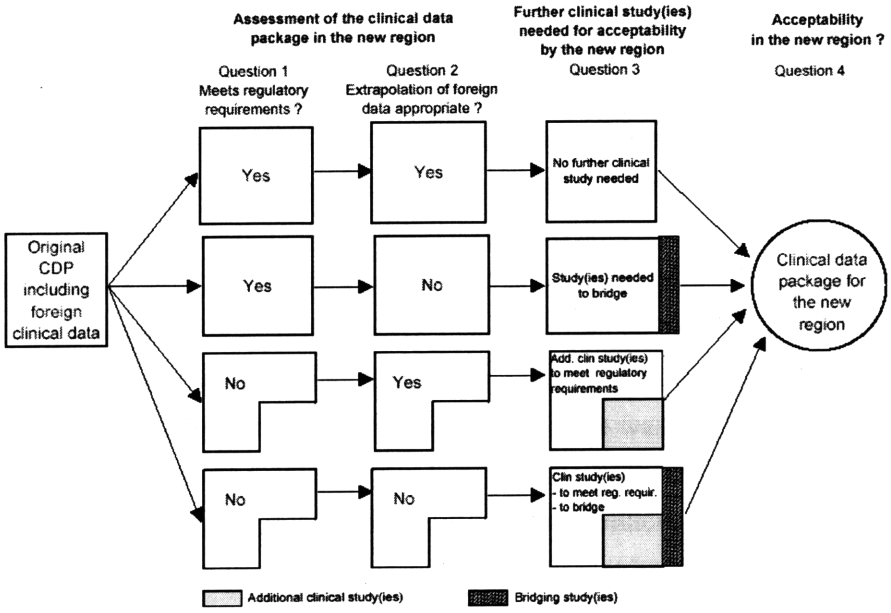
[5] Etienne Labbe estimated that at least 40 to 45 studies and 2,500 to 3,000 patients would be saved, while the introduction of drugs could happen two or three years earlier in the United States and five to six years earlier in Japan. See D'Arcy and Harron eds. 1998:349.

[6] Some examples include, first, clinical trials in different subsets of the population, such as patients with renal insufficiency, patients with hepatic dysfunction, etc; and, second, clinical trials using different comparators at the new region's approved dosage and drug-drug interaction studies (E5 guideline:3).

According to the guideline, bridging studies are required when a product is not granted a waiver for clinical trials in the new region.[7] A bridging study is defined as "a supplemental study performed in the new region to provide pharmacodynamic or clinical data on efficacy, safety, dosage, and dose regimen in the new region that will allow extrapolation of the foreign clinical data to the new region" (glossary 7). In addition, for safety reasons, a pharmacokinetic study in the new region may be considered necessary for products that need no bridging studies (4).

Fig. 6.2 Assessment of the Clinical Data Package for Acceptability



Source: E5 guideline. Appendix B:11.

When the regulatory authority is presented with the data, it will first request any additional data that will be necessary to make judgments on whether bridging studies are required (question 2 and 3). No exact criteria for whether a product is eligible for waiving bridging studies are specified in the guideline, but the applicant is encouraged, where possible, to consult with the regulatory authority "to determine what kind of bridging study will be needed" (ICH 1998: section 3.2.2:4). Even so, looking at the positive side of the guideline, these products are still "bridgeable" to the new region. As the guideline

[7] It must be noted that though the product may not be granted a waiver for any part of its application to the new region, data on it from a clinical trial done in the new region is still extrapolatable. In other words, there are, in practice, no criteria for whether extrapolation is possible. The key is how many bridging studies are requested and what on scale they are asked for.

states, in cases in which bridging studies are required, the acceptance of foreign data "may be achieved by generating 'bridging' data in order to extrapolate the safety and efficacy data from the population in the foreign region(s) to the population" (summary:7). This seems to assume that every product is bridgeable if it is possible to provide a smaller scale clinical trial—that is, one with fewer subjects enrolled that would be conducted in the name of establishing a "bridge." The size of such studies is another point. Although it was agreed that generally only one trial study is enough, in practice the guideline suggests that the sponsors do more than one in order to get approval (4).

The above procedure looks complicated, but its complexity should be assessed in the context of the issue it deals with. Racial difference is so touchy an issue that everyone should appreciate that this guideline overcomes the problems it poses at a small price. The ICH, in fact, was very proud of it. In its brochure titled "The Value and Benefit of ICH to Industry" (Nutley ed. 2000) the ICH listed the E5 guideline as its first and foremost achievement, claiming that the "costly and time-consuming activity [of clinical trials], frequently involving the repeat of long, resource-intensive Phase III clinical trials, is obviated in most cases by the introduction of this guideline" (3). A dramatic case that arose immediately after this assertion was the approval of Viagra by the MHW, which had blocked the import of drugs of this kind for over 30 years. Pfizer applied to the MHW for approval for Viagra at the same time that the E5 guideline was implemented, so it was an indicator for this policy. The result pleased the industry. With the help of a bridging study, it took less than a year to get the drug approved. John Nibliack, Executive Vice President of Pfizer, confirmed the value of this guideline, stating that because of the E5 guideline, "we did not have to repeat the Phase III trials in Japan" (3).[8]

The most cited case concerning racial difference and bridging studies is Aricept. It was one of the early applicants for bridging studies; Eisai, the manufacturer of the drug, followed all the steps suggested in the guideline, and the result was satisfactory. The example of Aricept can help explain how the drug review process specified in the guideline can be conducted. The following description is mainly based on a presentation by Takayama Chihiro, Director of Aricept Department t the APEC 2002 workshop titled "Impact on the Conduct and Outcome of Clinical Trials," and a paper about Aricept by Homma et al. from 2000.

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[8] Pfizer was not the only company to benefit from this guideline. In April 2000, AstraZeneca submitted a new drug application in Japan for its Triptan migraine treatment Zomig (zolmitriptan). It was the second Japanese new drug application to be submitted by AstraZeneca based on the importation of Western data using the E5 guideline. AstraZeneca was the first company to seek approval in Japan for the second generation of Triptan compounds for migraine. For details and other successful cases, see Usui 2002 and the special issue of *Pharm Stage*, vol.2 no.4.

Aricept, an acetyl cholinesterase (AchE) inhibitor that offers symptom treatment for Alzheimer's patients, was developed in the early 1990s. Despite its Japanese origin, the primary market was to be the U.S., where a controlled clinical trial on over 900 subjects was conducted. After FDA approval of the drug in December 1996, Aricept successfully penetrated the major European markets. This was followed by quick approvals in Asia by Thailand, Korea and the PRC. This called attention to an embarrassing situation. Although Japan is a developed country that has many elderly people living with and suffering from Alzheimer's, this "Japanese" drug had not been sold in its own market. Therefore, when the E5 guideline was enacted, it was one of first products for which the use of bridging studies was attempted.

According to Takayama, the process went smoothly. Eisai prepared the PK comparison between healthy Japanese and Caucasian American subjects (phase I trial). They claimed that the PK profiles of the two races did not show a "significant" difference in Cmax and AUC under the same standard conditions of measurement. Thus when the company first approached the OPSR, they confirmed that Aricept's behavior was the same and bridging was thus feasible. For the second consultation with the OPSR on the phase II trial, Eisai provided more information on responses to doses (1mg, 3 mg, and 5 mg per day for the Japanese) other than the two doses (10 mg and 5 mg for the Americans) that were applied in original studies done in the United States, and the company decided to use 5 mg as the dose for further evaluation.

Only at this point did Eisai enter a discussion on "bridging justification," which was done at the company's third consultation with the OPSR. Upon the conclusion of the second consultation, Eisai had designed an "incomplete" phase III study for safety and efficacy, using Japanese subjects and a single administration of 5mg per day, but a bridging study was still suggested by the OPSR. Testing two doses of 5mg and 10 mg, this study was conducted in a setting equivalent to that of the original study in the United States in order to claim that is was "identical" to the original and the data obtained thus comparable or able to be "bridged."[9] The results were satisfactory. Based on the above studies, the applicant claimed that analysis showed similarities in efficacy and safety in the U.S. and the Japanese subjects; thus it was agreed that the Japanese study could

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[9] Eisai's research team applied DSM-IV and Hachinski ischemic score diagnostic criteria. In addition, in accordance with the guideline, the study proposal covered possible factors that could involve intrinsic and extrinsic racial differences, such as 1) similar trial conditions to the foreign tests were incorporated based on the concept of bridging; 2) medical practices—the same diagnosis system was applied; 3) therapeutic circumstances, such as concomitant medication; 4) criteria for the inclusion and exclusion of subjects; 5) assessment criteria and assessment/analytical methods for primary endpoints—although the bridging concept had not been intentionally described in the original protocol, a similar primary endpoint to the foreign trial was employed; 6) treatment duration should be same for all subjects involved in the trial.

bridge to the data of the U.S. study. In the fourth and last consultation, the OPSR announced its approval of the drug. Aricept was finally imported into Japanese market in 1999.

The significance of the story of Aricept is that it demonstrated a standard procedure for the evaluation of bridging studies. We can trace its review process in fig. 6.2. Although after the consultation one bridging study was still requested, as seen in the scenario that shows a "Yes" response to the first question but a "No" to the second (in the second consultation), it recognized a racial difference by stating that a smaller does better suited Japanese patients. In addition, this case shows Japan's willingness to create a transparent environment for drug review. Unlike the old reviewing bureaucracy, which was often criticized as corrupt and opaque, the OPSR is a science-oriented, independent institution; its reputation was highlighted in its evaluation of the bridging study. As Hayashi Yoshikazu of the Pharmaceutical and Food Safety Bureau at the MHLW said, the OPSR ensures "the consistency of, and adherence to during the review of application, advice given in prior consultations provided by OPSR, which are based on MHLW policy" (WGDA Japan 2000: 243).

The foundation of the OPSR created in industry the trust necessary to send their applications to be evaluated for bridging studies, and the harmonization of clinical data could thus be achieved by rigorous adherence to the concerns raised in the guideline. According to the OPSR's statistical report (table 6.1), its performance seems good. Between 1997 and 2002 it offered over 1,000 consultations, of which about 32 percent were for bridging studies.

Table 6.1 Consultations Offered by the OPSR, 1997-2002

Year	1997	1998	1999	2000	2001	2002	Total
All cases	101	149	194	279	268	223	1214
Bridging studies	24	59	98	82	63	65	391

Source: Kazuhiko Mori's slide presentation at ICH6. http://ich.org.

Some might not be satisfied with the service offered, but, as I have argued repeatedly, this achievement needs to be considered in the context of the making of the E5 guideline and the debate over racial difference that it entailed. As one OPSR expert

told me, "At least we have science. For me, it could not be better to have it in our practice."

Where the Explanations End: The Reality of Bridging

Although the case of Aricept shows how bridging is possible, it also demonstrates its restrictions by showing how difficult it is to attempt to "bridge" racial differences. Two pieces of information need to be provided here. The first is an overview of how many drugs have been approved via bridging since the implementation of the E5 guideline. Up to October 2003, only 30 products had been approved out of about 230 NDA approvals, approximately 14 percent of the total.[10] The numbers speak for themselves; the reality is that the approval rate is low. Many drugs on this list were granted approval just before their patents were going to expire.

Let us take omeprazole as an example. Launched in 1988, this second-best-selling drug in the world used for treating stomach ailments has earned AstraZeneca billions of dollars since its American launch in 1988. With the help of patent term extensions or Supplementary Protection Certificates (SPCs) for this drug, its patent did not expire in the United States until 2001. KUDCo/Schwarz Pharma launched its generic version of omeprazole in 2002, the same year the MHLW granted approval to the company's proprietary omeprazole, Losec. Although Japan granted Losec patent extensions, these allowed only two years before their expiration in 2004.[11]

Secondly, it is correct that during the consultation Aricept was requested to provide only one new trial; but if we review this carefully, we can find that Eisai had already done some local trials, such as the PK study comparing Japanese and Caucasians. These were phase I and phase II trials, which were pivotal for bridging. We can agree that compared to the previous system, which required that all trials be repeated, bridging studies did

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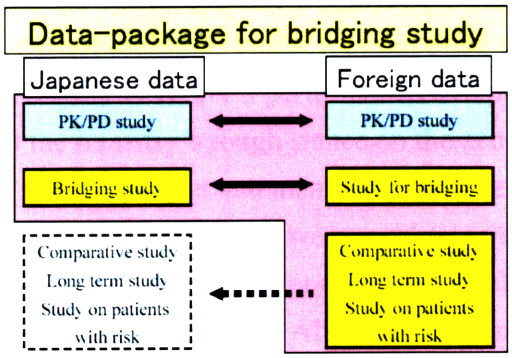
[10] They are sildenafil citrate, donepezil hydrochloride (approved in 1999), fexofenadine hydrochloride, anastrozole, oseltamivir phosphate (approved in 2000), zolmitriptan, sumatriptan succinate, sodium alendronate, insulin aspart, imatinib mesilate (approved in 2001), palivizumab, sodium risedronate, goserelin acetate, basiliximab, oseltamivir phosphate pediatric, eletriptan hydrobromide, omeprazole, three combination drugs (for the eradication of H. pylori), exemestane, gefitinib, brinzolamide (approved in 2002), satriptan nasal spray, leflunomide, infliximab (RA), imatinib (GIST), rizatriptan, tegaful+uracil+folinate (UFT), pramipexole, PEG-interferon α -2a, and verteporfin (approved in 2003).

[11] Omeprazole is a proton pump inhibitor that has racially distinct effects on P450 metabolic enzymes; and this had been noticed by the Japanese for a long time. In fact, in early 1990s Eisai had discovered this mechanism and had its compound rabeprazole filed with the NDA in Japan. However, because of the relatedness of the two compounds, Eisai was involved in a patent dispute with AstraZeneca when attempting to develop its rabeprazole in the United States. For more discussions on racially specific effects of this drug, see Chapter 7.

save some time and energy, but this savings was quite limited. This trend became clear from the OPSR's reviewing policy on bridging studies, as shown in fig. 6.3.

Fig. 6.3 OPSR's Interpretation of Bridging Studies



Source: Kazuhiko Mori's slide presentation in the 2001 APEC meeting.

Figure 6.3 illustrates how many trials are in fact required in the scheme of bridging. The essential data package for a bridging study, as indicated, includes not only the original clinical data obtained in the foreign region; it has to have Japanese PK data as well as some dose-response data and studies for bridging. Only when this information is ready can a smaller phase III trial called a "bridging study" be conducted.

Even the so-called "bridging study" requires a large number of subjects, almost as many as the original trials. Let us use Aricept again as an example. According to the study by Eisai scientists S.L. Rogers and colleagues (1998), only 473 patients were enrolled in the original Aricept trial done in the United States—162 subjects were given placebos, 157 received 10 mg Aricept per day, and 154 received 5 mg per day. However, in the Japanese study, which only included placebo and 5 mg per day groups, a total of 228 patients were recruited. In other words, all that Eisai really saved was the expense required to test patients with 10 mg per day Aricept.

It was understandable that global industry was not able to accept this practice. They seemed not to understand the underlying cultural division presented by this political compromise; instead, they asked for explanations of the E5 guideline that might favor their interests. As soon as the MHW implemented the guideline, it released a document in both English and Japanese listing the most frequently asked questions about bridging studies and answered industry questions one by one. However, industry was not satisfied. As can be seen in table 6.1, there were 391 consultations between 1997 and 2002; most of them were inquiries about how many trials could be waived based on bridging studies, but the responses disappointed drug manufacturers. Most of the applications were not

granted bridging studies waivers, and the scale of the bridging studies was so large and so expensive that they were not worthwhile.

These frustrations can be seen in a recent survey on the acceptance of foreign data using the E5 guideline reported by Masahiko Sato of DFPIA at ICH6. Although 40 percent of global companies use the E5 guideline in principle for all Japanese NDA applications, the results were not pleasing. Thirty four out of 59 companies who responded to this survey thought the MHW's performance was poor or very poor. They blamed this assessment on the ministry's tough stance on the acceptance of foreign standards and practices as well as its overstatement of the differences in clinical environments. They also complained that there were no clear criteria for obtaining scientific proof of the absence of racial effects, nor was there a clear way to harmonize Japanese information with existing global data. All these points meant that industry was in a difficult position: it needed to provide evidence of no ethnic differences in drug effects and at the same time risk the uncertainty of being rejected by the regulators. Drug companies doubted whether the MHW treated bridging studies scientifically; their inquiries referred to Japan's cultural attitude toward racial difference.

On the basis of a belief in the primary unity of all human beings, many thought that Japanese regulators had overstated the importance of racial variation in drug response. The "classic" study on racial difference I mentioned in chapter 4 came up again. For example, commenting on a hemophilia product awaiting approval in Japan, Neil Kirby of Genetic Institute said, "On the whole, there are greater intraethnic differences than there are interethnic differences" (as quoted in Hodgson and Marshall 1998: 14). Jean-Pierre Isal clearly expressed the frustration at Japan's regulatory policy after the acceptance of the E5 guideline by warning of two consequences. First, new drugs represent only 5 percent of total sales in Japan, compared to 57 percent in the U.S. and 25 percent in the EU. Second, of 149 drugs approved in the US between 1992 and 1996, 51 percent were not available to Japanese patients in 2000.

On the other hand, Japan had a different perception of the MHW's performance in bridging study evaluation. Uwoi Tohru of Yamanouchi Pharmaceutical commented, for example, that it was the idea of bridging studies rather than the MHW that should be blamed for this result. Interestingly, he shares the same idea as global industry, namely, that the concept of bridging studies is not scientific; however he has a different idea about the goal of bridging. He claimed in the 2001 APEC meeting that bridging studies represented "[the] wish to have immediate Japanese approval, and it leads to more economical/political [dispute] than scientific [ones]." For Uwoi, since a bridging study can be a political tool that connects one place to another, it could by the same token be

used as a way to separate two places by controlling the traffic between them. In fact, in a private speech to industry, Uwoi expressed this idea more directly. Predicting the fate of this guideline at the beginning, he said, "Let me prepare here the conclusion in case I do not have enough time: *forget bridging studies!*" (Uwoi 1998a, original emphasis). Those acquainted with Japan could see the problem rushing toward them. Stephen Barker, a senior pharmaceuticals stock analyst who has lived in Japan for over ten years, came to the same conclusion. "When the guideline was announced, I was a medical journalist," he said. "I went to Pfizer the next day, asking them whether this was what they expected. They just replied to me, 'It will be tougher now.' The new guideline requires everything repeated here; 'bridging' is an empty concept."

In the following let us focus on the aspects of bridging studies that are the sources of all the confusion. Before getting to this analysis, however, I want to clarify that these confusions did not result from translation. Although it is not unusual to make changes in order to write guidelines into local regulations,[12] this was not the case with the E5 guideline, which was an almost word-for-word translation, as confirmed to me by the translator Tominaga Toshiyoshi. The same was the case for the MHW's E5 Q&A document (1998c), which was also drafted by Tominaga. Although it is common in the Japanese legal system to have a Q&A document as a supplement to clarify regulations, in the case of E5 guideline it was intentionally published in two languages, showing concern for the foreign audience and their possible inquiries into this domestic law. The confusion over interpretations of the E5 guideline, I will argue, should not be considered as "misunderstandings" of certain concepts between different cultures. It is also far from the illusory dichotomy of a "scientific" West opposed to "unscientific" Asia. It should be understood as an extension of the conceptual division that arose in dealing with racial difference in a global setting. In order to resist a Western interpretation, the MHW's strategy was to clarify some selected concepts while leaving others unexplained.

For instance, the concept of extrapolation is a term that needs more explanation. According to the guideline, this is defined as "the generalization and application of the

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[12] The implementations of the ICH guidelines in Japan were not always direct translations of the guidelines into Japanese. Sometimes the MHW added extra regulations for Japan because it considered the guideline to be the minimum requirement. For example, in the Japanese version of the E6 guideline, the MHW added an additional clause on patients' rights. However, in the case of the E5, the MHW was very careful not to create any confusion about whether it was manipulating the guideline to add more requirements. As Doi Osamu recalled (1999: 16), "The [Japanese] content of the E5 guideline has to very clear so that no misunderstanding can be made on whether the MHW manipulated it in order to reject foreign data. We want everyone know that it is a guideline agreed to by the all parties but not formed by the MHW solely."

safety, efficacy and dose response data generated in a population of a foreign region to the population of the new region" (ICH1998: 8). This may suit our ordinary imagination of how a data set gathered in one region can be generalized to another; however, in practice it makes no scientific sense. As statisticians Goto and Hamasaki point out, if the foreign clinical data can be accepted as "bridgeable," it is not always necessary to conduct a bridging study, and then the inference of the data may be completed based upon the existing data alone. If the foreign data is not "bridgeable," meaning that it would lead to an incorrect extrapolation in the new setting, it is necessary to check the assumption to consider the sensitivity. It seems that the process of extrapolation is not suitable to the use of the foreign clinical data (Goto and Hamasaki 2002: 371-372, also see Liu 2003). Instead of openly rejecting this idea, however, the Q&A document chose not to offer any explanations.

Also unclear is the concept of similarity in bridging studies. The guideline lays out two instructions about the extrapolation of data generated from a bridging study. First, data should show that "dose response, safety and efficacy in the new region are similar," and second, if data indicates that a different dose in the new region results in a safety and efficacy profile that is "not substantially different from that derived in the original region," it will often be possible to extrapolate the foreign data to the new region (ICH 1998: 4). However, again, while this might fit with ordinary imagination, it makes no scientific sense. Technically speaking, Goto and Hamasaki have pointed out that the concept of similarity is confusing because in statistics it can refer to non-inferiority, equivalence, reproducibility, of no difference, or identicalness, which all have different meanings. The MHW's document addressed this matter in question 10, which asked if there existed a concrete standard to determine whether the dose-response, safety, efficacy, etc. of a drug are "similar" or "not greatly different" between racially different populations. However, instead of clarifying which standard it would use, the MHW only said that "it is impossible to suggest concrete standards to judge whether the cited features of a drug are 'similar' or 'not greatly different' across populations" (answer 10).

Meanwhile, on some points the MHW did make its attitude clear. First, it rejected any attempt to generalize rules for bridging studies. It only accepted case consultations on the basis of experience. The guideline states:

> for regions with little experience with registration based on foreign clinical data, the regulatory authorities may still request a bridging study for approval even for compounds insensitive to ethnic factors. As experience with interregional acceptance increases, there will be a better understanding of situations in which bridging studies are needed. It is hoped that with experience, the need for bridging

data will lessen. (ICH 1998: section 3.2.2:4)

The MHW explained this standpoint in more detail in the Q&A: it "has limited experience of basing its new drug approvals mainly on the data of comparative clinical studies conducted abroad. Conduct of a comparative study in Japan, therefore, should often be necessary for the time being" (answer 21). Thus, we see a consistent attitude toward all issues concerning bridging studies, such as criteria for additional trials (question 11) and considerations on extrinsic factors (question 15).

Second and more importantly, the OPSR rejected study protocols using a retrospective method. Although not written in the Q&A, this was an open secret among regulators and industrial people familiar with OPSR practice. On the surface, this was done for a scientific reason that industry did not want to admit: if the original study was met all requirements as a randomized, fixed dose, and dose–response trial, it was almost impossible to make a smaller replica afterwards called a "bridging study." Yet in reality the MHW silently protested industry's ignorance of the Japanese. It was not the OPSR's responsibility to provide evidence of ethnic differences; instead, it should be industry's job to show there were no such differences.

The E5 guideline again fell into deadlock. It led nowhere, as pharmacologist Helene Dumitriu concludes: "Industry may deplore the fact that the guideline provides no true harmonization of requirements" (142). As discussed in Chapter 4, the guideline established a superficial harmony on racial difference; however, it could not be put into practice until the underlying divisions were resolved. Although Japan could not openly argue against this guideline, it has said what it can in its Q&A documents and demonstrated its resistance in its actions. However, Japan did not always passively reject the current rules. In the second part of this chapter, I will show an alternative approach by which the MHLW is seeking to change this situation. However, industry could not wait and tried its own way, which will be the theme of next section.

Regressive Negotiations: The Return to the Bilateral Mode

Industry was the first party that became impatient with deadlock. As described earlier, while drug companies might know why the OPSR insisted on bridging studies, the problem was that most of the products the industry hoped to sale to Japan had been approved before the ICH guidelines were introduced. Thus it was impossible to expect the clinical trial data used for the application in the original region some years ago to be compatible with the bridging study requirements.

Industry started looking for evidence about the racially sensitive effects of

pharmaceuticals. The Pharmaceutical Research and Manufacturers of America (PhRMA) organized a working group consisting of clinical pharmacologists and led by Thorir D. Bjornsson of Wyeth Research. They intensively reviewed all scientific papers in the world literature on racial differences and their possible impact on drug effects. In this large work, 339 papers, mainly published between 1970 and 2001, were reviewed (Bjornsson et. al. 2003). The results of this study revealed nothing new; it just proved the intuitive impression that "only a few examples of suspected ethnic differences in pharmacokinetics or pharmacodynamic effects were found" (943). However, from this survey we learn the interesting fact that relatively few articles have mentioned ethnic differences in the past decade (960). This "absence" of discussions in academic field, in my opinion, should be understood together with the introduction of racial difference into the ICH negotiations. While discussing this issue, industry, the biggest sponsor for pharmaceutical research, wanted calm for the negotiations.

However, after few years of observation, the industry realized that the OPSR could not change its practice. The accusatory discourse on Japanese protectionism rose again. Elaine Esber, now working for industry, nicely summarized these open complaints in her presentation at the 2003 APEC meeting: "E5 has resulted in a request for more studies, rather than less," it was "a convenient excuse for requiring a local registration study and calling it a bridging study." "requests are for data, country by country, not as a region," "there are ulterior motives for requesting that studies be done, e.g., protect local industries," "E5 is being implemented as a trade barrier," "most companies are doing studies just to not get into an argument," "governments are not being flexible," and many other things.

It is thus understandable why racial difference was brought up as a topic of discussion in the trade-oriented MOSS negotiations, which I discussed in part in Chapter 4. When the global ICH was founded, the MHW intentionally directed all discussions to this platform and away from bilateral channels like MOSS. However, when the discussion on the E5 guideline fell into deadlock, the industry returned to this old channel. As shown in table 6.2, since September 1997, the acceptance of foreign data has returned as a topic in MOSS follow-up meetings. Obviously, it has been listed at the request of PhRMA, which hoped to put more pressure on the MHW via the USTR.

From this table we can see that industry resumed pressuring after the implementation of the E5 guideline. This phenomenon supports my observation in previous sections about the reality of bridging studies. It seemed that the industry could not wait for slow "academic discussions" in the bi-annual steering meetings; they hoped to intensify this pressure through this direct channel, which was more powerful.

Table 6.2 MOSS Follow-up Meetings, 1997-2000.

Time/place	Requesters	Main topics discussed
February 1997/ Washington	United States	Systematic reform of the Pharmaceutical Affairs Bureau (PAB) National Health Insurance (NHI) Insurance reimbursement process Price differences between Japan and abroad Nutritional food supplements and hard gelatin capsules
September 1997/ Tokyo	United States	Reduction in new drug application approval times **Increased acceptance of foreign clinical data for drugs and medical devices** Increased liberalization of nutritional supplements Review of government of Japan health care reform plans Reimbursement system for medical devices
	Japan	**Mutual recognition on GMP** Simplification of procedure of 510 k notification submission Simplification of the data submitted to make IND
March 1998/ Tokyo	United States	New drug application (NDA) process **Acceptance of foreign clinical data for drugs and medical devices** Review of government of Japan health care reform plans Reimbursement system for medical devices
	Japan	**Mutual recognition on GMP** Simplification of procedure of 510 k notification submission Simplification of the data submitted to make IND
April 1998/ Washington	United States	New drug application (NDA) process **Acceptance of foreign clinical data for drugs and medical devices** Reimbursement system (by function) for medical devices
	Japan	**Mutual recognition on GMP** Simplification of procedure of 510 k notification submission Simplification of data submitted to make IND
October 1998/ Tokyo	United States	New drug application (NDA) process **Acceptance of foreign clinical data for drugs and medical devices** Review of government of Japan health care reform plans Reimbursement system for medical devices

		Separation of the service component from medical device reimbursement
	Japan	**Mutual recognition on GMP** Simplification of procedure of 510 k notification submission Simplification of the data submitted to make IND
January 1999/ Washington	United States	New drug application (NDA) process **Acceptance of foreign clinical data for drugs and medical devices** Nutritional supplements Review of government of Japan health care reform plans Reimbursement system for medical devices Separation of the service component from medical device reimbursement
	Japan	**Mutual recognition on GMP** Simplification of procedure of 510 k notification submission Simplification of the data submitted to make IND **Mutual recognition on GCP**
September 1999/ Tokyo	United States	Approval process for drugs and medical devices **Acceptance of foreign clinical data for drugs and medical devices** Nutritional supplements Pharmaceutical pricing reform Reimbursement system for medical devices Separation of the service component from medical device reimbursement Health care services deregulation
	Japan	**Mutual recognition on GMP** **Mutual recognition on GCP** Timing of stability data requirement for NDA
January 2000/ Washington	United States	Approval process for drugs and medical devices **Acceptance of foreign clinical data for drugs and medical devices** Nutritional supplements Pharmaceutical pricing reform Separation of the service component reform Health insurance applicable reform Health care services deregulation
	Japan	**Mutual recognition on GMP** **Mutual recognition on GCP**
September 2000/	United States	Health care reform Recognition on epoch-making reform (drug price reform and insurance

Washington		medical supply reform) Transparency Health care services provided under health care reform Approval process **Acceptance of foreign clinical data for drugs and medical devices** Post-marketing Surveillance for drugs JIS (Japanese Industrial Standard) Nutritional supplements

Source: Adopted from The Working Group of Drug Administration, Japan 2000: 235-239. Emphases added by the author.

On receiving this pressure, the MHW tried to separate administrative issues from cultural ones. For example, in the third U.S.-Japan Enhanced Initiative on Deregulation and Competition Policy, the MHW explained the progress it had achieved in speeding up new drug approval. It claimed that the whole NDA approval process time had been decreased. However, concerning the acceptance of foreign clinical data, the OPSR's formal response was always: "the government of Japan provides opportunities for consultation with the Organization for Pharmaceutical Research (OPSR) and the like to promote the facilitation of acceptance of foreign clinical data based on International Conference on Harmonization (ICH) E5 guideline" (243). Obviously, Japan tries to push all "non-scientific" disputes raised by the United States back to the ICH track, which is supposed to be scientific and neutral.

On the other hand, the OPSR fought back with the mutual recognition of GCP and GMP, which appeared on the list for negotiation almost at the same time as the acceptance of foreign data. If we recall the "two big bangs" mentioned in the first section of this part, we know that the MHW had no intention of protecting any industry; instead, it tried to extend the "battlefield" to the regulatory sector, hoping to bargain on some respects of its poor environment for clinical trials. The FDA's pickiness in clinical trials, especially those conducted in Asia,[13] was an insult worse than any accusation for Japanese regulators, because its national credibility is being bluntly challenged. One

[13] Despite not being conducted in many countries, including some developed ones, it is a common practice for the FDA to validate factories and manufacturers overseas. No product by producers that is without proper validations can be imported into the United State. Although the FDA always claims that this is essential to protect their people's health, it is often criticized that it badly interferes with other countries' internal affairs.

MHLW official concluded that it is the FDA that should be blamed, since "all rules have been made at the ICH; what is left is only administrative work determined by the top of both side (of Japan and the United States)." An OPSR consultant told me that Japan cannot stand for not being trusted; he cried: "we cannot follow everything ordered by the United States." If mutual recognition of GCP and GMP cannot be granted, bridging will direct to nowhere.

Unfortunately, the FDA did not want to deal with these issues that the MHLW brought up. In fact, it did not either care about the E5 guideline, since it was not its business. As the most advanced country in drug regulation, the American standard led almost all ICH guidelines. For them, what were left might be only administrative problems, and from technical viewpoint they simply do not trust Japan's investigation. Thus, concerning the GCP issue, it responds that "FDA will continue cooperative activities regarding Good Clinical Practices (GCPs) especially in the ICH forum, and FDA will continue to respond appropriately to foreign regulatory bodies' requests, including MHLW's, for information regarding GCPs" (245). Like the MHLW does on the E5 guideline, the FDA push all disputes back to the ICH, otherwise they are only administrative problems. As a result, E5 and E6 could not be solved together in the context of bilateral negotiation; the only consensus achieved is that both had to be solved, and solved independently, in the global forum of the ICH. All things seemed to return to the place where the dispute on racial difference started.

However, this does not mean that the industry and the MHLW did not learn anything from this trip. The industry had known about the political orientation of this guideline, and they learned more from its practice. Even so, through these pressuring channels, they want to play safe in dealing with Japan. But, what we are concerned about more is the MHLW. How can they create an independent category of the Japanese race in clinical trials while escaping from the vicious circle where the same debates, the same reasoning; the same misunderstandings and the same frustrations were repeated? In the second part of this chapter, I will argue about how Japan intends achieve this goal by making a scientific move to the genome.

PART II
MAKING THE GENOMIC RACE PART OF BIO-GLOBALIZATION

New Wine in the Old Bottle: Recurrence of Global Drug Development

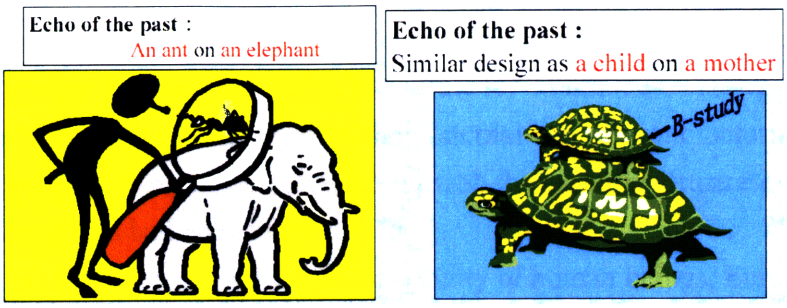
Let us start this part with the Japanese industry's perception of a bridging study. In 1997 the ICH Japan study group conducted a survey of Japan Pharmaceutical Manufacturers Association (JMPA) member companies on the E5 guideline. The result shows that although they had all read this guideline, only a few fully understood the meaning of the bridging study package and bridging studies (questions 13 and 14). Moreover, they believed that, first, bridging studies have to be done in the new region, supposedly Japan. Second, it would be impossible to grant waivers to foreign applications without doing any studies (questions 16 and 17). This situation had not changed a lot as shown in Masahiko Kato's survey in 2003. Japanese companies that would like to apply the E5 guideline was still few; Japanese clinical data was used in some cases in the West countries but this was still rare and not a core issue.

The above is surely not what the MHLW wanted to see when joining the ICH. As written in Chapter 4, the MHLW officials had an ideal view of harmonization where clinical data from the ICH regions can transfer mutually while each region remain to a degree independent. However, the making of the E5 guideline reflected a cruel reality that the flow of clinical data is in one-direction. A fear of being swallowed by the West rose among experts on drugs. Professor Sakuma Akira of the Tokyo Medical and Dental University described this anxiety. Using a metaphor of the myth of Kami Izumono, he teased that the bridging study should be the *kunihiki* rope to "pull" a piece of foreign land (data) to Japan nation. "But," Uwoi added: "the point is on which ground can the land be pulled to come from, if you think of the tug of war between England and European Continent" (Uwoi 1998a).

Concerning the MHLW's anxiety, Mori Kazuhiko of the OPSR used two analogies to sum up past practice for bridging studies, which was widely cited on related occasions. In the cartoons below (fig.6.4), the Japanese data was portrayed as either an ant on top of the huge foreign data of an elephant or a baby turtle (bridging data to be born) on the back of its mother (existing foreign data). These cartoons highlight two characteristics of Japanese's perception of themselves in global studies. First, the importance of the Japanese to the world, as seen in the sampling size, was extremely small. It is not comparable with its expectation as one of the ICH regions (left).

The second characteristic has to do with the developmental order, or level of advancement in medical research. Thus, only a mother can give birth to children; because of the backwardness of Japan's clinical environment, Japan will have to wait for advanced drugs until after they are available in Western countries (right). For Japan, bridging studies were not what it expected from the ICH as a place for making harmony. It is regional discrimination.

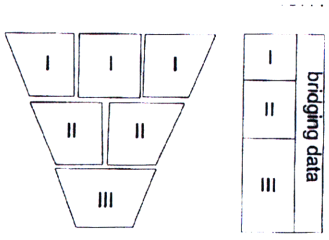
Fig. 6.4. Echo of the Past: Impression of Japanese in Bridging Study



Source: Mori Kazuhiko's presentation in the APEC 2003 meeting, Taipei.

Thus, based on the understanding of bridging studies, the MHLW's request on racial difference is clear. Instead of exhausting all the characteristics that make a Japanese "Japanese," they asked for enough recruitment of the Japanese subjects and for the same trial design as conducted in the original region. According to their interpretation, there is a two-stage transformation when dealing with racial difference, and bridging is the product of the first stage. Though useful, bridging did not perfect the idea of harmonization because it helps only those that have done clinical trials in one region, supposedly the West, and considers only whether this data is acceptable to the new region, supposedly Japan. In other words, it favors only a certain region but not all regions. Thus, as bridging finished its mission, a better program was needed to achieve real harmonization.

Fig. 6.5. *Left*: Proposal of Global Clinical Development: the "1-2-3; Asian-Black-Caucasian" model; right: the "bridging to all" model.



Source: Adopted from IFPMA 1998:350, Figure 4.

The program the MHW proposed was global drug development. It was definitely not a new idea. It origin can be traced back to ICH1. W. L. Thompson replied when asked the role of multi-center, multi-national studies in assessing efficacy: "I think the goal

should be to have a single protocol applied across all three cultures and that this is a much more powerful design, that doing serial small studies and attempting to put them together with a meta-analysis. Whether we can achieve enough harmony, to allow a single protocol to be used, is a difficult question...." (D'Arcy and Harron eds. 1992: 416-417). At that time "global" is a rough substitute for "multisited." However, the later developments about racial difference, including internal and external factors that may affect this, complicated this ideal project. Along with the tiresome, frustrating discussion, the nuance of the global had changed and split.

Based on ethnic diversity and the primary unity of human beings, European experts provided its version of global drug development at the ICH4 as a next step to get rid all national influences. As held in the ICH4, the panel on "planning a global clinical development aimed to list philosophy and principles with regard to ethnic factors, as if all would be easily overcome after bridging studies was applied (D'Arcy and Harron eds. 1998: 330-331 and 349-350). A rough principle was suggested for such a plan. In order to obtain enough information to judge whether the New Drug Application (NDA) in assessment is ethnic sensitive, it would possibly to have a requirement for different phases. For the phase I, it would require the PK/PD to be done separately, as shown on the left of fig. 6.5, or that there be one main PK plus a bridging study (right). For phase II, it would require a comparative does-response analysis concerning at least two races (left), or a main trial plus a bridging study for the local. The most innovative part is for phase III, where it would require only a single trial either done on a race, if no ethnic sensitivity was found, or done in a multi-ethnic, multi-center fashion (left), or, again, one main trial plus a bridging study (right).

On the other hand, based on national difference, Japan has a different perception of global drug development. The concept of globalization by the MHLW, as I mentioned, is a status of mutuality where the Japanese are properly represented in a simultaneous manner. It is a consistent standpoint stemming from a very early stage of the discussions on racial difference. For example, at the ICH 2 Naito Chikayuki brought up the idea to have phase III and/or II studies done at the same time, but this proposal was declined. Later when the bridging approach was decided, Japan suggested prospective global drug development as a separated option yet this was eventually declined (Uwoi 1998a).

Japan's attempt finally transformed into a vague section in the E5 guideline and this was articulated in the form of bridging studies. In the section titled "developmental strategies for global development," it states the possibility of conducting a main study and bridging ones in parallel:

> Ideally, this characterization should be conducted during the early clinical phases of drug development, i.e., human pharmacology and therapeutic exploratory studies. In some cases, it may be useful to discuss bridging study designs with regulatory agencies prior to completion of the clinical data package. However, analysis of the data within the Complete Clinical Data Package will determine the need for, and type of bridging study. (ICH 1998: section 4:6).

It is an interesting statement; the key to understand it is the timing of the consultation. This is because it does not indicate an exact time point where it is best to consult the regulatory agency and what should be required for this; it gives the regulatory authority the freedom to lead the way that industry develops its clinical trials.[14] Thus, as Naito recalled, "It is suggested, though in a very abstract form, that when a drug was being developed, a multi country or multi site clinical trial can be conducted prospectively" (Naito 1999: 5).

Let us see Japan's plan. On what to consider during the recruitment of local subjects, the guideline mentions that for the global development, "studies should include populations representative of the regions where the medicine is to be registered" (section 4:6-7). The Q&A provided by the MHW indicates the number required. When asked on the number of subjects required for detecting adverse effects (question 24), it confirms that three hundred patients are necessary if the safety profile of a drug is totally different between the Japanese and the foreigners. It also added another condition when less Japanese subjects are recruited before approval that "the applicant should supplement in the post-marketing phase."

On the simultaneity of clinical trials, although Japan realized that the bridging study approach presumes a sequential process of clinical trials in the world, it tried to "synchronize" them. It did through both positive and negative approaches. On the positive approach, the MHW strongly encouraged applicants to do the studies to be bridged and the bridging studies in parallel. It writes: "it is possible, however, to conduct clinical trials to construct a clinical data package to be bridged and a bridging study in parallel" (answer 4). As discussed in the Chapter 4, bridging studies were originally proposed as a way to judge whether further studies are required, yet it now in itself has become a requirement for adding local data and a new platform on which a small scale of "global clinical trial" is possible. The negative approach, as I have mentioned in previous part, was to decline all bridging studies that applied a retrospective approach. It became

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[14] In the Q&A on the E5 guideline provided by the MHW, it was asked that whether it is possible to give a concrete description of an appropriate bridging study, including its size, design, etc. (question 20). Yet, the MHW hesitated to clarify this.

an open policy, as Naito Chikayuki claimed in 2003: "[s]o far, such retrospectively created bridging data according to the lists have never succeeded in making a sound bridging" (Naito 2003: 150S). It would be clearer if we consider the two ways together. Hayashi Yoshikazu comment this way when reviewing OPSR's E5 review: "in general, retrospective application of Japanese clinical data collected before the E5 guideline was issued might not be successful for bridging purposes. We have observed, however, an increase in the number of prospectively well-designed bridging studies" (Hayashi 2003: 134S). In his reasoning, bridging studies is always considered transitional. It is a process to help the development of a drug and moves toward a "globally-synchronized" development.

The domestic industry's attitude was ambiguous about the MHLW's attempt. Far from hoping for government's protection, some JMPA member companies wanted to know how to step out of Japan through bridging or global drug development. In the beginning of the year 2001, an editorial of *Yakujinippo* entitled "spontaneous development among Japan, United States, and Europe; the pharmaceutical industry in the twenty-first century" record two different voices concerning the future of Japan's E5 policy (January 2 2001). On the one hand, the JPMA welcomed global drug development, thinking one day it will be possible to conduct clinical trials in three regions with a single protocol, and apply for marketing in each of them at the same time. On the other hand, it complained that, so far, the mutual recognition of the GCP had yet to be achieved and this impeded Japan's bridging study policy. It argued that although industry could understand that bridging studies functioned like a requirement by the local authorities, yet "after near two and half years of working by both regulatory and industry sides, no agreement has achieved on the criteria by which foreign data can be judged similar enough with Japanese data." For them, the global drug development approach will be a null promise if no concrete steps are set.

The Necessity to Move to Genomics

So the MHW had the idea of global drug development, but the problem was how to make it a workable project. What should they do? It needed to separate itself from the European suggestion, which is based on ethnicity but not nationality. Furthermore, even the division of ethnicity was problematic. Early discussion of the E5 topic (see Chapter 4) had "proved" that individual variance is larger than interethnic difference. Although under the scheme of populations, this difference is still meaningful using gene frequency.

This project needed to have a clear criterion to identity where global drug development can be applied.

Unfortunately, the MHW did not yet have such a plan. In that *Yakujinippo* editorial it reported that the expert's reply on this policy was that bridging studies were transitional. However, he did not say more about future plans. He just said that if the interethnic difference is smaller than individual variances within a race, it is possible to conduct a global trial with a unified design; however, he did not show in what situation racial difference is trivial and thus can be ignored. Uwoi Tohru has already predicted this problem: "neither does the MHW nor the E5 guideline write anything on how a prospective global drug development can be conducted" (Uwoi 1998a). Uwoi further criticized that Japan needs a direction for this approach; otherwise it would fail to convince anybody. He warned: "we want a real global strategy; it will be bad if it ends up with strategies (such as bridging study) for enterprises."

At the beginning when the E5 guideline was implemented, the MHW really did not know their direction. The long and tiresome debate in the making of the guideline had legacies that could be used as the scientific foundation for their project, but they had no idea which of these should be chosen. Two strategic trajectories, one named "cultural" and the other "biological," present different concerns about this project. The cultural trajectory followed from the discussion of extrinsic factors and has a clear focus on the locality of the region. The MHW used this to qualify overseas Japanese, who might possibly replace "true" Japanese as representatives of the Japanese race, in bridging studies. In the Q&A on the E5 guideline, it states that overseas Japanese can be used in clinical trials in principle "except where differences in diet and the environment are expected to alter the drug's pharmacokinetic behavior" (answer 26). This trajectory can go to an extreme, such as Naito Chikayuki's claim in interview that from medical point of view, he would agree that naturalized Westerners can be regarded as native Japanese after three generations, since "their life style and food would be the same as us, the Japanese."

Although the cultural trajectory was useful in defending the extrapolation of foreign data into Japan and in showing the importance of locality, it failed to serve as an approach to the new platform of global drug development. It did so for several reasons. First, if the MHW insisted on it, it would be forced to list as many as possible cultural or social factor that needed to be taken into account, and, when included, what weight should be granted to each. It would face a technical muddle of numerous factors similar to the situation of European experts when applying the triage or decision tree for anchoring where racial difference resides. Second, if the MHW emphasized these factors too much, it would make any unified global protocol impossible. The more local factors

involved, the more limitations there would be when synthesizing them in a meaningful statistical model. In other words, it would badly hurt Japan's wish to allow their clinical data applicable in other countries. Third, the cultural trajectory would drag global drug development away from the multi-ethnic frame into one that was multi-nation for administrative purpose. It was not impossible, because the MHW had already done this as part of its bridging study policy that requested "sufficient" recruitment of Japanese subjects for every bridging study. However, it would face strong objections from Europe and the United States if the MHW insisted that same number of local subjects were required in global drug development, because it would be judged unscientific and would not be acceptable.

The biological trajectory is an extension of the discussion about intrinsic differences between foreigners and the Japanese. Of course, the MHW always insisted on this difference, and Europe's global drug development project had also appreciated this difference as a strategy to blot out the influence of any government. Thus, the point was not whether people could recognize biological characteristics of Japanese, but how to articulate it in a way that can relate these characteristics (Asian) to a nationally defined group (the Japanese population), while making global clinical trials possible. It was upon this concern that genomics was called in. It must be clarified that the MHW did not intentionally develop genomics in order to solve solely the E5 problem. Basically, Japan's decision to participate in the Human Genome Project was a complicated process, which deserves independent research (for example, Fujimura 2000). Nonetheless, the official promotion of this genomic study of the Japanese did have an identifiable effect on the MHW's E5 policy, which became clear later in announcements on related occasions.

Let us briefly introduce genomics and its relationship to pharmaceutical industry. Along with the completion of the Human Genome Project, pharmacogenomics was claimed a concept that would refine the relationship between drugs and patients from a group-to-group match to a promising one of individual-to-individual targeting. Through this promising vision that the genomic claimed to give, there was a huge gap between the present situation and the future dream. To explore specific gene variations is one thing, to reflect them back to the genetic map is quite another. Donna Haraway has pointed out the informational gaps that are present when the human genome databases are exhaustively used to represent the species in totality as well as a specific form of individuality; this worry led to the Human Genome Diversity Project, a project devoted to "save" some useful information on extinct races from vanishing human gene pools (Haraway 1997: 247-250). But, along with such an endeavor there were other information gaps in the field

of pharmaceutical research, such as how to identify the populations that have genes with clinical meanings.

As was usual, the industry should be considered the pusher for this move, and the ICH is not an exception. For this, journalists John Hodgson and Andrew Marshall provided a nice report. According to them, Marisa Papaluca Amati of the European Agency for the Evaluation of Medicinal Products (EMEA) said that at present there are no guidelines in Europe that spell out the requirements for pharmacogenomic data, though as an ICH presenter she confirmed its importance in the consideration of ethnicity. She says: "If exposures of patients to experimental drugs are much reduced, then that is a good thing... I hope the effect of [harmonization under ICH] will be to reduce the number of clinical trials of experimental drugs.... Pharmacogenomics will also save some unnecessary exposure" (14). This attitude is also held by the FDA, according to Etienne Labbe. He commented that any such document would be premature: "we have not reached an agreement [under the ICH] on the basic rules for drug development" (14). Apparently, both Europe and the United States were happy to endorse the value of genomics, but they did not want to be the pusher. Amati said it frankly: "that is the realm of drug developers." FDA's Collins responded in the same way: "This (genetic) information is very useful to us. It is in companies' best interest to provide us with it." The ICH did not seem to like this move, because, as Labbe concluded: "this topic would complicate ICH harmonization" (14).

However, the Japanese government decided to take on this task and the MHW made it part of its E5 policy. The Japanese involvement in genomics is through an unusual inter-ministerial project called "Millennium". Starting from 2000, this five-year project aims at the reformation of Japan's science, technology and society in the twenty-first century and covers several fields such as a fiber-optic communications network throughout Japan, monitoring system for environmental changes, and research on human genome (Prime Minister, Japan 1999). As medical policy analyst Hiroi Yoshinori pointed out, this was the first time the government had a clear policy frame to promote the quality of its medical care from the basic research to bedside (Hiroi 1997, 1998). In addition, it was regarded a project whose aim was to "speed-up the industrialization of biotechnology."[15]

The informative framework about the Japanese genome was constructed by the two

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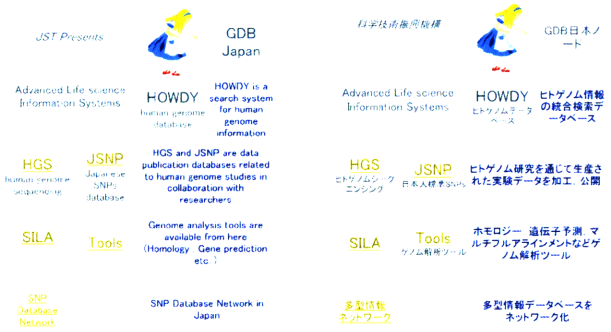
[15] This strategy became explicit in the Outline of Biotechnology Strategy drafted by the biotechnology strategy council led by Prime Minister Junichiro Koizumi. The council had been discussing a national strategy to develop biotechnology into a core industry by stimulating R&D activities in the pharmaceutics, medical equipment, agriculture, food processing and microorganism sectors (Prime Minister, Japan 2003).

projects. Since 2000 and with it planned to finish by 2004, the Japan Science and Technology Corporation (JST) has conducted a multi-institutional project on the Japanese genome. Using the symbol of Alice from *Alice's Adventure in Wonderland* (fig.6.6), the whole project of Advanced Life science Information System (ALIS) seems to represent wandering Japanese who want to find herself in the world of the genome. As the diagram shows, ALIS incorporates several fundamental projects, such as the international collaboration on the human genome database (GDB Japan node and HGS), the structural initial data library of amino acid residues (SILA), human organized whole genome database (HOWDY), and database of Japanese Single Nucleotide Polymorphisms (JSNP). Each project involves three to five research institutes from industry and the academia in Japan.

Fig. 6.8. English and Japanese Homepages of the ALIS Project



Source: http://www-alis.tokyo.jst.go.jp/index.html (left) and http://www-alis.tokyo.jst.go.jp/index_ja.html (right).

I will then focus on two projects, HOWDY and JSNP, which will demonstrate the issues that we are concern. The work in the two areas was conducted by the bioinformatics division of the JST. HOWDY was developed by the JST with the help of Fujitsu lab and first released in July, 2000.[16] It is a computational platform on which the previous database on the human genome can be integrated and cross-referred. Or, describing it in terms of internet accessing, HOWDY can be understood as a searching engine for search engines that retrieve human genome data in public databases. Furthermore, it has powerful design of object-oriented modeling. Not only the names or the alias of nucleic acids can be keywords for searching; the sequences obtained can be further analyzed and corrected. The crucial function that HOWDY offers is a link

16 The source for the following introduction to HOWDY and JSNP is Hirakawa et al. 2002.

between the realms of information and that of practice in life science research. It enables life scientists to move their front to genomic studies, furthering leading their way into the world of human genomics.

As a database open to the public, the usefulness of HOWDY has to be understood through the JSNP. The JSNP is a repository of DNA polymorphism data for the Japanese.[17] It began in 2000 and was supported by Millennium Project. Prior to this project, the MITI had already received generous funding for cDNA and SNPs programs as well as those by the Science and Technology Agency and the MHW (ATIP 1999: 4). Yet under Millennium Project, the project was carried out by collaboration between the Human Genome Center (HGC) in the Institute of Medical Science (IMS) at the University of Tokyo and the JST.

The mission of this undertaking was to identify and collate up to 150,000 SNPs from the Japanese population to construct a basic data set to identify relationships between polymorphisms and common diseases or the reaction to drugs. As such, emphasis has been placed on the identification of SNPs that lie in candidate regions that may affect phenotype but which would not necessarily directly cause disease. In order to construct an infrastructure for genome-wide association studies of common diseases or drug sensitivities among the Japanese, the JSNP project has been systematically exploring common variants by re-sequencing genomic regions containing candidate genes in specific DNA samples.

According to Haga et al. (2002), JSNP database was formed by gene-based screening; it is based on locus-specific PCR amplification. It can pin down specific regions of interest and explore variation in areas such as promoter regions or coding elements. Although more feasible than a genome-wide screening, this approach still requires extensive genomic sequence information to cover the whole genome. Even so, the researchers adopted it, because the HOWDY project can provide the necessary help. Up to the year 2002, a total of 154 Mb, corresponding to approximately 5 percent of the human genome, had been analyzed, and 174,269 SNPs and 16,293 insertion/deletion polymorphisms within gene regions have been identified. As a pioneering experiment to make racial difference visible, the JSNP project gained significant international attention.

However, we need to look at how the HOWDY and JSNP can be related to our concerns about the ICH. Intended to be open to the public, both databases indicate

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[17] SNP is the most common form of DNA sequence variation. They are useful polymorphic markers to investigate genes susceptible to diseases or those related to drug responsiveness. A small subset of SNPs directly influences to the quality and/or quantity of the gene product, and produce severe side effects with drugs. For a brief review on research on SNPs, see Shastry 2002.

Japan's ambition to redefine the Japanese race and to publicize it to the scientific community. As Hirakawa Mika of the JST nicely concludes about this trend: "The SNPs in JSNP will be the baseline data for Japanese medical and pharmaceutical research and further development of the database will be continued" (Hirakawa et. al. 2002:161). These efforts have clear implications for the MHW's E5 policy, because this genomic race will be the basic unit for global drug development. Despite its original biological determinism, this new racial definition can make the Japanese a distinct category in global clinical trials.

This distinction has two meanings in the context of global drug development. First, it is expressed at a higher standard that is undeniable even by the West. Nakamura Yusuke, Professor at the Institute of Medical Science, University of Tokyo and the coordinator of the JSNP, is perhaps the best person who can explain this. When asked about the existence of the SNPs that can be found only in the Japanese, he answered that a full survey has yet to be completed, but to his knowledge he thought from 20% to 30% of the Japanese SNPs do not belongs to the Japanese exclusively. However, concerning the importance of the JSNP study on drug development, Nakamura said: "we do know that the Japanese have different enzymes for drug metabolism than the Americans and Europeans. Even so, up to now we have called this difference a vague term *taishitsu* (ethnic characteristics). To consider it scientifically as the genetic polymorphisms, we have to clarify the SNPs that can only be found in the Japanese that are related to drugs" (Nakamura 2002: 14-15).

The second meaning of the distinction between the Japanese genome and genomes of other races is one that is practical. As Nakamura states, some SNPs do not belong to the Japanese solely. However, as a population, the Japanese can be defined as the collection of these SNPs found within this group of people. This is a "digitalized" genomic definition of the population that moves away from an "analogical" description of genetic frequencies. Thus, if global drug development has to be conducted upon the ethnic diversity, the MHW will prefer a classification based on this definition, because so far only the Japanese population is qualified to offer such information. In fact, at the beginning of this project, some experts had predicted the possible use of this database (*Yakujinippo* January 1 2001). Taniguchi Toshiichiro of Shinshu University, for example, said that "still, for obtaining information useful for the Japanese it is necessary to create a Japanese genome (while the United States is a reference)." Itakura Mizuo of the Genome center, Tokushima University, and Takeshita Akira of Kyusho University, expressed the same idea. Itakura said that it is important to study in themselves the polymorphisms among the Japanese, so that the target population of "common diseases" can be explicitly

identified. Tekeshita claimed that a database has to be established for the Japanese exclusively.

Thus, notwithstanding cultural concerns, the MHW was ahead of other countries in its move into genomics. Not waiting for the completion of the JSNP project, one of its officials claimed convincingly: "from now on the intrinsic factors of racial difference can be replaced by the genome."

New Tool and New Channel

Although the MHLW (renamed from MHW) pursued a new definition of Japanese race, there were at least two problems they had to solve. The first was how to make this new standard fit into their project of global drug development. As I have mentioned at the beginning of this chapter, genomics could be a vision too far from the industry. The MHLW had to show the variability of some possibilities that make this genomic race sound real in clinical trials. Second, the MHLW had to persuade other ICH parties to accept this standard. As we read in last section, the Europe and United States seemed not to be enthusiastic about its early application and the ICH seemed not want to tackle it soon.[18] This section will describe the how the MHLW tried to solve the above problems together. As we will see in the following discussions, Japan on the one hand developed a theoretical framework that served to make global drug development possible as it wished. Meanwhile, through some personal connections, it established an informal channel with the FDA to negotiate the technical issues about this project.

Let us deal with the scientific framework first. Technically speaking, in order to conduct a global clinical trial, the MHLW required a theoretical toll to transform the genomic information into meaningful variants and factors that were countable and reproducible. It has not yet had any formal name for this statistical method created to serve this need, though some called it "statistics for the post-genomic era" or "genetic statistics" (Kamakura 2001). In order to clarify my argument on the drug development, in the following I will call it genomic biostatistics. Of course, statistics is not a new area in terms of global drug development. In Chapter 2 I had discussed its role in the current practice of clinical trials, and the concerns of statistical methods have remained an important topic at the ICH since its beginning. For example, the E9 guideline was formed

[18] This was until ICH6, where this conference started dealing with some issues about biological products and gene therapy.

to establish a methodological guideline for clinical trials that recruit subjects from more than one site;[19] some concerns also appeared in the E6 guideline with regard to how good clinical trials should be conducted.

However, compared to the mainstream discussion about the conflicts raised in statistical methods used in "Japanese style" clinical trials, only few Japanese statisticians pursued the approach that the MHLW favored. Among these scientists Takeuchi Masahiro, Professor of the Division of Biostatistics, Kitasato University, was the youngest and most promising. He seemed to be the "Mr. Right" of the moment. Before returning to Japan at the request of the MHW, Takeuchi had very few connections with statisticians in Japan. He was educated at Boston University and earned his Ph.D. degree in biostatistics at Harvard University. After that he was recommended to work at the FDA as a statistical reviewer of anti-cancer drugs. His American personality and working experience made him the best "post-E5" expert to help the MHLW get away of the deadlock of bridging. Thus, although originally he was interested in a medical university located in Western Japan, the MHLW asked him to work in Tokyo so that he could visit the MHLW frequently. "I am highly involved in this institution," he admitted.

Takeuchi has a different viewpoint on the ICH. His American training told him that to insist on "Japanese style" of clinical trial would not work. Quality, instead, is the term he would like to emphasize. Unlike other statisticians who related the E9 with the E6 guidelines, he insisted that it was the E5 guideline that should be discussion with the E9 guidelines; the former gave a chance to exchange qualified data, and, the latter, as the perquisite, guides how to produce the data (Takeuchi 2001). After his return in 1998, the Symposium on Global Drug Development Techniques (hereafter the Kitasato-Harvard Symposium) was the place where Takeuchi gradually realized his attempt to combine genomics and global drug development; it was, too, a new and informal channel for the MHLW that allowed them to talk about this new idea with their American colleagues.[20]

Although this symposium later received sponsorship from the MHLW, these serial symposiums were initiated through Takeuchi's personal connections with his advisor and colleagues in the United States.[21] When asked, he put it in a Japanese way: "when I was thinking whether I should return to Japan, I called up my pals at Harvard. They

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[19] Although this guideline is important for making a multi-sited clinical trial, which is related to the global drug development project, in order to keep my argument flow moving smoothly, I will leave more discussions about this guideline to Chapter 7.

[20] These symposiums have been all held, all at ANA Hotel, Tokyo, from October 5-6, 2000, October 22-23, 2001, October 2-3, 2002, October 28-29, 2003 and October 25-26, 2004.

[21] The proceedings of the first three symposiums have been published (English with Japanese translation) as *Bridging Strategies* (2001), *Bridging Strategies and Pharmacogenomics* (2002), and *Simultaneous, Worldwide Development Strategies* (2003). All are published by Dizitaru puresu, Tokyo.

encouraged me to go and promised to back me up wherever I was. And this is what they promised." He kept in touch with Steven W. Lagakos, Professor of the Department of Biostatistics, Harvard School of Public Health, after his return, and the first symposium was held in 2000 with sponsorship by the Pfizer Health Research Foundation.

I pointed out that the Kitasato-Harvard Symposium is a *de facto* Japan-U.S. channel to solve the deadlock of bridging between the MHLW and the FDA, and Takeuchi did not deny it. "It is not specifically for the FDA; it's for many people, industry, for example," he replied: "but, in this symposium we do release some information that would be improper for the MHLW to speak out." It is safe to claim that this symposium functions as an arena for technical discussions on behalf of their governments. In each symposium there were open seminars and close meetings, which satisfied everyone's needs. The former acclaimed possible changes in the MHLW's policy on the E5 guideline and the future of drug development; the latter provided a chance for these experts to exchange information in a more private atmosphere, which was neither the multi-national ICH nor trade-driven MOSS.

Four symposiums from 2000 to 2003 witness the gradual formation of the global drug development program. As written in the welcome note addressed by two organizers, the initiation of this symposium was a response to the impacts that the new issued E5 guideline would introduce:

> The adoption by countries of recommendations from the International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH) has set the stage for important advances in drug evaluation worldwide. In particular, the E5 guidelines, issued in August 1998, allow data resulting from clinical studies done in the West to be used by regulators in other parts of the world, including Japan, for consideration in the approval of drugs in their own countries.

Nonetheless, the symposium hoped to shift the research body to global drug trials, as interpreted by the ICH in the following way: "The ICH recommendations raise the specter of global clinical trials in which one or more international studies could be used for registration of a pharmaceutical in multiple nations." Arguing against the "west-center; east-peripheral" structure of globalization I mentioned in Chapter 4, in which clinical information flows through a one way canal from the West (Caucasians) to the East (Japanese), this symposium nicely echoed the MHLW's vision of globalization where every nation (race) can be equally treated and respected.

Even with this ambition, this symposium took its steps slowly. The following table

can give us a broad sense about the trends at this symposium, showing the movement from bridging studies to the genomic approach and global drug development. In the following let us trace this trend year by year (table 6.3).

Table 6.3 Themes and Goals Presented in the Kitasato-Harvard Symposium, 2000-2003

	Theme	Sessions	Goals
First symposium (2000)	bridging study	1.global harmonization 2. ethnic differences 3. bridging strategies 4. future strategies and challenges	Discussions on technical issues on bridging study
Second symposium (2001)	Bridging strategies and pharmaco-genomics	1.bridging strategies: overview 2.bridging strategies: the west experience with bridging 3.regional/global clinical trial 4.ICH: practical implementation of E5 guidelines 5.pharmacogenomics: advances in understanding 6.pharmacogenomics: impacts—clinical and regulatory	Discussions on important issues: ICH E5 and implementation in individual Asian countries, EU's regional implementation, explaining ethnic and other factors, statistical challenges, genomics: its understanding and use in drug evaluation process
Third symposium (2002)	simultaneous, worldwide development and pharmaco-genomics	1.simultaneous/worldwide development strategies: overview 2. simultaneous/worldwide strategies: new challenges 3. simultaneous/worldwide strategies: ICH-E5 4. more concrete plan and actions based on ICH agreement, APEC report and today's discussion 5. pharmacogenomics: drug discovery and drug development based on the	simultaneous/worldwide development strategies

		genetic analysis. 6. implementation of global development programs.	
Fourth Symposium (2003)*	advance global drug development	1. global program: is there a reality? 2. regulatory updates and clinical trends 3. practical use of ICH guidelines for bridging/global clinical trials 4. OMICS: genomics, proteomics and metabolomics-how can they be used to enhance product approval 5. other novel technology update: modeling technique, biomarkers, disease Surrogates, data mining	Advance global drug development by discussion of emerging trends, technology updates, and novel paradigms

* It has a satellite meeting regarding QT prolongation effect titled "QT symposium" before the formal program.

Source: Adopted from the Kitasato-Harvard Symposium website. http://www.pharm.kitasato-u.ac.jp/biostatis/Khsympo_main.html.

The symposium of the year 2000 presents a conventional format. As its subtitle "bridging study" shows, sessions were organized in a fashion covering issues regarding the overview of the ICH and the possible impacts of the E5 guideline, especially the bridging approach. Also covered were the problems created by the bridging study strategy and its coming challenges, but there is nothing surprising. They seemed to know the ultimate goal but they had no idea how to get there. No sessions, even papers, concentrate either on genomics or global drug development. Indeed, as claimed in the preface of the meeting, the mission of this symposium was modest to "address a variety of topics relating to bridging strategies." Yet this statement had a clear explanation of the dual orientation of this occasion: "[B]ecause of the global nature of the issues to be discussed, it was felt to be important the both Eastern and Western perspectives are elucidated" (Takeuchi and Lagakos 2000). Obviously, in this situation Japan represented the East and the United States played the Western counterpart; their experience sharing about bridging studies would lead to more harmonious global drug development by means of biostatistics.

Some threads can be found in the second symposium about the shift to global drug

development. On the part of bridging studies, we see a shift of the discussion from basic research to the sharing experience of the reviewing process. Meanwhile, the way of discussing the E5 guideline changed. They started seeking other factors, such as genetic variations, that were able to explain more precisely and convincingly intrinsic racial differences, namely, the genomic move. On the other hand, global drug development appeared in the sections on "multi country trials" or "global clinical trials." In order to carry out meaningful global trials, there were discussions about how statistics could help. Another theme that appeared is pharmacogenomics. Apparently it was too new to discuss the practical applications at that point, but participants felt that it was a necessary field in order to make global drug development realizable. Although these signals were too weak to call huge attention, there was a move towards global drug development. In their welcome Takeuchi and Lagakos wrote: "the E5 guideline ... enables the extrapolation of Western clinical data to new regions of the world. In addition, the availability of pharmacogenomics information is likely to play a prominent role in future new drug development... The two concepts can lead to profound effect of drug development programs worldwide. It is therefore very important to create a forum for discussing the multiple issues surrounding these concepts." In fact, this statement became the theme statement for following symposiums.

As Takeuchi pointed out, the direction toward global drug development and genomics became clear at the third symposium. Flagging its theme as "Advancing Global Drug Development Techniques: Simultaneous, Worldwide Development and Pharmacogenomics," this symposium achieved following two agendas. First, it confirmed the "two-stage" evolution of clinical trials from a bridging study to a global drug development. Lagakos pointed out this shift clearly in his presentation slides. He compared bridging studies and global trials and indicated the distinctions that the former was serial and, evaluated and expanded existing information to create an evaluation of the risks/benefits of a drug in a new region, while the latter are concurrent studies and presumably all regions will benefit from each study and thus there is potential to shorten time needed for worldwide availability of effective new drugs. Thus, Lagakos concludes: "bridging studies are by their nature imply a sequential versus simultaneous development/evaluation strategy. Whenever possible, simultaneous studies will produce information more quickly and be beneficial to a broader audience since bridging studies really only intended to help the new region."

Meanwhile, pharmacogenomics eventually became one of the main topics of this symposium. Seeming to echo the completion of HOWDY and JSNP, these sections were designed to test whether genomics can serve as a scientific base for global clinical trials.

Although the discussion was limited by the progress in this area of science, we can feel the optimism from the presentations. Lagakos also pointed out the potential of pharmacogenomics as "apparent associations (e.g., ethnicity) at a more causal level; identifying patient subgroups who are more/less likely to benefit from treatment;" thus, the next step for this approach would be to "combine genetic information with other information to see if apparent associations between ethnicity and outcome variables were explainable by the genetic information."

The above agendas were fully developed at the 2003 symposium. In fact, almost no paper solely on bridging studies was presented; on the other hand, the sections about global clinical trials and pharmacogenomics had grown. Practical procedures were proposed as well as the possible scientific approaches, genomics, proteomics and metabolomics, and other new techniques such as biomarkers, disease surrogates, for example, were discussed.

What is perhaps more explicitly about this trend is the re-interpretation of bridging studies. Unlike an alternative approach where they were compared with the global drug development, it is portrayed a transitional process toward global drug trials. In Takeuchi's presentation titled "lessons learned from three global clinical trials," he reasoned why bridging is needed and why it is transitional:

> The main purpose of the bridging study is to show a similar profile of a tested drug in new regions to the one derived from the foreign data. .....The concept of the bridging strategy simultaneously, makes global drug development possible. The bridging strategy is just a 'one-way process' and we can extend the idea to the 'two-way process'. The global drug development can adopt the 'both way process' simultaneously and show no difference in the two factors among regions.

The first half of the above message was not new; it reiterates that bridging studies were proposed to solve the problems of ethnic differences. What was interesting was the second half. It was the first time that the statistical relationship between bridging studies and global drug development was clarified. Takeuchi claimed that global drug development was nothing other than "simultaneously" bridging studies. In this manner, a presumed "center-peripheral" worldview was carefully questioned by highlighting its primitive, one-way nature, and for this reason it must be "upgraded" to a more advanced, both-way approach of global drug development.

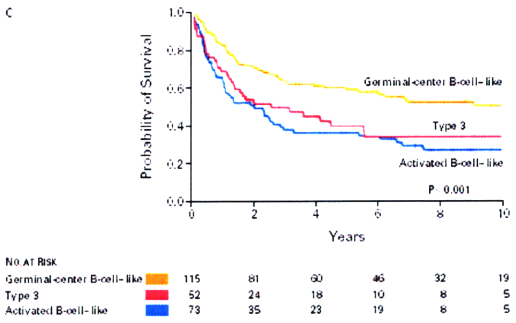
It seemed like Takeuchi and the MHLW had figured out a workable plan using these symposiums. Statistics was the new tool; and the Kitasato-Harvard symposium was the new channel. They shared the same vision and both agreed that it has to be achieved by a

scientific program that first, has Japan as the Asian representative in all clinical trials of a global scale, and, second, retained as much visibility for the Japanese as possible. In the next section, I will further discussion in detail how this discourse works.

Seeing Race in Genomics: What Science Has and Has Not Yet Said

Although the approach of genomic statistics is pervasive, we do not yet know in detail how it is to be applied to clinical trials. In the following I will take Takeuchi's presentation at the 2003 APEC meeting as an example allow such an explanation. At first glance, the main goal of this study is to build two statistical models that can estimate more clearly the dosage-efficacy effect in a mixed target population. The PA model is applied to a population when individual variance (or random effects) can be ignored, while SS model is applied to a population when variability among individuals exists. Since SS model requires more mathematical assumptions and hypotheses to correct possible biases, the conclusion suggests that the PA model be more appealing in a clinical trial setting. Like many papers in this field, the presentation involved complicated differential equations and functions. However, if we paid more attention to the logic of why these questions are raised and the assumption made, we are able to read some implications between the lines.

Fig. 6.7. Subgroups of Diffuse Large-B-Cell Lymphoma According to Gene-Expression Profiles



Source: Rosenwald et. al. 2002:1939, Figure 1.

The key thing to understand in this paper is the E5 guideline, through which we see concern about racial difference all the way from the beginning. In the introduction section, Takeuchi briefly reviewed the ICH, the E5 guideline, global drug development and intrinsic and extrinsic factors that define the racial difference. He then posted the research

question: does a mixture of different groups make the pharmacokinetic study data inadequate? Of course, in a sense, every person is different. What is new in this study is to point out how to sort out, to give these differences an order. For this reason Takeuchi introduced the idea of "molecular profiling" from a recent research in the *New England Journal of Medicine*,[22] pointing out that the genetic profiling can provide the material base required to explain these differences.

This figure, which is often used in Takeuchi's recent presentations, shows the gene-expression profiles of three subgroups of diffuse large-B-cell lymphoma. According to original study, the subgroups were formed from 240 patients with the disease by a hierarchical-clustering algorithm that groups the lymphomas according to the expression of 100 genes that distinguished between germinal-center-B-cell-like, activated B-cell-like, and type three diffuse large-B-cell lymphomas. Fig. 6.7 shows the Kaplan-Meier estimates of overall survival after chemotherapy among these patients, according to the gene-expression subgroup. In other words, there is a correlation between genetic expressions and cancers as well as that between with gene expression and their clinical outcomes.

It is an amazing study combining basic research and clinical investigation; however, while citing this figure in his genomic biostatical agenda, Takeuchi silently reversed its logic in terms of the relations between group and individuals. As we know, in this study, the subgroups were sorted from unrelated individuals by similar expressions in selected genes (as indicators). By PCR processing, they were grouped for scientific reasons as to show possible statistical meanings in the research. If we borrow anthropologist Paul Rabinow's concept of "biosociality" (1996, Chapter 5), the logic of this research nicely demonstrates this transition where individuals are unified in some biological ways but still remain independent and free in social situations. However, Rabinow also reminds us that the older forms of bio-identity, such as race, have not disappeared (103), and this can be well seen in Takeuchi's agenda. When using the result of this study to explain the genomic differences among races, Takeuchi has assumed a pre-existing cultural category of race in which every member must share some similarities with others in his/her genomic expressions. Takeuchi's thought reflects a primary distinction of race, which should be dealt with before that of the individual. This distinction also matches the MHLW's scheme of global drug development, which consisting of distinct groups of populations in the world.

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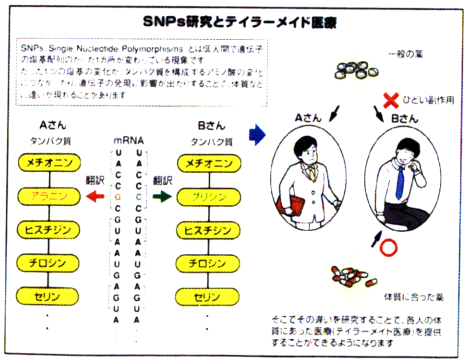
[22] Rosenwald et. al, "The Use of Molecular Profiling to Predict Survival After Chemotherapy for Diffuse Large-B-Cell Lymphoma," *N Engl J Med*, Volume 346(25), June 20, 2002: 1937-1947.

Holding this assumption, Tekeuchi goes ambiguously back and forth between individual genome and population genetics. According to his statistical models, he differentiates groups of similar gene expression and then to build a statistical model that combines the data generated. According to his presentation, the problem of racial difference can be solved if the target populations grouped by their gene expression are well defined. Only with adequate treatment of each target group can more specific results be achieved. In the end, an argument about how the "clearly defined population" helps to leads his discussion to the conclusion, Takeuchi reverses the result again by saying these studies can make sense of the genomic expression in a population. As the slide reads: "PK, PD and PPK study play an important role to investigate the relationship between dosage and efficacy, dosage and adverse event, and *possibly clearly defined target population*" (my emphasis). Although the above sentence looks confusing, I would suggest that the statistical tool Takeuchi formulates has, in fact, its cultural use; it provides a way to identify a "target group" by looking at its responses to a certain agent. Knowing which genomic information should be chosen from the group becomes important, since it will be the indicator to reduce the statistically individual differences and then the PA model becomes applicable. Coincidently, it was exactly the goal of the Japanese genome project.

Fig. 6.8 Idea of Tailor Made Medicine with SNP Studies



Source: Prime Minister, Japan 2003: 50

It is not until we reach this point do we realize the strategic position genomics now has in the discourse on global drug development. As anthropologist Joan Fujimura's precedent study on the rise of Japan's Human Genome Project suggests (2000), culture should be considered in a particular practice at a particular time and space, in which it is "both a heuristic device for discussing local and global actions and movements and a

concept that is being continuously produced through actions and discourses about these actions" (84). Even so, unlike Fujimura's observation where Japanese scientists inject a specific set of Japanese value on life into this transnational project, in our story about drug regulation, the cultural importance of genomics should be understood in two contexts. First, by using a burgeoning genomics, the MHLW draws a beautiful vision that centers on "tailor made medicine," "customized medicine," or "order made medicine." It is a latest trend that nobody will openly deny. In fact, Japan promotes this vision widely on many public occasions as well as in official reports, such as that of Millennium Project and the Outline of Biotechnology Strategy (fig. 6.8). Although promising, this goal cannot be achieved without going through a group approach on the human genome. On the other hand, the language in population genetics shows its limitations. The frequency of individual genetic traits is not enough to catch the complicated phenomenon of disease as well as the diversity of human beings. In order to make sense of the racial difference as a sum, researchers realized the need to have a broader knowledge of the expression of all genes, namely, genome.

A new "two-stage" transition is scientifically completed. Takeuchi and Lagakos claimed in the welcome note of the 2001 Kitasato-Harvard symposium that "the availability of pharmacogenomics information is likely to play a prominent role in future new drug development, especially as regards individualized, or tailor-made medicine." However, this goal has to be achieved through the traditional understandings of population genetics and, thus requires a national project for study the gene expression in a population. Race becomes a necessary existence for this transition.

So the following is what the MHLW said about its scientific concerns on the drug development in the future. Takeuchi shared with me his vision on how racial difference should be dealt in clinical trials: racial difference must be identified at phase I, in which twenty subjects from each major race should be recruited. According to their genetic profile, different protocols will be applied and conducted in each region in the phase II study. With this dataset, a simultaneous global phase III can be performed. He concluded: "to be honest, in this coming fall (2004) we are expecting to form a guideline scientific and clear. We are about to be ready."

Even so, there are some technical problems that need to be solved. The first is the problem of external factors, those that cannot be reduced by genomics. For this, the MHLW has no solution but local trials. Narikawa Mamoru, the former MHLW officer on international affairs commented in the 2001 Kitasato-Harvard Symposium while introducing the Japanese gnome, that extrinsic factors still have to be analyzed in each

region where the drug is to be marketed (*Yakujinippo* October 29 2001). His opinion was supported by Sato Daisaku, the current representative on the E5 policy. Regarding this problem, Takeuchi has formed a solution by applying "true bridging." What he provided to me was a combination of one main study and several "bridging" studies. In order to consider possible racial differences, the main study is a simultaneous global clinical trial, which has to include every genomic group, such as Caucasians, blacks and Asians, and should be conducted in a form of a dose finding trial, that is, a phase II study. In order to confirm the possible influence of extrinsic factors, some "bridging" studies can be arranged in the region (country) where the product is to be marketed. "Only through this way we can leave the touchy extrinsic factors on the back burner."

Another problem is the amount of Japanese subjects who can be recruited for the global drug development. Takeuchi left this open. "I know industry do not like our current practice on bridging study, which recruits too many Japanese subjects. To be honest, I do not really care the number of subjects (of course it has to have some); instead, I will argue for the quality of the trials. Japan cannot keep clinical trials done in Japan without improving its environment." "But, do you worry, as many MHLW officials have told me, that the results of trials done in Japan fails to show statistical significance?" I checked. Takeuchi replied that Japan has to face the global era. "I work with many industries and know that we cannot block the flow of business," he said. "We have to realize our current position so that we know how to start from there." In fact, the MHLW has been preparing as well. At the Kitasato-Harvard 2001 Symposium, the MHLW claimed that in response to the acceptance of foreign data, it would be more and more important to build a monitoring system, that is, phase IV trials (*Yakujinippo* October 19 2001). With the help of the information technology and the national health insurance, this system has developed into a mandatory process for drugs that may have side effects on the Japanese. "It is asked that, say, the first five thousand people who use this drug have to report to the MHLW their reactions," Takeuchi explained.

Perhaps it is not mature enough to form a solid guideline, but so far; so good. However, I still wonder why the MHLW is willing to abandon its insistence on the recruitment of the Japanese race. Because, according to the above agenda, it has almost accepted the original plan that the EFPIA proposed at ICH4, an agenda that based on ethnicity not on nationality. What Takeuchi proposes is a total deregulation of the Japanese race. Does the MHLW forget its mission to preserve the largest presence possible of the Japanese race in these trials?

The answer is a certainly "no". There is, in fact, something that the MHLW does not

say. Donna Haraway has noticed that genomics is a way to define human species, which has moved away from the traditional category of individuality and collectivity. However, she has not yet elaborated on what is really happening under this cultural promise. Daniel Cohen, chief genomics officer at Genset, proposes a new and ambitious approach to mapping disease and drug response genes. "It is clear that familial studies and positional cloning is not the way forward in unraveling complex disease," says Cohen. "[What] you need [is] a systematic genome-wide mapping effort that will enable the dissection of complex gene pathways involved in drug responses and disease" (quoted from Andrew Marshall 1998:8). Cohen is right to expand on this possibility, yet what he does not say is that except for industries that can smell the profit generated from this map, who else would dare to spend such an amount of money just to set up a database?

Japan does. This country is willing to spend as much money as needed to prove their racial solidarity in the global era. For example, Nakamura Yusuke mentioned the European study on SNPs, which included Caucasians, Blacks, and Asians, eight subjects of each group, criticizing that no polymorphisms can be found because of the "noise." The Japanese SNP study, instead, carefully chose twenty-four Japanese grouped into eight samples so that every sample can be identified. Through this way the SNPs can be found (Nakamura 2002: 14-15). Unlike the traditional approach where individual variance is analyzed with a reference to interethnic difference, the genomic version we have introduced, the SNP database, groups the ethnic and individual differences together. As I have written repeatedly, scaling is not the point in the use of genomics in pharmaceutical studies; the point is that no individual difference can be found without any reference, and vise versa.

Returning to the case of racial difference. Pharmacogenomics is certainly a science that does not belong to Japan exclusively. However, almost no country would be able to afford this information, especially Asian countries. Thus, although this framework does not indicate which population group should be chosen to represent Asians, in reality there is only Japan, the only Asian ICH country such an advanced technology, which is qualified for this task. This is why Takeuchi can remove the bar of cultural "protectionism," since scientific genomics will replace it. Benefited from its advance life science, Japan does not worry to compete with other Asian races in the global era.[23]

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[23] In fact, the cost of making such a genomic data is not that large. The commitment is. In Taiwan's case, if it was willing to, it could afford this approach across a wide range of ethnic groups. However, no such a commitment was made among these genomic scientists. Thanks to Professor Ralph Kirby at National Yang-Ming University for discussions on this point.

Perhaps we cannot easily ignore the power of the state, and Japan's attitude on race represents the most salient example.[24] Etienne Labbe, who has been working a long time with the Japanese as the E.U. representative on E5, teased the Japanese that "they are still convinced that Japanese have a 'pure genome' compared to other populations (they live on an island and do not 'mix' with any foreign populations!)." Labbe's comment maybe right; yet, what he does not know is that the Japanese really mean it and have turned it into both a scientific discourse and a business program. When I reminded Professor Takeuchi that in his explanation of global clinical trials that he always uses "Japanese" is where he should have used "Asians," he gave me a charming smile and said: "well, yes. But do you think it will make any difference if I do?"

CONCLUDING REMARKS: WATCHING GENOMICS MOVE IN THE ICH

At this point, we can draw some conclusions concerning Japan in the post-E5 era. These can be divided into two sets of problems, one theoretical and other practical. The theoretical questions stem from Donna Haraway's three-configuration description of how the human species is conceived in the past and the present. As I have written in Chapter 4, this notion is useful as a frame of reference to capture the main social and cultural concerns of an episteme and the scientific tools developed to serve this need. However, as an interpretive framework this frame does not show us the mechanisms by which one configuration changes to another, and in what field the paradigm shifts take place. This is especially the case when we apply Haraway's observations to a specialized field, such as the world of proprietary drugs, and to a global setting for the making of this paradigm, the ICH. From this viewpoint, this chapter, along with Chapter 4, represents a detailed "slow-motion" ethnography that supports Haraway's argument on one hand, and indicates the limitations of its implications on the other.

The first theoretical conclusion we can draw from this chapter is the ambiguous "delay" between the time that of public expectation or imaginings about science and its actual application. Haraway has argued that in the development of modern biopolitics, there is not always a one-way diffusion from science to society; in its diffusion to society, scientific knowledge is constructed and reproduced with metaphors outside of its own language and epistemology, giving rise to a mutually constitutive relationship of political

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[24] Another recent case concerning the complicated aspects in the relationship between the state and race can be seen in Iceland, a country also proud of its pure racial composition, which attempted to "capitalize" the genomic information of its nationals with the help of a biotech company. For an anthropological analysis of this project, see Pálsson and Rabinow 1999.

economy, symbols and science (Haraway 1989: Chapter 10). Although in a simplified vision of science and society, it is possible to assume an interactive situation where the two move hand in hand, this ethnographic study of pharmaceuticals shows that the construction of ideas about science does not translate into immediate application, because scientific ideas belong to different apparatuses of reproduction. It is true that the promise of genomics may evoke a political economy of science that will result in more funds being invested in research and research facilities; nonetheless, this does not mean that the industry will simply immediately apply this concept to drug production. The pharmaceutical industry is already a monopoly business, and it has no reason to risk its current profits just for the advancement of science.

Second, this chapter shows the cultural and social reasons for a move to the genomic. These reasons have often been ignored by some researchers, who fail to address them from a non-historical, anti-cultural viewpoint. Considering the move to genomics rather than a total shift or Kuhnian switch of worldviews, this chapter identifies the locality for the move in the field of the ICH. The necessity of "breaking" the drug approval requirements consensus, as I have discussed, is not always commercial—it can also be cultural and political, the result of active participation or of passive resistance, as in Japan's insistence on its racial difference. As described in this chapter, the MHLW did not only create a scientific program that could serve its cultural concerns; it tried to make this program a reality in order to solve the deadlock on bridging studies. Some attempts, though still only a few, have been made in the name of establishing global clinical trials (*kokusaikyodochiken*), such as for the AT1 antagonist for type II diabetes (RENAAL test) and the ACE blocker for preventing recurrent strokes. Meanwhile, more pressure has come from the other side of world. Shimatani Katsuyoshi of Pfizer, for example, indicated that despite their own ethnic diversity, the United States and the EU have recently tried trials that used a unified protocol and gave reasonable weight to ethnic factors; thus he warned that it is possible that Japan will be excluded from the global drug program because there is no visible effort to decrease the number of repeated clinical trials (2002: 711). All of this reveals a complicated reality that cannot be reduced into a mechanical image of the world.

As far as practical problems are concerned, this chapter has brought a clear ethnographic focus to how and in what way Japan's voice can be properly heard. I not only analyze the content of what the MHLW said, but give equal attention to the way Japan's voice is expressed. I stated in Chapter 4 that the MHLW intended to use the science-oriented, global ICH as the place to deal with the problem of racial difference. Following this argument, the first part of this chapter described the dynamics of a

dialogue in which the industry tried to force Japan back to the bilateral MOSS trade negotiation forum. Paralleling these channels, the second part of the chapter singled out an informal "express" channel between experts at the MHLW and the FDA for the project of global drug development.

Even so, looking at the practical aspects of this move, all disputes have to return to the global forum of the ICH, and genomics was not encouraged as a way to solve the deadlock. The West had its own ways of dealing with this problem. In the Steering Committee meeting of May 2001, both industry and the MHLW were concerned about the clarity of bridging studies. An informal expert working group on "Ethnic Factors in the Acceptability of Foreign Clinical Data" was formed in February 2002 to discuss issues on the guideline and its implementation. There were two reasons to open this discussion, as Robert O'Nell of the FDA pointed out: first, "general agreement that misunderstanding and confusion still exists regarding the intent of and advice in E5 and its implementation," and second, "general sense among industry sponsors that their experiences support the position that E5 is not being adhered to." In order to fix this problem, questions and answers about the E5 guideline were needed to "identify key questions and topics for which consensus answers can be provided to all regions." The purpose of these efforts was "to clarify the situation and help move us forward" (O'Neill's slide presentation at ICH6, see the conference website at http://ich.org).

Japan perceived this discussion differently. It seemed that the MHLW could not wait for the genomic frame to arrive.[25] On the one hand, Japan wanted to avoid being excluded from the trend of integrated clinical trials in the West. On the other, it hoped to form a policy to allow the products to be developed after the implementation of the E5 guideline, and it was expected that a bridging study approach would not be suitable for this. To fulfill these goals, the MHLW had to have a guideline backed up by the ICH. Of course, another concern about the timing had to do with patents. An OPSR consultant said to me, "Don't you think that it is time for promoting global drug development? Indeed we had troubles in asking industries to make bridging studies for the products that have been approved a long time ago, but it will be gone soon. You know that most of the patents are about to be expired." This assumed that the industry would support this change.

As discussed above, the MHLW planned to propose a revision of the guideline in

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[25] Naito Chikayuki also mentioned the pressure from the industry side (Naito 2002: 94). However, according to the discussion of this chapter, I don't think industry was a crucial factor in the idea of global drug development. It is worth noting at this point, though, since it confirms again one of this thesis' main arguments: the MHW had different concerns than industry.

the Steering Committee meeting in Tokyo in 2001, specifically requiring simultaneous phase III clinical trials that recruited enough Japanese subjects. Naito Chikayuki summarized the need for revision (2003a). He wrote that the goal of the E5 guideline was to efficiently introduce new medicines which were already approved in other regions. The guideline had only described in principle how data could be extrapolated from one region to another. Even so, "It would be seem possible and efficient to assess potential regional differences as part of a global development program, i.e., for development of data to occur simultaneously in various regions, rather than sequentially" (152S).

In the proposal on global drug development, as Naito said to O'Nell personally in the meeting, what was important was that global drug development be "appropriately conducted with a single protocol and with a sufficient number of trial subjects in each region"(152S). Three possible scenarios for global drug development were received and listed by the OPSR (Naito 2003b: 93). Naito's comments on each proposal are shown in table 6.4.

Table 6.4 Scenarios on Global Drug Development

	Scenarios
1	Conducting different phase studies in each of the 3 ICH regions. For example, phase I in Japan, phase II in Europe, and phase III in the United States.
2	Conducting phase III trials in three ICH regions, recruiting the necessary numbers of cases in total, but only a few in Japan. For example, a trial that recruited 100 subjects among which only three were Japanese.
3	Conducting phase III studies in three ICH regions, with enough subjects in total and enough analyzable cases in Japan. Two scenarios follow: A: Having already conducted dose-response test in Japan. B: No full does-response test done in Japan, but instead a test based on the dosage applied overseas.

Source: Adopted from Naito 2003:93, Table 1.

The first and second scenarios were turned down, Naito claimed, because they totally ignore ethnic factors and regional differences and thus could not be accepted. As

for the third approach, although it was potentially acceptable, one condition needed to be added: the Japanese sample size must be "large enough to allow clinical analysis done solely by them, since it is the only way to consider the regional difference" (94). Further more, on the dose-response test, Naito suggested that the B scenario was more adequate because in some cases the Japanese PD data is not consistent with foreign data, and thus a single does test is not sufficient. From this comment we can see that the MHLW preferred a type of global drug development that satisfied two conditions: enough Japanese subjects enrolled and a separate does-response test done in Japan. The former was the bottom line and the latter was strongly argued, but all were negotiable.[26]

Two meetings were held, as O'Nell recalls,[27] and the issues of the acceptance of clinical trials from non-ICH regions and global drug development were discussed. At the first meeting the participants recognized the contribution of the E5 guideline and asked each regulatory authority, especially the MHLW, which had the most data, to report on its experiences of bridging studies. But the touchiest issue discussed was whether clinical data received from Asian states other than Japan (for example, Taiwan or Korea) could be accepted. It was proposed by O'Nell, since he had clearly indicated that the spirit of the E5 guideline was "intended to permit the requesting of one 'confirmatory' phase III clinical trial (bridge study) in the region (*not specifically defined, nor meant as 'country'*) if needed or if necessary to extrapolate" (ICH6 presentation, emphasis mine). He wanted to separate nation from race, but Japan rebuffed this effort by claiming that it was "beyond the scope of the ICH." The reason for this objection, as Naito explains elsewhere, is that the ICH guideline was formed for the exclusive purpose of dealing with regulations among the United States, Europe, and Japan; thus a data package created outside of the area should be considered independently by the regulatory authorities through which the product is seeking to be for marketed (2003a: 149S-150S).[28]

This situation continued when Japan proposed the discussion of global drug

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[26] For example, elsewhere Naito emphasized that the sample size had to be large enough to allow an assessment of the impact of racial difference, but this did not mean that the sample size should be very large for statistical analysis. Besides, if a separate Japanese dose-response trial was impossible, an alternative would be to have a simultaneous "global" does-response trial, like the global Phase III trial, to determine whether Japanese patients would need a different dose regimen. See Naito 2003.

[27] The first meeting was held in Brussels on February 6-7, 2002, and the second was in Washington, D.C., on September 10-11, 2002. According to Uesaka Hiroyuki, one more meeting, a teleconference, was held on July 21, 2003. It was held to confirm the content of the Q&A by three regulatory bodies with the participation of the industry.

[28] I was heard at the 2003 APEC meeting that Japan is considering the acceptance of clinical trial data using Korean and Hong Kong subjects. However, I confirmed later from the officials, it turned out the use of non–Western "foreign data", thus Japanese data is still required. Even so, for the GCP concerns, these data are subjected to the site-inspection by the MHLW and are judged on a case-by-case base.

development. It expected a guideline that could be made to ensure sensitivity to Japanese racial uniqueness. But the FDA that turned this proposal down, claiming that it was "potentially beyond our scope" (Naito 2003b: 93). It was suggested that instead Japan's proposal be added along with bridging studies as a drug development strategy option. These compromises resemble what Naito had first proposed ten years earlier. After all, the West did not understand what Japan had insisted so strongly on. In 1993 the rejection of this proposal led to the endless entanglement over racial differences that gave birth to the ambiguous guideline. Ten years had passed—the same scenario was happening again and it was not clear what consequences would be. As I argue repeatedly in this thesis, it is an anthropological problem. When the ultimate hope of making Japan, the United States and the E.U. equal partners was rejected, it was impossible to expect Japan to compromise its state and national integrity. As a result, only a simple Q&A document was agreed upon. The second meeting determined that the regulatory bodies—the MHLW, FDA, and EMEA—would be responsible for developing this document. The final document was signed off on October 15, 2003, and reported to the Steering Committee at ICH6.

We can see misunderstandings, or, I would argue, quarrels, in this Q&A document as it was first released at ICH6 in Osaka in November 2003. It was accompanied by an implementation working group assigned at the second meeting in September, and only ten questions were listed. Japan's request was written into the first question as "I am planning to develop my new drug globally. Does E5 provide guidance for this approach?" And the answer is a long one. The first part includes all the requirements that Japan asked for. Unfortunately, however, it is not a guideline, as the FDA and other participants did not back this approach. As we see in the second and third paragraphs, complicated concerns about ethnic difference are mentioned, and there is a recommendation to discuss these with the local authority for any specific requirements, but none of this differs significantly from the original guideline.

Next, O'Nell's requests, along with those of global industry, are listed (questions 4, 5, and 10). They usually start with the phrase "I believe that my drug is insensitive to ethnic factors and that there are no significant relevant differences in extrinsic factors," and the answers are the same as the ones provided in the MHLW version of the Q&A: polite, encouraging, but making no concrete promises. The last question clearly states this problem: "E5 expresses the principle that, as experience with interregional acceptance of foreign clinical data increases, there will be a better understanding of situations in which bridging studies are needed and that it is hoped that, with these experiences, the need for bridging data will lessen. Is this principle still valid?" The answer is as follows: "Yes, this

is the expectation. The accumulation of experience by each region with implementation of the E5 guidance continues to add to our understanding of situations in which a bridging study would be considered necessary by a new region. The expectation continues to be that, with this experience, the need for a bridging study will lessen."

Nobody was satisfied with this compromise, but it was all they could achieve. It seemed to reach the point where science could not provide decisive answers. It could only complicate the social landscape in which it was just one of the ways that the parties involved expressed their concerns. Even the experts did not have any idea why things go this way. They were lost, as Naito frankly concluded in his report on the MHLW's current standpoint on the acceptance of foreign data, which is still the same and has the "three repeats" specified in the original law back in 1985 (for details, see Chapter 4, n.25). He writes, "The 3-B scenario was thought [to constitute] no change [from] the 1985 amendment. However, standing on the same side as our nationals, we consider only the drug's efficacy and safety in terms of their interest. For this thinking the guideline has to fall in that direction" (2003b: 94). Recording the attempts made to move to genomics, I do not think that nothing has been achieved since 1985. I will argue, however, that what remains unchanged is the mentality of such attempts. For good or for ill, Japan will be the last nation-state in this global world.

Chapter 7
Composing Our Voice by Biostatistics: Anchoring Taiwan on the Global Networks

> If we are global, there will be no need for bridge[s].
>
> John Lim[1]

> Unfortunately, pharmaceutical biotechnology is not a traditional industry. It requires vast investment, an integrated system of policy regulation system on pharmaceuticals and close cooperation among government, academy and industry. Taiwan seems has everything required; and everyone in charge is elite. However, their efforts are antagonistic when they work together—even worse than a tray of loose sand (*yipan sansha*).
>
> Shaw T. Chen and Keith Chan[2]

PART I
SAVING BRIDING, SAVING THE STATE

Voice and *Fasheng* (Voicing) in the Bio-Global Era

This chapter intends follow up Chapters 5 and 6 on the subject of voice and voicing in the global era. It will follow from Chapter 5's analysis of how the Center of Drug Evaluation (CDE) made Taiwan an institutional voice in discussions on racial difference and drug regulation. In order to make this voice heard, it created a global network through which to articulate its policy on bridging studies. This chapter will also follow from the description in Chapter 6 of the failed attempts by the Ministry of Health, Labor and Welfare (MHLW) to replace bridging studies with global drug development. The deadlock on bridging studies, in this sense, made Taiwan's voicing possible; its strategy was to separate race and the state, and this influenced the post-E5 negotiations between the United States and Japan.

All these issues can be seen in the discussion of U.S.-Japan Market-oriented, Sector-selected Discussion (MOSS) follow-up meeting of April 2001. At this meeting, the United States requested a reconsideration of the definition of "Asian" data (*Yakujinippo* [Pharmaceutical News] April 6 2001). Although the MHLW interpreted the use of the word "Asians" in the E5 guideline as referring to the Japanese since Japan was the only

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1 In the slide presentation at the 2001 APEC meeting, Taipei, May 25 and 26, 2001.

2 In "Taiwan Senjiyaoye Menrin Weiji: Fajan Tingzi Buchien; Jingjengri Liushi" (Taiwan's pharmaceutical biotechnology facing crisis: development ceases; competitive power loses), p.2.

Asian country invited to the ICH, the United State hoped to reconfirm the definition of "Asians," extending it to apply to the people of other East Asian counties. In making this request the U.S. had in mind Taiwan and Korea, two states implementing the E5 guideline at almost the same time as Japan.

However, these two states had different concerns about racial difference. Like Taiwan before the introduction of the ICH guidelines, Korea required a low-standard but mandatory phase III study with a certain amount of local subjects for every new drug to be imported. Furthermore, medical institutions there were not allowed to participate in multinational trials. However, efforts were being made to improve its review standard. In 1998, it had raised its drug regulation agency from a headquarters to an administration known as the Korean Food and Drug Administration (KFDA). This new institution soon adopted the ICH guidelines, mainly the E5 and E6 guidelines, and put them into practice.

According to Kim Hoon-Kyo's presentation at the 2001 APEC meeting, this implementation was considered an important reform, for it accepted the concept of bridging studies and permitted national-level trials. Three more guidelines were adopted in 1999 indicating the material required to apply for waivers of local clinical trials. Even so, Western industry was most concerned with was KFDA's policy on Asian racial difference. The E5 guideline glossary indicates that the complete data package should contain "clinical data that fulfills the regulatory requirements of the new region and pharmacokinetic data relevant to the population in the new region" (7). The crucial point is how to define relevance in terms of race. We know that the MHLW defines this data as produced from studies on Japanese living in Japan. Korea, at this point, had the same stance. Although the KFDA accepted data from studies done with oversea Koreans, basically it recognized only Koreans for "Asian" data.

Apparently, when global industry started dealing with East Asian countries other than Japan, Korea was presented as an example of what they would not like to see. It was argued in the MOSS meeting that if all Asian countries improved the standards of their review policy while insisting on local clinical trials, this would create serious problems. The total number of subjects required would increase, as would the time for marketing. Korea was thus blamed for this rigidity on the subject of racial difference. Although it was one of big Asian markets able to afford advanced medicines, it was threatened with abandonment if it insisted too much on racial difference.

In contrast to Korea, Taiwan presents another kind of example, an example of how the "politically constructed" guideline could still work. The "scientific" foundation of the CDE's policy on bridging studies, as introduced in Chapter 5, is a "politically motivated" paper that identifies the genetic relationships among races in East Asia. Even so, the CDE

incorporated it into its discourse on the scientific evaluation of bridging studies and included it in its policy. We can assume that PhRMA would like to use this policy to balance out the "conservative" practices of Japan and Korea.

Just as Chapter 5 starts with an evaluation of Taiwan's voice to the world, this chapter briefly evaluates its voicing, or *fasheng*, in a local political context. Although the CDE now has an institutional voice heard by the global, there are at least three limitations in terms of voicing. First and foremost, the agency of voicing is problematic. As analyzed in Chapter 5, we cannot identify any distinct voice that could be heard before the foundation of ICH-Taiwan. However, even after Taiwan had founded the ICH-Taiwan committee and later a semi-governmental institute, the CDE, there was still no clear agency for voicing. This is a situation in which, to borrow from feminism, "the personal is political." As a state policy, drug regulation is commonly the business of a government department, such as the MHLW or the Food and Drug Administration (FDA). However, it is problematic to assume that the CDE is representative of the Taiwanese government, for two obvious reasons. First, the Taiwanese government it is supposed to represent does not represent anything from the viewpoint of global politics. Even in APEC, which the CDE used as a global stage, Taiwan is identified by the non-governmental name "Chinese Taipei." Second, because Taiwan has failed to win global recognition as a state, on some occasions the CDE's claim does not truly reflect the result of discussions within the government, but an opinion strategically formed in order to make a voice heard.

Second, Taiwan's voicing is limited to certain conversational contexts. Although the CDE successfully makes an effective claim about racial difference and bridging studies, which were one of the most "troublesome" concepts in the ICH guidelines, there are still many important drug regulation guidelines, such as E6, E9, S3, S4, M1, M2, and many others. Even so, in addition to the E5 guideline and bridging studies, there has been almost no chance to hear from the CDE in global settings.[3] Taiwan's voicing to the ICH was in fact exceptional; it happened only when the Western countries and global industry failed to make an agreement with Japan. Even so, its voicing was limited to restricted conversational contexts, like an actor who has only few lines in a play, no matter how important they are. Let us use an example from drama: if Tom Stoppard had not written *Rosencrantz and Guildenstern Are Dead* (1963), how many people could remember the two friends of Prince Hamlet who have no lines in Shakespeare's famous play?

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[3] However, Taiwan presents as a loud, important voice on the subject of the E5 guideline and bridging studies. It has even been a regular guest in the Kitasato-Harvard Symposium series since its beginning. In addition, as I will introduce in the second part of this chapter, Taiwan developed a new field of statistical methods for multi-sited studies that is now also globally recognized.

The third limitation concerning Taiwan's voicing is the temporality of the conflict on the E5 guideline, the only stage that the CDE is able to use. Though it was feasible, it was not the CDE's proposal that made the ICH decide to keep bridging studies. They were kept because they considered the ultimate solution to disagreements about global drug development. Although up to ICH6 this problem had not been solved, it is about to lose its importance, because, as Naito Chikayuki has pointed out, all the drugs that need bridging studies to combine existing data with data required for the new regions will soon lose their patents. Because of Japan's insistence on racial difference, firms developing drugs after the implementation of the E5 guideline have noted the importance of recruiting Japanese or at least Asian subjects for clinical trials. Thus, it seems likely that in a few years bridging studies will be history.

Even so, this does not mean that bridging studies will be of no use to the world. In the following I will briefly introduce the dynamics of the bridging study policy with regard to both ICH and non-ICH regions. As described previously, global drug development will be the solution to problems of racial difference for ICH regions. Although no agreement has been reached about how global trials should be conducted, there is a consensus that a certain amount of Asian clinical trial subjects will be required due to concerns about racial difference. Then the problem will be which Asians have the potential to be used in these trials. The Japanese, based on the MHLW's insistence, should have first priority. However, as introduced in Chapter 6, Japan still has problems conducting trials that meet the requirements of the E6 guideline. It will also cost a lot of money and time to recruit enough subjects to satisfy a globally acceptable trial. Therefore, as long as Japan cannot adjust its clinical trials system, an opportunity is available for other Asian states that can offer both the environment and subjects required.

This is what Shaw T. Chen, a senior reviewer at the FDA who has long been involved in Taiwan's ICH initiatives, and Keith Chan, a veteran of the pharmaceutical industry, argued to their nation in the article quoted at the beginning of this chapter. There is a substantial need for Asian subjects and there are many states that have shown an interest in the burgeoning business. On the other hand, bridging studies are still useful for non-ICH states that want to keep some local clinical trials or clinical data on local subjects. In this sense, Korea is the best example. Unlike Japan, which is still conservative about conducting Western-style clinical trials, Korea quickly did away with restrictive regulations on clinical trials. For example, in order to keep more local trials, it even allows different phases of clinical trials (for example, phase II and phase III) to be conducted at the same time. As long as this need exists, bridging studies are a necessary

framework.[4]

However, among these non-ICH countries, not everyone is capable of or interested in addressing the topic of racial difference. Not many countries are rich enough to afford these advanced drugs. Even among those that are able to pay for them, their markets are often too small for them to be able to bargain for more trials. The global industry's attitude toward these states is clear: no more clinical trials should be requested or they will give up these markets. One PhRMA person told me in private that although the ICH may have the mission of improving world public health, basically they do not want their guidelines to apply to all countries, because this would slow drug sales. This poses a tricky problem for Asian regulatory authorities, because they need to decide whether racial difference should be taken into consideration, and, if so, how it can be dealt with. Obviously, depending on whether or not the county decides to adopt the ICH guidelines, we see different responses to the problem of racial difference. In fact, except for Korea and Taiwan, almost no countries take it into account. Most member states of the Association of Southeast Asian Nations (ASEAN), even the richest such as Malaysia and Thailand, say clearly that they cannot maintain such a high standard, and they worry about the possible loss of accessibility to the latest drugs.

Meanwhile, two other countries in this region that are able to afford these drugs, Singapore and Australia, remain uninteresdted in this topic, despite the fact that one's population is over 80 percent Han Chinese and the other's over 30 percent Asian. The reason for this decision, on the surface, seems to be simple: as stated by John Lim, Singapore's Director of Center for Pharmaceutical Administration, "if we are global, there will be no need for bridge[s]." But underlying this claim is the complicated racial composition of these countries. Singapore, for example, has three major ethnic groups—Han Chinese, Malays, Indians—along with various others, all of whom are quite different one from another. Once the government decides to deal with racial difference, they will have to do so for all differences. However, current research is limited. Some ethnic differences in drug effects have been discovered for the Han Chinese and the Japanese. However, as yet, very few differences in drug effects have been found for either Malays or Indians.

After a brief evaluation of Taiwan's voicing in the ICH and a general survey of the issue of bridging studies inside and outside of the ICH regions, it should be clear what is

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[4] However, this does not mean that Koean insdutry is ready to catch up with such a high standard. To my understanding, Korea does not have any strong pharmaceutical firms due to its weak foundation for clinical research and development. After the introduction of these guidelines, most companies were unable to manage their their production as they suffered from heavy penalties ordered by the government.

important about the change in Taiwan's clinical environment after its adoption of the E5 guideline and the CDE's efforts to "save" bridging studies. The first part of this chapter will focus on the dynamics of the introduction of bridging studies. The immediate trade-off, as we will see, is the possible loss of local trials because of the extrapolation of foreign clinical data. There exists a possibility that Taiwan could gain more local trials as part of the global development trials for Asian subjects. However, a painful transformation might be experienced in the change from local trials to racial trials.

With this understanding, the second part of this chapter will deal the CDE's two actions in response to international dynamics surrounding bridging studies. The CDE would like to create more collaborative conversations—in addition to the existing APEC platform—with the hope of discussing issues other than the E5 guideline. The two actions are interrelated; the former is an attempt to win Taiwan more global attention by amplifying the use of bridging studies in non-ICH regions, and the latter can be seen as a desire to establish an administrative network of regulatory authorities in which Taiwan could be recognized as an integral entity. These actions cannot be purely political pursuits; the ICH guidelines have given the CDE a framework by which to speak. Thus any agenda provided by the CDE has to have scientific meaning and must also be of strategic use in order to be attractive to other countries. As we will see, biostatistics is the tool that makes this vision possible.

Making Bridging Studies Workable: Taiwan as Exemplary

Let us look at Taiwan's E5 policy first. Aware of the possible impacts on the accessibility of advanced drugs, four years of transition were planned. A three-year grace period was given after the "double twelve" announcement on bridging studies in 2000. As bridging study evaluation became mandatory for every product that was seeking a market in Taiwan in 2003, one more year was given during which bridging studies remained optional but only if the applications were not granted waivers.

However, what makes Taiwan globally known is the CDE's attitude toward bridging studies. The CDE has claimed to global companies repeatedly that it would never be an unconditional requirement. An early report shows that 60% of the first twenty applications were judged ethnically acceptable (Lin et al. 2003). The updated results on the bridging cases in Taiwan are as follows: among sixty-two cases that sought for evaluation between January 2001 and August 2003, forty-nine were granted waivers for further clicnial trials (Yi-jin Chou's slide presentation at the 2003 Kitasato-Harvard Symposium).

The key to the above result is the independent consideration of race. For a state that has no formal recognition, the only way to build its credibility is to have a universally acceptable standard such as science. The CDE has always claimed its technical orientation, emphasizing a neutral standpoint on processing the NDAs. Its high percentage of waivers gives a clear sign to pharmaceutical industry and ICH guideline makers that no "non-scientific" concerns are involved and there will be no applications that require extra clinical trials due to such factors. In fact, the CDE follows closely the rules of the game set by Europe and the United States; the high rate for waiver is just one example, for it fits the FDA's previous survey on drugs that may have racial effects. It shows how the E5 guideline can be "scientifically" realized.

For example, using the ideas put forward during the discussion that failed to be added to the text of the guideline,[5] the CDE designed a flow chart and a checking list for applicants, helping them to know its policy and the criteria for judging ethnic sensitivity (Hsiao et al. 2003). Concerning the process, the rational of the "algorithm" is clear and can be characterized by four steps, and it is also transparent. First, is the question of whether the drug is eligible for waiving bridging studies with reference to DOH announcements on waiving clinical trials? If the NDAs falls within the category that requires submission of information proving no existence of ethnic differences, it should be evaluated by following steps. Secondly, the quality of data is tested; any submitted data package that fails to meet the regulatory requirement is advised that amendment is required.

The third step and the most important concerns ethnic sensitivity. A bridging study will not be required under the following conditions: 1) sensitive on neither extrinsic or intrinsic factors; 2) Taiwanese subjects have been enrolled in a multi-center trial; and 3) no racial differences are found between Asians and foreigners in terms of the dose-response reactions and the efficacy/safety profile (that is, the foreign data is extrapolable to Asian region). The fourth and last step is applied when a MDA is judged ethnically sensitive or considered to have safety concerns. In this case, a local clinical trial is required. It can be a PK and/or PD study or any clinical study that can demonstrate the efficacy and safety of the medicine, and its protocol should be created in consultation with the CDE before it is conducted.

The checking list is a reference for product sponsors so that they can know the

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[5] They are mentioned as an appendix to the E5 guideline. For the discussion of these thoughts on racial difference, see the part II of Chapter 4.

rationale of the regulatory agency on judging whether a product is deemed to need a bridging study. Again, it is transparent and open to consultation. There are two kinds of concerns in the list. The first is administrative in order to provide information about current application status of the product, such as whether this product is applying to other states, whether clinical studies have done with Asian subjects, and whether post-market surveillance data is available if it has been marketed. The second concerns are scientific to order to self-evaluate the characteristics of the product. Twelve items are asked on whether the product being applied for is possibly ethnically sensitive, such as non-leaner PK performance, steep PD curve, narrow therapeutic dose range, high potential of drug-drug reaction, metabolized by enzymes known to be a site showing genetic polymorphisms, specific bioavailability profile (drug use, dietary habits), disease epidemiology, and other important factors (medical practice). In order to make the reviews more efficient, the CDE requires the documents submitted to indicate the paragraphs or sections containing important information, such as the comparison between different races. Furthermore, each item asked for should have a descriptive summary or brief description of enclosed information according to the checking list.

On the other hand, the CDE provide clear explanation for those that fail to waive bridging studies. In fact, this is another aspect that needs to be considered, namely, the integrity and fairness of its practice. Between 2000 and 2003, fifteen products were requested to have bridging studies (two products withdrew during evaluation); everyone was given good reasons for the judgment.[6] Chu Mong-Ling, Director of the CDE, provided an explicit description of the criteria, which consist of five kinds of problems: 1) efficacy concerns, such as the abuse of antibiotics; 2) safety concerns, such as extremely high dosage difference between United States and Asia; 3) a lack of familiarity on the Asian market, such as new drugs with a narrow therapeutic range; 4) sensitive PK/PD characteristics; and 5) inadequate data to meet Taiwan's regulatory requirements. For the CDE, bridging study evaluation is a purely technical problem.

A case often cited for the CDE's E5 policy is omeprazole, which I have introduced in Chapter 6. Despite there being no adverse effects reported, it is race sensitive. Study shows that poor metabolizers of omeprazole, who are classified as CYP2C19 genotypes, have a higher plasma concentration of omeprazole and thus a higher efficacy for

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[6] According to Yi-jin Chou's presentation at the 2003 Kitasato-Harvard Symposium, the reasons include the followings: malqualifeid pharmacokinetics (PK) studies, differnce found in PK data, non-leaner PK-patterns, lack of Asian data, potential drug-drug interactions, insufficient dose-response information, suspected differences due to medical practice (such as antibiotics abuse), and unclear metabolisms.

anti-Helicobacter pylori (H. pylori) therapy.[7] It has been revealed as racially sensitive among Asians. The incidence of poor metabolizers is reported between 15% and 25% in Asian populations compared to the 2% to 5% found in the Caucasian and African-American populations. Moreover, the Asian population has a higher percentage of H. pylori infections than does the Caucasian population (but not African Africans, which it is endemic due to poor water supplies).

Taiwan, particularly Chern Herng-Der and his colleagues, has taken up the topic of CPY2C19 since 1998. According to one of their preliminary studies, the prevalence rate of CYP2C19 poor metabolizers in Taiwan is about 15%. Further, the efficacy of dual therapy with omeprazole and amoxicillin was significantly higher in CYP2C19 poor metabolizers than in extensive metabolizers (Yang, Chern and Chen, 1998). As the Mey Wang of the CDE summarized at the 2003 Symposium on Statistical Methodology for Evaluation of Bridging Evidence, omeprazole is characterized as the most salient example due to its non-leaner PK behavior above 40mg, low oral bio-availability of 30% to 40%, high bound rate to plasma protein at 95-96%, extensive metabolism by CYP2C19 (where the AUC in Asians is two to four times than of Caucasians) and rather flat pharmacodynamic (PD) curve and does-response curve.

Even though the racial effects of omeprazole are clear, the CDE does not follow the OPSR in making a quick conclusion that omeprazole requires a bridging study. Mey Wang presents the reasons for its waiver. Using simulative approaches, she points out that an operational criterion for bridging study evaluation is possible (Wang et al. 2003). In order to make the simulation resemble reality, Wang introduces variables, including not only factors such as racial differences but also many others, such as minimal effective concentration (C_{min}), maximum effective concentration without adverse effect (C_{max}), therapeutic index (C_{max}/C_{min}, TI), and treatment success rate (P). All are considered important to the therapeutic dynamics.

The simulation is conducted with considerations of efficacy and safety, testing examining how other variables changes while fixing one variable. The results suggested as follows: considering efficacy, when TI of an applicant is wide (for example, from 4 to 8), there will be no need for a bridging study if the interethnic and intraethnic variations are within a reasonable limit (for example, interethnic variation smaller than 2.5% or intraethnic variation smaller than 0.8%). In addition, efficacy would not be a concern

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[7] Belonging to the P450 family, CYP2C19 is a genetic polymorphism that has been widely studied since the 1990s. In addition to its effects on omeprazole, it is responsible for metabolisms of S-mephenytoin, methylphenobarbital, phenytoin, diazepam and its active metabolite desmethyldiazepam, warfarin, phenytoin, lorsortan, tolbutamide and several non-steroidal anti-inflammatory drugs, and many others.

when the proportion of poor metabolizer and interethnic variation falls within a reasonable limit (for example, interethnic variation within 3% and 10% and/or poor metabolizers are within 1% and 15% in a certain population). As for safety, whether a bridging study is required depends on the following factors: therapeutic index, seriousness of an adverse event, the rareness of that event, and total prescriptions.

In summary, guided by a biostatistical approach, it is suggested that applicants supply more "key parameters" in order to achieve a better bridging evaluation. As for the case of omeprazole, Wang shows how it could be waived a bridging study on the above principles. Given the fact that omeprazole has no serious adverse effects (only headache, abdominal pain, and some minor complains), the CDE made a decision based on the following considerations. First, because the drugs estimated therapeutic index is as high as 12, no bridging study is required regarding to safety problems. Second, because the value of interethnic variation and intraethnic variations falls within a reasonable range (10% and 0.3%, respectively), efficacy would not be a concern.

Although its decision is still controversial, the CDE's attitude toward bridging studies is clear. The industry certainly appreciates this approach, for an Asian state, it hits at the Organization for Pharmaceutical Safety and Research (OPSR) for its "non-scientific" practice. The European and American experts appreciate the CDE, for it shows how the method they proposed for racial difference is workable. Elaine Esber, one of the ICH founders, openly praised Taiwan at the 2003 APEC meeting based on the waivers reported. She pointed out that the CDE has revealed why it is important to strengthen the regulatory capability and how much this can change and increase acceptance under the E5 guideline. Chern Herng-Der buttonholed me with this confidence: "good policy needs a solid scientific base; we are proud of the transparency of our bridging policy." As a state that as yet gains no general international recognition, the CDE seems to consider the ICH as a global stage for those who pay respect to science and other universal virtues.

Trade-Offs for Bridging: Dislocated Government and Fragmented Policy

The CDE wins itself and Taiwan a global visibility, but this was not achieved without any cost. The pay-offs for the CDE's high waiving rate for bridging studies, as I have just introduced, are multi-fold. First of all, while following industry's expectation, it risks the possible loss of local trials that were originally requested by the administration. Furthermore, if the CDE can waive most bridging studies and welcome other Asian

clinical data, industry will naturally apply to Taiwan with the clinical data they have from other Asian counties that have requested local studies.

Among those who do not agree with the CDE, Professor Hu Oliver Yoa-Pu at National Defense Medical Center is typical. Serving as the chairman of the Advisory Committee on Pharmaceuticals (ACP), Hu openly expresses his disappointment with the CDE's high waiver rate. As a government technocrat, Hu insists that more stringent criteria should be applied for bridging study evaluations. He admitted that there is no evidence showing the need for bridging studies in the cases being waived; however, he reminds me: "there is no evidence either to let these applicants waive bridging studies." As discussed in Chapter 4, there is a cultural division between Japan and the Western countries in terms of racial difference, but in Hu's opinion, this is a gray area in which the government should play a more active and strategic role in order to keep more clinical trials in Taiwan. He suggests, for example, an "unarticulated" percentage, by which Taiwan decides that applicants required bridging studies, should be set by the advisory committee, while leaving the CDE more scientific-oriented. "In this sense, the advisory committee should not be an administrative 'appendix' to the business of drug regualtion; instead, it should be the ultimate safe valve for Taiwan's drug regulation," Hu adds. A relatively high inconsistence rate between the CDE and the advisory committee on pharmaceutical affairs seems to support this comment.[8]

Hu's opinion reveals the "non-scientific" function of that regulatory authority as means of protecting the domestic industry. As discussed in Chapter 6, the OPSR is often perceived by industry as the source of a "non-tariff barrier" for foreign products. From this point of view, the CDE seems to have "abandoned" the hope of strengthening its domestic industry,[9] and they have already felt this pressure. They argued that the government's welcome attitude toward the ICH would shift the whole impact directly on to the burgeoning pharmaceutical companies, which are too small and need time and tariff protection to grow. Chang Hsiu-Gang, president of Purzer pharmaceutical, Inc., compares the difference between Taiwan and Japan in terms of their policy on drug development and regulation (*ICH-Taiwan Bulletin* 3). Chang pointed out that the

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[8] This thesis notices, yet will not deal with, the conflicts between the advisory committee and the CDE. This committee is a quasi-administrative-quasi-academic institute on drug regulations that is commonly seen in Asia. Thus, after a professional technical agency like the CDE is introduced, every government faces the problem of how to treat two organizations of the same function. In the case of Japan and Taiwan, they tend to leave the both in parallel. Applications have to be approved first by the CDE and later the advisory committee, and sometimes their opinions are not consistent. A recent estimation of this percentage of disagreement in Japan was about 5%, while in Taiwan it is much higher at 20% to 30%.

[9] Here it is noted that the industry refers to proprietary drugs, which are, in fact, the minority of this sector.

Japanese government has successfully delayed the rapid import of Western pharmaceuticals by slowing down the adjustment of its regulations as taken from the ICH negotiations. It is what he calls the "Japan model": the MHLW grows together with the industry. It provides the time necessary for companies to modify their production system from copying to research and development intensive. Meanwhile, the MHLW has learned how to achieve scientific, high quality regulations of drugs.

However, the CDE did not follow this model. It chose to let industry confront the world of harsh global competition. "From the viewpoint of industrial development," writes Chang: "it is like forcing local athletes to reach immediately the standard of the Olympic Games." According to Chang, this policy has had limited impacts on Taiwan's drug industry up to now, since it just beginning to develop products other than generic drugs. However, it effect will be seen in a long run. Taiwan is at risking of having no local pharmaceutical company in the future. Even so, Chang does not blame the government too much. Using C.K. Yang and Chi Cheng, two legendary Taiwanese athletes that won medals in the Olympic Games, as goals, he expects a few, but not many, companies will survive this tough challenge. "We have no time to argue for the chances we have lost," he concludes, "chances will be given to those who work hard."

Chang's comment reveals a subtle inconsistency, if not contradiction, about Taiwan's promotion of its biotechnology industry. Like Japan's Millenuim project, Taiwan's "two-billion; two star" plan, a national plan for globalization, featured newly emerging fields, information technology and biotechnology/pharmaceutical, as two promising sectors to establish. Under the Executive Yuan's Biotechnology Industry Promotion Program, some initiatives have been taken.[10] Certainly, the CDE is incorporated into this program. By only looking at this side, many may be happy with the government's effort to establish a state-sponsored industry based on high technology. However, the establishment of institutes and programs will mean little if no integrated effort is taken. Also, it is not an all or nothing situation; bridging studies are a salient example to show how manipulation of policy is necessary. It is absolutely correct for a government to create better regulations on drugs in order to protect the nation's health, but fine adjustments are required in deciding when and how much they should be introduced given there is a goal of also protecting domestic industry. Unfortunately, it

[10] These interministral projects include the Biomedical Research Center established by the Industrial Technology Research Institute, the National Science and Technology Program for Biotechnology and Pharmaceuticals by the National Science Council, and the Executive Yuan's One-Stop-Service Office for Biotechnology Industry.

seems to have missed the right timing and the pressure is on.

This inconsistency is more obvious in Taiwan's policy on the CRO industry.[11] As I have written previously, the deregulation of administrative clinical trials in Asian countries will force them into tough competitions where the number of clinical trials done in one country is not decided either by its population, its market size, or how "odd" its racial composition is. As a newly established business, the number of local clinical trials is based on the state's ability to recruit enough human subjects in a short period of time, the ability to execute qualified experiments, the ability to review protocols for clinical trials and the ability to provide advisement during trials. Apparently, the CDE has showed this ability and its E5 policy is a declaration of the liberation of clinical trials. Although the high waiver rate provides Taiwan with a way to import more drugs in a timely fashion, a potential risk could rise from this too early welcoming of the pharmaceutical industry. If Taiwan minimizes the number of local clinical trials, it may lose the potential to build up its own CRO industry.

Considering the advancement of medicine in Taiwan, CRO seems to be a promising industry to try. However, was it too early for the CDE to open this gate to competition? With respect to this criticism, Chern Herng-Der thinks that the CDE should not be the one blamed. Concerning a policy that waives bridging studies for these drugs and how this will make influence Taiwan's clinical trial environment, Chern (2002) defends: "the CDE ... found that in 2000 the DoH received about 85 applications, but up to November 2001 it has received 122. Thus, the number is increasing." Furthermore, Chern pointed out the improvement in the quality of clinical trials because these, include more pre-phase IIIa trials and multi-national trials. He concludes, "While insisting on a policy that promotes necessary bridging studies and waives unnecessary trials, this has not resulted in decrease in the quality and quantity of local clinical trials."

Does a bridging study create a "win-win" situation for Taiwan and global industry? Because the CDE extended the grace period to the end of 2003, it is hard to reach a

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[11] As an element in the value production chain of pharmaceuticals, the history of CRO in Taiwan is fairly short. It was not until 1997 that Taiwan had formed a market able to attract the long term investment of some international companies, though the famous Panlabs Taiwan Ltd., which was an addition to Panlabs Seattle, was founded in 1970. Later some local companies join this battlefield, yet almost no one could balance their deficit after few years of operation. For example, the first CRO in Taiwan has been claimed to be, More Biomedical, which was founded in 1994. Yet it could not attract enough local cases and was acquired by Quintile 1998. According to a report made in 2001 (Chiu 201: 136), only 10 to 20 percent of local CROs have entered the global market fully. Most of the studies are post-marketing trials and for registration use, presenting a weak and depressed infrastructure for this sector. I thank Professor Ralph Kirby at National Yang-Ming University for the history of Panlabs Taiwan and the CRO industry.

conclusion on this trend at this moment. Even so, we can see some clues in terms of the number of clinical trials and their content. In terms of the amount of INDs and NDAs, according to Kuo Benjamin Ing-Tiau, the executive secretary of the Joint Institutional Review Board (JIRB), the number of trial has decreasing to about two third in 2004, the true "first year of bridging studies" (table 7.1). Chern Herng-Der confirmed this to me: at the time point of September, only seventy or so applications have sent for reviews compared to one hundred in the past. Worse, the fact that the local companies have almost disappeared is most worrying.

Table 7.1 Clinical Trial Reviews in Taiwan, 1998-2004

Year/cases	1998*	1999	2000	2001	2002	2003	2004**
IND	12	42	90	131	102	134	49
NDA	9	18	24	34	60	67	38

*start at the quarter 4. ** up to the second quarter.

Source: the CDE website at http://www.cde.org.tw.

However, Kuo reminds us about which type of clinical trials have contributed to this decrease. In the past over the half clinical trials conducted were trials on bioavailability and bioequivalence, which did not have much academic value. What is crucial for bridging study policy should be the number of phase III studies, which is considered to be more meaningful.[12] Judging by this standard, the numbers do not decrease as critically. Although Chern and Kuo have different understandings of this number; Chern thinks it is slightly decreases but Kuo thinks such trials are gradually increasing; but both agree that Taiwan has chosen to transit from a "meaningless" registration or listing trials to "meaningful" global trials. Kuo showed to me the number of cases that have applied to the JIRB, Taiwan. "Since the application fee is expensive, thus only global trials can afford this," Kuo explained; we see that the number of phase III trial applications has increased, as a trend, from 2000 to 2003.

According to Kuo, it is what Taiwan needs. "You cannot ask for the same number of meaningful trials in Taiwan as a site. It needs time and requires more improvements in the

[12] There are many factors by which to judge whether a study is meaningful, such as the number of hospitals involved and the quality of the trial sites, how many patient are enrolled, the methodology used, and whether it has international participations. Thus is hard to give an exact number of how many trials are considered "meaningful." Yet, according to Chern, about half the trials can be said meaningful to the CDE.

environment. More importantly, before all tasks are taken, our government has to be clear about whether it would like to consider clinical trials a 'business'," Kuo pointed out. Indeed, the CDE's E5 policy does contribute to competition with other Asian countries and to the transformation of clinical trials from tests for administrative uses to those that have an academic contribution and a business value. Unlike the pharmaceutical industry, which has to make its own products, what CROs sell are various services from basic research to clinical applications. Since this is so, even Taiwan cannot have its own brand that can still build up by itself into a strong business, like the semi-conducting industry of twenty years ago.

Thus, what is at stake may not be the timing of this decision but whether the Taiwanese government was prepared for this transformation. Unfortunately, it has not been ready. Kuo recalled a public debate about whether Taiwan should include the CROs into its promotion program. In 2004 the advisory board of Taiwan's "two-billion; two star" plan decided to add the CROs into the main industry to promote them.[13] Concering the strategies for the biotechnology industry, adviors noted that the island was falling behind regional competitors such as Korea and Singapore. They recommended that an independent body was needed to steer the future direction of life sciences in Taiwan, namely, a "Biotech Industry Strategy Consulting Committee," in order to consolidate and integrate often overlapping government biotech promotion organizations and research institutes. Furthermore, this committee should be set up and headed by a strong and influential industry leader.[14]

However, some government officials disagreed. Wang Hui-Po, then the Director General of Pharmaceutical Affairs, openly criticized this policy in a newspaper (*Zhongguo Sibao* [China Times], May 24 2004). Entitled "All People become Guinea Pigs?" Wang claimed that Taiwan is too small to be self-contained, thus importing drugs is evitable. It is the government's responsibility to introduce a global standard to guard the safety of the drugs imported. However, "to have good regulations on clinical trials" is not "to promote the industry of clinical trials." A small state like Taiwan needs not risk its people by testing the most advanced products on them. Furthermore, any industry based on human's bodies is unethical and inhumane. "It will be an international joke if we are proud of this kind of industry," she warned. Although Wang has gained support from

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[13] For the conclusions and suggestions from this meeting, see http://www.stag.gov.tw/content/application/stag/freeformat/guest-cnt-browse.php?ico=4&cnt_id=327.

[14] In fact, it has been listed as an issue for discussion at the SRB since 1999. Yet not enough actions has been taken to form a robust economic body like other regional competitors.

some medical authorities,[15] most people expressed their disagreements.

At the case of clinical trial, the Taiwanese government's attitude is disoriented. Not only it has the double-checking system of the CDE and the ACP, there are three checking points for each clinical trial application. After consulting the JIRB, it has to be re-checked by the CDE, and, before it is conducted, each hospital that conducts trials reserves the right to review clinical trial applications. All these repetitive works badly weaken Taiwan's competitiveness. This self-conflicted situation has not improved as I write this thesis. Kuo replied when asked whether the E5 guideline or bridging study policy is an issue in the development of Taiwan's clinical trials: "I do not think bridging studies themselves are a crucial factor. In fact, it helped us to earn some meaningful studies, which I appreciate. Let me put it this way: if our bureaucratic environment shows no improvement, we are about to meet the limitation of the trials we can take."

Kuo's warning exactly touched the fundamental problem of Taiwan's governance, which explains both the CDE's success and its "failure" to build Taiwan as a place to hold clinical trials. Policy analysts tend to separate one policy from another, estimating the results and the influences by each of them. However, this functionalist viewpoint assumes two things that do not fit into Taiwan's situation. First, despite its existence as a well-functioned polity, Taiwan is not a formally recognized by the world as as state. It cannot join any formal organizations of states as well as hold official dialogue with most countries of the world. Since this is so, at most global occasions, the individuals who can be accepted are considered to speak on behalf of this state. Thus, unlike Japan's bureaucracy where every bureau is independent yet contained by other bureaus, Taiwan's political situation grants technocrats flexibilities in dealing with international affairs. Sometimes personal creativity can even circumvent any systemic agreement. Due to the lack of the integrity of the national identity, the Taiwanese government does not have an institutional mechanism to check every policy it has made a decision on. In order to make Taiwan visible, sometimes it has to leave the person in charge to make the decisions. If readers still remember what I mentioned in Chapter 5, it was these individuals who "institutionalize" their arguments and gave Taiwan a robust voice.

The second problem concerning Taiwan's situation is the fragmented nature of its policymaking. This is why the CDE alone has failed to give birth to a good environment for clinical trials. Of course, this is not unusual for some huge bureaucracies, such as that of the United States; however, for a small state like Taiwan it is a serious problem. Since

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[15] See, for example, the article by Andrew T. Huang, president of KFSYS Cancer Center in *Zhongguo Sibao*, May 26 2004. Like Japan, Taiwan has its problems with the ICH GCP standards. However, I would like to leave these discussions to future studies.

individuals can have their own opinions on global affairs from their perspectives, these may be contradicting with each other and problems arise when these people try to realize them through the bureaucratic system. Each policy may be creative and excellent, but as a whole they just cannot work together as an integrated agenda. Shaw T. Chen and Keith Chan, senior consultants of the CDE, expressed their frustrations in a recent article about this problem and point out the necessity of a light, responsive government (Chen and Chan 2005). The point is not whether clinical trials, or in a broader sense, drugs should be considered a business; instead, what at stake is whether Taiwan can form an integrated policy that is comprehensive and robust enough to put together all parts toward an achievable goal. They point out that while new institutes, such as the CDE, are pushing Taiwan to move forward, other institutes pull it back. They cry: "Please give up the burden of old system as soon as we can and form a small yet flexible one that fit Taiwan as a vibrant island."

Yet, these are far beyond the control of any single institute, such as the CDE. Chern Herng-Der, who forwarded the above article to me, did not tell me his intention. He only said: "We cannot wait for others anyway." As one of the aspects to present Taiwan to the global, the CDE seemed to insist on what it thinks is best for the state, and to achieve this goal it would like to keep moving forward alone.

Unstable Voicing: Two Challenges from Outside

Even if the CDE can get rid of the factions within the domestic realm and focus only on its international relations on behalf of Taiwan, it has problems in terms of its voicing ability. In the first section of this part I have introduced three limitations on Taiwan's voice in the world of the ICH, here I shall point two direct challenges that will destroy the CDE's previous achievements.

One challenge, as I have discussed in Chapter 6, comes from Japan's ambitious promotion of global drug development. Unlike Taiwan, the MHLW has a full presence at the ICH. It can lead the discussions, draft new guidelines and form a working scheme that favors its cultural agenda. When Japan insists on its "mandatory bridging for all" policy, asking future products for perspective, the global data package in which the Japanese presence is necessary, the CDE is losing. As described previously, drugs have about five years on average of marketing time before their patents expire. Thus, when almost all the drugs in question have lost their patents, there will be of no point in applying for bridging evaluation. Although the MHLW has participated in every meeting of the APEC network

since its beginning and collects information about Taiwan's E5 policy, there has, in fact, been limited communications between Japan and other non-ICH country states. The main field for negotiation, for the MHLW, is always the global ICH and not regional meetings. In addition, its market is large enough to allow bargaining on these issues alone. As one Japanese professor involved in the MHLW's E5 policy told me, the MHLW has no interest to interfere in other countries' E5 policy.

Meanwhile, global industry is tired of this discussion. Since the CDE has shown that bridging studies are a scientific, workable agenda, and Japan already known this, they do not need it anymore. Some of them might assume that the APEC meeting is a place where Taiwan's experience can embarrass Japan to change, but apparently this strategy does not work. Along with the rise of global drug development, they wonder whether the APEC meeting is a worthwhile conference to attend. I witnessed a blunt question at the ICH GCG meeting in 2003. After the CDE's announcement of the coming APEC meeting, one EFPIA member asked: "Putting aside of the E5 guideline and bridging studies, can you just tell us what is new in this meeting?" Of course, the deadlock about the revision of the E5 guideline gives the CDE some time, but the signs are clear that it must create new agendas otherwise the APEC meeting that will attract people.

The other challenge to bridging studies comes from the non-ICH region, of which Singapore is exemplary. Singapore was relatively behind in following the development of the ICH, whose guidelines were not introduced, along with the foundation of an administrative authority on drug regualtion, until the new mellenium arrived.[16] It did not only miss the debate over the E5 issue, which Japan was hugely involved in the early 1990s, it also missed the chance to form a professional and independent institute, like Taiwan did in the late 1990s.

Even so, this does not mean that Singapore has no way to catch up with other countries. In fact, Singapore has not followed the way Japan and Taiwan. Its strategy is to ignore racial difference so that it can "skip" the dispute over bridging studies. It considers clinical trials nothing but strictly business. It welcomed the E5 guideline and does not reject global drug development. As a country consisting of various ethnic groups, Singapore claims to provide the best site for clinical trials to study Asian people, but does

[16] Singapore did not introduce drug registration until the Medical Act of 1987. According to this law, new drugs could only be registered if they had been already been approved in major developed countries, and this administrative system remained the same until 1998 when a center for drug evaluation was established. This center later became one of eight professional centers of the Health Science Authority (HSA), but still remained small.

not apply the results to its nationals.

I have argued elsewhere that Singapore presents itself as a business "node" in the global network of proprietary drugs and it seems to want to be a global state with no local characteristics. The network exists and therefore the state lives (Kuo 2004). The above vision refers to a contrasting image about that state compared to Taiwan in terms of its spatial imagination of the world. As discussed in previous section, Taiwan maintains a relatively huge and inconsistent bureaucracy on drug regulation. Considering Taiwan as a land hosting many people rather than a global business point, the CDE's main mission is to improve its medical standards and public health but not to make CRO an attractive business. It might be hard for Taiwan to accept Singapore's view on the state. However, Singapore's stance is a threat that other Asian countries cannot ignore, especially countries that genuinely insist on the racial difference of their nationals.

Let me briefly introduce Singapore's strategy on drug regulation, whose mission is "to develop the Republic into a regional medical and life science hub" (Wong and Lim 2003: 17S). In one way, it follows closely the leading countries and organizations. As part of the second-tier drug approval system, Singapore is hoping to be able to accept the results made by these authorities in order to shorten the time to drug accessibility from the primary reviewers. To achieve this goal, Singapore sets a high standard for its dossier format and review requirements comparable to that of the ICH. More importantly, it designs an "express" route of review process, which claimed in its presentation, for the submissions of drugs that have been approved by the HSA's benchmark regulatory agencies.[17] The aim is clear: since it is hard for Singapore to be a primary reviewer in the world, it hopes to the first country in East Asia that has access to the latest drugs marketed in the most advanced countries.

On the other hand, Singapore has enhanced its connections with other Asian counties through regional organizations, especially ASEAN. Even ahead of the ICH regions, the recent involvement of the ASEAN common technical document (ACTD) enables it to have an administrative platform on which drugs can be freely registered within its member states. When the ASEAN Implementation Working Group on ACTD was formed in 2002, Singapore was appointed the chair, leading the realization of the ACTD implementation. This group has achieved a firm timeframe for full implementation, twining system programs allowing information exchange for specific areas. One cannot say that Singapore is the only player to make this happen. However,

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[17] These agencies are the FDA, Medicines and Healthcare Products Regulatory Agency, Therapeutic Goods Administration, Australia, European Agency for the Evaluation of Medicinal Products, and Canadian Health Canada.

the only thing we can be sure of is that Singapore will definitely benefit from this homogenous market of pharmaceuticals if we think together of the strategic position for the state's global industries. It deregulates all requirements, including those on racial difference, so that it can have the most advanced products available as soon as the West. In addition, it engages in regional networks, such as the APEC and ASEAN, to make "pathways" through which these products can be sold in other Asian states.

There are cultural reasons why Singapore's proposal is a threat to Taiwan. For global industry, Singapore is one of the two entry points (other than Hong Kong) into East Asia. This is not only because it used to be a part of the United Kingdom, but because the English environment helps Singapore to maintain its ties with the former motherland and her ex-colonies. In fact, the English language is itself a tool that makes the Westerners comfortable. When asked about the company's recent strategy in Asia where it absorbed an independent firm in Singapore, a CRO person told me: "Westerners still feel more comfortable talking in English. Think of this, if a yellow face can speak fluent English with an Oxford accent, this gives our customers more confidence." If Singapore decides to give up all racial concerns and focuses only on clinical trials management and R&D, such as its famous "biopolis," it will be attractive to all CRO companies and a tough competitor for Taiwan.

We have seen some signs of this trend. In 1998 Taiwan signed up to an agreement with the world's second largest CRO company Covance, asking it to help Taiwan to build up a CRO industry. Some training courses were arranged after this project was included in the five-year plan for the development of biotechnology in 1999. Yet, this cooperation seems to have ceased, and Covance has moved its Asian base to Singapore. In addition to Covance, Taiwan also signed with Quintile as strategic partners in 1999, yet no further steps have been seen since then. It wants to catch all, but fails to do anything. Meanwhile, Singapore, a semi-democratic state, shows a surprisingly high efficiency in maximizing its ability for competition. Its stance of ignoring bridging studies also demonstrates a feasible way to dealt with racial difference.

What will the CDE do? It cannot be like Singapore and dismiss all requirements on racial difference, since they are required and it cannot go back. The bridging study agenda, though workable, will be soon replaced by Japan's global drug development. If the CDE cannot solve these problems, its voicing ability will soon be gone.

PART II VISIONING THE STATE; VISIONING BIO-GLOBLIZAITON

At the Frontier of Bio-Globalizing World: "Regionalizing" Bridging Studies

The previous part of this chapter asked a question at its end of the CDE: while Japan and Singapore propose their worldview concerning racial difference and drug regulation, what will Taiwan do after bridging studies? Before analyzing the CDE's project to respond these challenges, let me first summarize two characteristics of the bridging study agenda.

The first characteristic is about its underlying concern on racial difference. Originated from Japan's sensitivity to their bodies, bridging studies should be applied to countries that sincerely consider themselves to have a relatively homogenous racial composition and having strong awareness of their difference from other regions. Even so, except for Korea and Taiwan, not many Asain counties qualify the above provision for political concerns. To use Singapore as example, although the Chinese are in an absolute majority in this country, some policies are imposed to achieve harmony with the other three major ethnic groups. Surrounded by counties dominated by different races, Singapore has to eliminate all possible friction in the name of racial discrimination. Of course, for this reason, bridging studies are not on its agenda.

The second characteristic of bridging studies, which also originated from Japan, has to do with its administrative function. In the case of Japan, it is practiced like an administrative requirement when applying foreign data into a new region where this product is seeking to market, thus indicates a dichotomous view that divides the world into "the local" and "the foreign." Apparently, no one likes this view, including Japan, for different reasons. As discussed in Chapter 6, while the industry hopes to penetrate this administrative barrier by global trials, Japan attempts to achieve a true world harmony by providing simultaneous global drug development that keeps every race, especially the Japanese, distinct. No matter for what reasons, they all agree that bridge studies are bilateral thus should be transitional in order to achieve globalization.

With an understanding of the above characteristics, the CDE's strategy for the global challenges is clear. When questioned about topics other than bridging studies in the 2003 APEC meeting, Chern Herng-Der replied confidently that regional harmonization on regulatory science would be the theme for the coming meeting and for the future ones. Based on Taiwan's success on bridging study evaluations, the CDE tries to extend its use from single countries to a region. The reputation that the CDE has earned on bridging studies has given it a token by which to make such a claim; thus to promote this "Taiwan experience" to other state is its immediate mission. In other words, it wants to "regionalize" bridging studies.

The paper "Reinventing drug regulation in the Asia Pacific Region: Taiwan's experience and a vision for the region" explains in more detail about how a regional platform on drug regulation can be founded by individual agencies (Jao et al. 2003). For understanding exactly Taiwan's strategy, we should pay equal attention to the paper's content as well as to the way it is narrated. The first half of this paper reviews the initiatives taken by Taiwan to establish a high-quality environment for drug regulation, and the second half brings up a proposal to promote harmonization and cooperation in the Asia Pacific Region. Although these reforms have been discussed in Chapter 5, it is worthwhile to note how they are narrated in this paper. Quite far from describing a series of contingent actions taken through personal connections, this paper uses a formal yet positive tone, giving readers a sense that all is well thought out and planned, the concept being achievable by a strong and effective government.

This impression can be easily seen in its description of the CDE. In the section of the introduction on the CDE, it describes that it was modeled after the FDA, the best of the best in the world and thus is capable of providing full-time expertise in both preclinical and clinical reviews with a transparent, reliable and authoritative approach. As a regulator, it has to hold to a global class standard to facilitate participation of global clinical trials. In addition, it is both an educator of the public and the leader that guides pharmaceutical research by examining the need for special regulatory requirements. It is proud of the highly qualified staffs it has recruited, which includes "fourteen physicians, eighteen professionals with Ph.D.s, and twenty-one professionals with bachelor's degrees and other backgrounds" (Jao et. al. 2003:43S). It is an outstanding team that cannot be seen in Asian countries outside of Japan.

This paper then uses another important characteristic of Taiwan's CDE to persuade its readers, the in-house reviewing system, which not so many countries can afford. It copies the FDA's Center for Drug Evaluation and Research (CDER), where a substantial group of professionals are maintained to provide a responsive, high-quality service. Though it is expensive to maintain such a group of professionals, it is insisted, according to its deputy director Chern Herng-Der, that this is necessary in order to improve the ability of the regulatory agency. "No one is born a professional in this business; so we have to train these personals ourselves," Dr. Chern said: "through proper trainings these reviewers can build up their expertise in two years."

The full range of the service that the CDE provides reflects its ambitions. Except for the "routine" works of the new drug application (NDA) reviews and consultations, it offers protocol reviews of the clinical trials similar to the FDA. Other major tasks include

cooperation on the clinical trial adverse drug reaction evaluation (the phase IV study) with National Adverse Drug Reaction Reporting Center, that of the national genomic project (gene therapy) with the National Health Research Institute (NHRI), and that of traditional Chinese medicine project (the guideline on the evaluation system of Chinese herbal medicine) with the Department of Health's Committee on Chinese Medicine and Pharmacy. The CDE seems to be the research and development department of Taiwan's pharmaceutical industry; it has done through the reforms of the regulatory science.

Except for reviewing the CDE's achievements, the above introduction part of this narrative has its strategic use. By reorganizing these historical events and facts, it tries give an impression that a strong regulatory agency is the key to boosting a country's medical research and drug industry. Following this argument, this paper describes the CDE's relationships with first-tier reviewers. In order to catch up with the first-tier reviewers, this paper write, some efforts have to be taken to exchange updated information and reviewing experience. Like Sigapore, it is claimed that the CDE has established partnerships with the FDA, EMEA, MHRA, OPSR, TGA, and Medical Products Agency in Sweden.

Again, the above description is not quite new as discussed in Chapter 5. However, what should be noticed is the way that it is narrated. Unlike Singapore's reliance on its administrative or informative ties with these benchmark agencies, the CDE provides another global vision about international liaison based on scientific knowledge. In fact, this view was emphasized more in my interviews with the CDE officials, such as its director Chu Mong-Ling and deputy director Chern Herng-Der. They believe that only by forming a strong and responsible agency can a true partnership can be established with these institutes, and they tried their best to make the CDE such an agency. Chern once told me: "you have to be strong first so that you can win true respects from Western countries. You have to have some information made on your own so that you can exchange it for more information. It is our perspective to the world of regulation."

So far we have gone through the "Taiwanese experience" part of this paper. Its overly positive tone may not be normal to some readers but is familiar to those who understand Taiwan public heath in the 1960s. As I have argued elsewhere (Kuo 2005), it is a nostalgic narrative on the "golden age" where many similarities can be found in the tone of these achievements in public health, such as the international cooperation and exemplary success. However, here this tone has a function other than "self-bragging." As a part of the narrative technology, a positive tone is necessary, because it gives an example of how a country that has a weak environment for pharmaceutical industry and biotechnology can achieve success, and this success will become a foundation for a

making a regional strategic alliance.

In the second half of the paper, readers are told the CDE's proposal to extend its influence, forming an alliance of regulatory authorities based on a development model. On the surface this model resembles the one Eruopean Union attempted back to the late 1980s; yet, the underlying reason it holds is different. The need to cooperate, as indicated, is to increase bargaining power while negotiating with industry: It is reasoned: "the Asia Pacific Region represents an immense and highly populated area, but it is also a region with small individual markets, weak regulatory authorities, primitive local drug industries, and poor infrastructures for clinical studies. Thus, except for Japan, the region has been excluded from the ICH and has no independent voice in the global drug evaluation process; the region's local needs are often ignored during new drug development" (Jao et al. 2003: 47S). In order to clarify serious misunderstandings by other "more advanced authorities"[18] and to express their needs, the regional economies must form a unified market for new drugs, and a strong, harmonized regulatory system would facilitate its formation. It is expected that it will "account for population differences in drug response, promote local drug industries and meet regional needs for new drugs" (47S).

From the above description, we can easily identify that the ASEAN states and Asian member states of the APEC are the paper's expecting audience. Contrasting Singapore's imagination of an "unpeopled" state, the CDE continuously reminds these countries about the realities of their populations and health of their citizens. Meanwhile, by bring back the old notion of populations, it rejects Japan's too-quick move to genomics. According to the CDE's vision, a certain number of clinical trials are necessary to provide information for the use in public health and there is also a chance to be equal with these ICH countries by improving the standard of local industries. It writes: "if the Asia Pacific region is inspired to be an equal partner with the current ICH members, scaling up is the only way to achieve regional harmonization. The benefits will outweigh the risks" (Jao et. al. 2003: 48S).

The CDE then shows how the cooperation among regulatory authorities can be achieved. In short, it should be achieved by a sort of the division of labor. Limited by budget and resources, the paper points out that it is hard for each agency to maintain a high review quality while offering consultations covering all specialties. Therefore, the

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[18] It is said that these counties are not able to conduct reliable reviews and consultations. For example, in a questionnaire re to the global industry about their interactions with regulatory authorities in East Asia, it was reported that companies gave poor overall reports on Korea and Taiwan, though the quality and clarity of the advice from Taiwan should be noted. See Anderson et. al. 2003:111S.

aim of the cooperation would be to pool the resources and collaborate. The harmonization of the "non-ICH" Asian states can be achieved by following steps. The first step is certainly to recognize racial difference and negotiate issues related to bridging study policy, in which Taiwan's experience can be help. Based on their experience with bridging studies, various collaborations can be conducted, such as the exchange of reviews (for examples, Taiwan for the reviews of drugs on gastrointestinal diseases, Singapore for those on hematological diseases), collaboration on inspections (for example, the Good Clinical Practice inspection), joint review of NDAs, and consistent postmarketing monitoring. Only after these are done, it should be possible to mutually recognition drug approval, the final step of harmonization. The ultimate goal, it claims, is an agency similar to the European Agency for the Evaluation of Medicinal Products in the European Union.[19]

Perhaps we should stop here and clarify some issues about our concerns on racial difference and bridging studies. In fact, we see some interesting points in this vision. First, as we have read in Chapter 5, Europe was the first region that noticed the problem of racial differences in drug regulation and tried to provide a solution by administrative recognition across the member states. Basically the CDE's idea for this regional approach shares the same concept that the harmonization must be an administrative one so that every agency can share the work load and enjoy a certain independent existence. However, what is different from Europe's proposal is the introduction of bridging studies. Every agency that wants to join this "bridging study" alliance has to commit the clinical significance of racial difference but do not overact it.

Second, I have written at the beginning of this section on the two characteristics of bridging study developed in the context of the ICH. However, the CDE carefully avoids them in its proposal. For example, although it recognizes racial difference, it underlines local factors (for example, extrinsic factors) when encouraging mutual recognition of reviews among these countries. Furthermore, although working like a pure administrative recognition, this alliance emphasizes a division of labor based on the local conditions and specialties of each agency, which can be said to be racial concerns. In short, the CDE tries to build a network through bridging studies, but within this alliance there will be no need for bridging.

The ideal vision thus goes as follows: the Asian countries that have the potential to

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[19] In fact, the CDE proposed a change of name from the APEC Joint Research Project on Bridging Studies to the APEC Network on Pharmaceutical Regulatory Science in 2004.

offer high quality reviews on drug regulations will work together while maintaining the integrity of each individual agency as specialists in certain fields. Based on mutual recognitions, the harmonized regulations will lead the Asia Pacific region to an EU-like market large enough to bargain with global industries, allowing them to minimize the clinical trials done especially for this area. Also, the performance of these regulators empowers them to be qualified reviewers, granting the possibility of dialogue with the most advanced countries, Japan, United States and the EU. Where should Taiwan be? Obviously, it is supposed to be one of the leaders of this regional network, a position somewhat like it currently occupies in the APEC network.

Here we see the full display of this interesting vision. If Japan, as discussed in Chapter 6, tries to provide a new scientific standard to preserve its imagination of the nation-state, the science provided by the CDE equips Taiwan with a political vision of globalization; it is all about the politics of *fasheng*. The proposal by the CDE is one of multiple goals. At a practical level, it can be understood as an attempt to improve the bargaining power of the non-ICH states when asking for more clinical trials from global pharmaceutical industry. However, this multi-nation collaboration, again, confirms Taiwan's existence as a *de facto* state. We should read carefully that in this proposal the CDE not only asks for cooperation on the racially sensitive drugs issue related to the E5 guideline; instead, it is pursuing an "EU-like" organization where every member is equally treated as an independent entity. Finally, after entering into the stage of the ICH, the CDE does not want to be treated just as an "exemplar" of the E5 guideline; it wants to be an "equal partner" of the first-tier countries. For this purpose, it has to amplify its voice by gathering more countries that are in the same situation. It seems not to care much about whether other countries are able to spend such money; its robust economy pushes it to insist on the equality with the most advanced reviewers.

Bridging studies are a chance, probably the only chance that the CDE cannot miss. It is fully aware that Taiwan is standing at the frontier where the global ICH starts "formatting" the world. Within the tensions inside the ICH and between the ICH members and non-ICH regions, it has to grab this flexible position and do something before all is settled. The regional network based on bridging studies is what it can offer. In fact, the scene is much like a repeat of history, where Taiwan was both the frontier of the falling Qing Empire and that of the rising Japanese Empire. Reading the CDE's proposal, we seem to find a twenty-first century version of the announcement of the Taiwan Cultural Association in the 1920s, which claimed that Taiwan was a "central station of the world." Unlike Japan's attempts to preserve the distinctiveness of its race,

Taiwan focuses on its statehood, trying to preserve its integrity by projecting itself into a network. That is the ultimate goal of the CDE while it embraces globalization.

The Necessity of Biostatistics

The CDE's proposal to make an Asian regulatory platform is interesting, yet one thing needs to be clarified about the reality of clinical trials if we take the Asia-Pacific region as a whole. As pointed out by Suchart Chongprasert of the Thai FDA at the 2002 APEC meeting, "Participating more in all phases of global clinical drug development should minimize the need for bridging studies, but Asia must be more united." In other words, although the regulatory routines can be done through mutual recognition among individual agencies, clinical trials have to be done in a collaborative manner.

This is why biostatistics became the solution to the above problems. It meets the CDE's need for three reasons as they concern the functionality, availability and strategic meaning of Taiwan. In the rest of this section I will introduce them one by one. The first reason, as we have read previously, is simple that in Asia-Pacific region there exists a wide range of states that differ in terms of their development status and health needs. Thus, except for applying a unified, globally accepted standard to collect the data required, the product sponsors have to provide a cross-sectional framework to incorporate the data from the various sources. Obviously, biostatistics is designed for serving this need.

The second and third reasons why biostatistics was chosen are more complicated and require more pages to explain. The second reason concerns the reality of the ICH negotiation. As I have written in previous chapters, the ICH is a monopolist, hierarchal conference in the name of "globalization." The decisions and information goes only one direction from the ICH members to non-ICH regions in order to make sure they will not be changed. Thus, unlike the ICH member Japan that can employs new sources, such as genomics, to support its project, the CDE has to find its tools in the existing guidelines. Fortunately, biostatistics is one of them.

In fact, as the main place that addresses biostatistical concerns in clinical trials is the E9 guideline. Its importance, as I mentioned in Chapter 2 and 6, refers to its position in the development of modern clinical trials and the increasing need for a large scale trial that crosses the traditional boundaries of hospitals and centers, cities and regions, and even states and populations. A background about the discussions concerning the E9 guideline should be provided here. Entitled "Statistical Principles for Clinical Trials," this

guideline was drafted from a note for the guidance of "biostatistical methodology in clinical trials in applications for marketing authorisations for medicinal products" in 1994. Like the E5 guideline, the E9 guideline also has its MOSS origin (for details about this negotiation, see Chapter 4) and this is found in two documents entitled "guidelines on the statistical analysis of clinical studies" (drafted in March 1992) and "guideline for the format and content of the clinical and statistical sections of a new drug application" (drafted in July 1988). Even so, under the context of the disputes over racial differences, the E9 guideline can be understood as a new theoretical frame that makes international participation in clinical trials possible.

Let me introduce two issues about this guideline related to our concerns. The first is the concept of "multiple centers." Traditionally, this approach was desirable for it can make trials more efficient. But, considering the generalization of the results to Asia, this concept provides a base to incorporate Asian subjects that were originally excluded from global trials. The E9 guideline points out two reasons for doing multicenter trials:

> Firstly, a multicentre trial is an accepted way of evaluating a new medication more efficiently; ... Secondly, a trial may be designed as a multicentre (and multi-investigator) trial primarily to provide a better basis for the subsequent generalisation of its findings. This arises from the possibility of recruiting the subjects from a wider population and of administering the medication in a broader range of clinical settings, thus presenting an experimental situation that is more typical of future use (Section 3.2:12)

According to the above description, an internationally participating trial is workable. Although it would create possible biases due to the various medical settings of the sites for the clinical trials, the guideline allows this approach with restrictions. The only requirement for a multicenter trial is that it has to be conducted by a single protocol (section 3.2: 13 and glossary: 34).

Even so, it was able to announce the settlement only after the following two problems were solved. First, although racial difference is recognized and a method is provided for this, it still requires experience to know whether it should be considered a variable in the trial, or as an adjustable factor that belongs to the sites. For example; the intrinsic factors (for these factors, see fig. 4.3 and table 4.9) are relatively well defined and more likely to be variables in the study. Yet, the extrinsic factors, which are closely related to the environment where a trial is conducted, have yet to be identified for measurement. In other words, rooted both in the biological characters and social matrix, racial difference cannot be easily extracted from the "background noise" of the centers.

The second problem, which is related to the first, arises from a poor definition of

what is a center and how they should be considered a multicenter trial. As each investigator should be responsible for the subjects recruited, a "center" is naturally defined by either investigator or a medical institute, and based on this, the statistical protocol is designed for measuring the center effects. However, the situation is more complex in multicenter trials, where the subjects are recruited from several hospitals located in different cities and states. One investigator may recruit subjects from several hospitals; one investigator may represent a team of clinicians who all recruit subjects from their own clinics at several hospitals. Excluding individual factors (for example, investigators), there are also institutional factors, such as the medical environment and the local habits, which are ambiguous and easily mistaken with the "extrinsic factors" of racial difference. Among those that should be taken into account as characteristics inside of a center, but which variables are inconsistent from one center to another are problematic. Any attempt to tell apart the former from the latter will challenge the definition of what the basic unit of clinical trial is.

The second issue concerning the E9 guideline is the number of samples required for such a trial. It is especially a concern for the industry because of the high cost of adding subjects in clinical trials; they want to know the minimum number of subjects that is considered sufficient. According to the guideline, no additional subjects are required theoretically to perform a multicenter trial, as no site effects are noted. It only rules that the total number of the subjects recruited should be large enough to provide a reliable answer, thus it ought to be determined mainly by the primary objective of the trial (section 3.2: 16-18).[20] When the appropriate sum is assessed, several statistical items have to be specified in the protocol.[21]

Compared to regulations on the total number of subjects, few are written on how many subjects each center needs in a multicenter trial. It only addresses the following concerns from the quality perspective, namely, the need to show meaningful information and the effect due to the center chosen (section 3.2:13-14). For example, the sample size should large enough so that the differences between compared treatments are unbiased estimates. Further, a limited numbers of subjects per center will make it impracticable to include the center effects in the statistical design. Also advised is the need to avoid excessive variation in the numbers of subjects across the centers, since if it is found

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[20] It is noted that when the sample size is determined on other basis, the safety of drug, for example, it has to be made clear and justified. See Section 3.2:17.

[21] These concerns include a primary variable, the test statistic, the null hypothesis, the alternative hypothesis at the chosen dose, the type I and II errors, and the approach to dealing with treatment withdrawals and protocol violations. In addition, assumptions and factors that would affect the power of the statistical results have to be taken into account.

necessary to take this into account, there will be heterogeneity of the treatment effect from center to center. This heterogeneity, as it writes, "may be identified by graphical display of the results of individual centres or by analytical methods, such as a significance test of the treatment-by-centre interaction. ... In the presence of true heterogeneity of treatment effects, the interpretation of the main treatment effect is controversial."

For the people who only read this guideline, it may not be necessary anything immediately concerning international clinical trial. Hinted from chapter 6, we know this guideline is originally a product to "correct" the Japanese style of clinical trials. Even so, it intends to avoid over-interpretations that can be used like the controversial E5 guideline. As is written in its introduction, "the focus of this guidance is on statistical principles. It does not address the use of specific statistical procedures or methods. Specific procedural steps to ensure that principles are implemented properly are the responsibility of the sponsor." It leaves a gray area for interpretation and presents a good source for the CDE to formulate its multi-state project. As the guideline suggests: "such a trial would be a confirmatory trial in the later phases of drug development... It might sometimes be conducted in a number of different countries in order to facilitate generalisability" (section 3.2:12). As the MHLW's attempt to wrap up all factors related to the Japanese using a genomic categorization of race as part of its global drug development agenda, the CDE can also wrap up all the local factors into a functional category of "state" in order to "facilitate generalisability."

Although the E9 guideline provides a good source for the CDE, it still requires qualified scientists to work these interpretations out. This requirement leads to the third reason got the use by the CDE of biostatistics. It did so for strategic reasons. The credential to serve as a multicenter trial, as the guideline rules, is as follows: "the actual responsibility for all statistical work associated with clinical trials will lie with an appropriately qualified and experienced statistician" (section 1.2:2). In addition, the statistician should have "a combination of education/training and experience sufficient to implement the principles in this guidance and who is responsible for the statistical aspects of the trial" (glossary: 39). Even so, compared to discussions about other guidelines, Japan, as well as other ICH members, does not work much on this arena. According to my personal survey in the PubMed database about papers about the E5 and E9 guidelines, only handful papers are available between the foundation of the ICH and 2004, most of

which are not academic papers but reports and letters.[22]

The above background provided us with some sense of Taiwan's advantage, which I will introduce in the following. As a new and small branch, biostatistics requires two kinds of training and experience, statistics and clinical research. Thus, as there are very few jobs on offer, there were few statisticians capable of conducting clinical trials in East Asia when it encountered the ICH. In the case of Japan and Taiwan, some statisticians are teaching in Department of Statistics and some in the schools of public health, but there are few and only less experienced persons working for industry. However, they are different from other Asian states concerning the pool of global intelligence; both have recourses overseas, especially in the United States.

In Chapter 2 I have mentioned the urgent need for statisticians by both the regulators and the industry, which in fact facilitated the stay of Asian scientists. In the late 1970s or early 1980s, after receiving their bachelor degrees, which may have been in mathematics or statistics, these scientists left Asia, moving to the U.S. to earn their Ph.Ds. After that, they chose to stay in the United States, and many chose the regulatory agency and pharmaceutical industry. Of course, not many of them knew clearly what biostatistics was, as one Taiwan-born FDA official admitted when interviewed. He reminded me that there was an economic regression and it was hard for foreign Ph.D.s to find jobs. For him, after earning a doctoral degree in chemical engineering, it was suggested to him that he pursue a M.D. degree in order to find a better job. "Otherwise I had to leave this country." Another medical scientist joked: "the Americans assume that Asian are good at mathematics, thus we can do these repeating, trivial, and boring jobs that few Americans are willing to do." These PhDs thus started their new careers in the United States.

For Taiwan, it is a significant pool of intelligence. Shaw T. Chen has done a personal survey on the Asian-American staff at the FDA and other national health institutes while serving as the president of Parklawn Asian Pacific American Community, a social group for Asian scientists in the East coast. He told me that Korea, India and Taiwan are the three countries where most of these scientists come from. As table 7.2 shows, these so-called "overseas scholars" (*haiwai xueren*) filled in the fields of academy, industry, and government.[23] Some are senior professors at leading universities and some

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[22] Before the implementation of the E5 and E9 guidelines in 1998, only nine papers were published concerning the ICH. Even after 1998 there were only eight with the keywords of "E5" and "ICH," eight with "E9" and "ICH," and four with "ICH" and "bridging studies" shown in either the title or in the abstract.

[23] The names and affiliation of the statisticians mentioned are basically from the publications of the ICSA. Because not every ICSA member is from Taiwan, I only listed the people identifiable by the spelling of their names, their biographical profiles, and other related sources.

are in the FDA or the NIH. More importantly, there is an increasing population working for big pharmaceutical companies. They seemed to be clearly aware of their identities as immigrants and minorities working in a small field.

The International Chinese Statistical Association (ICSA) is the realization of this identity. It is a small yet firm society officially founded at the 1987 Joint Statistical Meetings in San Francisco. Although with the term "Chinese" in its name, this Taiwanese-dominated association is open to all individuals and organizations in all statistics-related areas in the world. As declared in its constitution, the ICSA is dedicated to educational, charitable and scientific purposes. In addition to general meetings and workshops, every year since it was founded, it has organized symposiums on applied statistics, which later developed into the section on biometrics.

Table 7.2 Taiwan-born Statisticians and Medical Experts Mentioned in *ICSA Bulletin* and other materials, 2002-03

	Name	Position and Affiliation
Government	Shiew-Mei Huang	Deputy Office Director for Science, Office of Clinical Pharmacology and Biopharmaceutics CDER, FDA
	Sue-Jane Wang	Division of Biometrics II, Office of Biostatistics, CDER, FDA
	Shaw T. Chen	Associate Director for Special Product Review-Botanical Drug Products, CDER, FDA
	Yi Tsong	Office of Biostatistics, CDER, FDA
	James HM Hung	Division of Biometrics I, Office of Biostatistics, CDER, FDA
	James J. Chen	Mathematical Statistician, Division of Biometry and Risk Assessment, National Center for Toxicological Research, FDA
	Darrel Liu	National Institute of Child Health and Development, NIH
	Kimi Feng-Ying C. Lin	National Institute of Child Health and Development, NIH
	Chuang C. Mike Chiueh	Senior Pharmacologist (Principal Investigator), Laboratory of Clinical Science, NIH
	L. J. Wei	Department of Biostatistics, Harvard University

Academy	Kung-Yee Liang	Professor and Graduate Program Director, Dept. of Biostatistics, Johns Hopkins University
	Shau-Ku Huang	Associate Professor, Department of Medicine Johns Hopkins Asthma and Allergy Center Unit
	Irving K. Hwang	Harvard Clinical Research Institute
	Leon Tseng	Medical College, University of Wisconsin
	Cathy Wu	Director of Bioinformatics, National Biomedical Research Foundation, Georgetown University Medical Center
	William Wei	School of Business and Management, Temple University
	Shu-Pang Huang	Department of Statistics, North Carolina State University
	Weichung J. Shih	University of Medicine and Dentistry of New Jersey
	Jun Shao	Statistics Department, University of Wisconsin
Industry	Shien-Chung Chow	President, U.S. Operation at StatPlus, Inc.
	Frank Shen	Director, Clinical Discovery Biostatistics and Data Management, Bristol-Myers Squibb Co.
	Gordon K.K. Lan	Senior Research Scientist, Central Research Division, Pfizer Inc.
	Kao-Tai Tsai	Aventis Pharmaceutical Inc.
	Shu-Yen Ho	Director, Respiratory Section, Biostatistics and Programming, RTP, GlaxoSmithKline
	Hung-Ir Li	Eli Lilly & Company
	Don Chen	SynAm
	Keith Chan	GloboMax
	C. Chun Chiueh	C.E.O, FarEast Algae
	Wenlii Lin	ADImmune

The ICSA became an important resource when Taiwan's environment improved. For these scientists, the reason for this return is far more complicated than just a "go-home" calling. A Taiwanese FDA official reasoned the calling it a "returning home" phenomenon "can give the wrong impression." Nonetheless, it goes something like this: "We all know that there is an invisible ceiling for Asians in the United States. I know that I would not be promoted to any higher position, for which I think I am more qualified than many persons born in America and I am still young and productive. Since the U.S. cannot give a chance, why don't we return to a place where people need me more?"

Now I have reviewed the reasons for the necessity for the CDE to use biostatistics. It is a tool for large-scale trials and the existing guideline that has space for interpretation. Moreover, Taiwan happens to have a pool of knowledge available to fill this need. In the following two sections I will describe how these statistical models were formed and through what channel they can be heard.

Making Bridges; Saving Bridging: The APEC Statistical Symposium

In a similar way that the Kitasato-Harvard Symposium functions as an informal channel between the MHLW and the FDA, the CDE establish a scientific symposium attached to the APEC meeting for its proposal (Symposium on Statistical Methodology for Evaluation of Bridging Evidence, hereafter the APEC statistical symposium). However, we should be clear that this symposium cannot be considered a "second channel" between the CDE and the FDA or a "direct channel" between the CDE and the ICH, because commonly neither the FDA or the ICH need to talk to Taiwan. The U.S.-Taiwan trade negotiations seldom touch issues on standards thus for the FDA there is no need to go through issues with the CDE. In addition, the ICH has claimed that it does not deal with issues with a single country outside of the ICH regions.

Even so, a symposium was achieved and I witnessed some exchanges of information and ideas among experts from the United States, Japan and Taiwan. In this section I will analyze why this channel could be established and how it works to save bridging studies. Let us discuss first the interactions between statisticians in Taiwan and Taiwanese statisticians in the United States, which, in my opinion, can explain the establishment of the APEC statistical symposium. In last section I have mentioned a phenomenon where many Taiwanese scientists chose to work in the United States after earning their degrees, but we cannot forget the people who decided to return after graduation, which started in the late 1970s. When qualified Ph.D.s had few positions being offered, some people chose to return to Taiwan and develop their career as educators and pioneers in new fields. This generation is crucial for two reasons. First, they have no difficulties with English and maintain more or less connections with the United States. Second, when biotechnology became a focus of Taiwan's science and technology policy in the 1980s, they became major experts and researchers. When the ICSA was founded, most of them joined and formed an international network of knowledge.

The contacts intensified. When Taiwan was able to afford travel grants for attending

international conferences and to organize conferences, these people reunited. Along with the preparation of the NHRI in the 1990s, the Biometrics Section of the ICSA was approved during the 1993 ICSA Board Meeting and formally established in January 1994.[24] With the increasing importance of biotechnology, the purpose of this section was to pursue the objectives of the ICSA with special interest in biostatistics, biopharmaceutical statistics and their applications. In addition to publishing newsletters, reporting meeting, announcements, activities and other events within the section, its U.S. members often tour to East Asia, helping local industries and regulatory agencies. These tours shows the hierarchical nature of this network where the information pours from the United State, the center, to peripheral Taiwan through personal connections. The "overseas scholars" are invited to Taiwan as keynote speakers or supervisors and the professors and researchers working in Taiwan go to the United States to update their knowledge. Anyway, this network is vitalized by these activities.

The ICSA served as a center making contacts between the experts from the United States and Taiwan. This is true not only of the early symposiums and conferences of the ICSA, which were held at the FDA and the NIH, since 2000 it has held some symposiums on biomedical technology, inviting researchers and professors to Taiwan.[25] Although Taiwan still has no strong environment for clinical trials and research, the network of biostatistics has equipped it with an excellent tool to develop its strategies. Immediately after the time when the APEC networking initiated, Taiwan was granted an opportunity to join the biostatistical discussions between Japan and United Stated and later formed its own forum.

The first meeting was the 2000 Kitasato-Harvard symposium. As introduced in the Chapter 6, it was an informal channel between the MHLW and the FDA, thus is not open to the public. However, because Robert O'Neil, the director of the Office of Biostatistics, FDA, could not present the statistical concerns on bridging study,[26] L.J. Wei, one of the founders of the ICSA and a member of the preparatory committee of the symposium, suggested Taiwan's Jen-pei Liu of National Cheng-Kung University as a replacement. As a veteran statistician with more than sixteen years experiences of clinical research and

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[24] Before then they organized panels included drug stability and management in the pharmaceutical industry as the first applied statistics symposium held in 1990 and collected papers on biostatistics in the first issue of the ICSA's journal *Statistica Sinica* in 1993.

[25] In fact, biostatistics becomes one of the most "productive" disciplines among pure science in Taiwan. As reported in the APEC statistical symposium, a professor of bio-statistics he knows well contributed numerous of SCI papers that count one seventh of what his university produced last year.

[26] As the FDA representative to the E5 EWG, O'Neil had been involved in the drafting of the E5 guideline. For his activities in the EWG and the ICH6, see Chapter 4 and 6.

development, Liu is proficiency in statistical computer software and has a well-established publication record in bioequivalence study. More importantly, however, he has closely followed the E5 guideline and been involved in CDE's statistical reviews since its establishment. Not only has he made some presentations on bridging studies, he was requested to write entries for the *Encyclopedia of Biopharmaceutical Statistics* (Marcel Dekker 2000; revised edition 2003), one of the first ever on this field. Liu became the only presenter not from either the United Sates or from Japan.

In addition to Liu's presenatation, Wei used his personal connections to reserve for Taiwan five seats at this symposium. An observation group led by CDE's Chern Herng-Der attended the symposium and knew the organizer of this symposium Takeuchi Masahiro, who became a regular presenter at the APEC statistical symposiums.[27] Through watching this channel worked, evryone learned. As for Professor Liu, he was impressed by the OPSR's explanation of its bridging policy, which had not been yet openly claimed: the same protocol, the same quality, more subjects recruited (Liu 2000). Also he found that statistics might be a point where Taiwan could cut through. He wrote: "all have discussed for what goals which bridging studies should be requested and the ways to evaluate their effects. However, there is no convincing study on the sample size and data assessment. The United States and Japan have large different ideas on bridging studies from Taiwan, showing a huge space for development. Besides of listing explicitly the bridging studies required, we have to speed up to complete the methods of data assessment."

Liu's idea gained realization in the series of the APEC statistical symposiums. Sponsored by the ICSA and the CDE, and hosted by the NHRI, the first symposium was held on May 23 2001 as an annex of the 2001 APEC meeting. Its goal was to solve the technical problems associated with the evaluation of bridging studies. It was a small, focused, workshop-like symposium, since they believed that statistics was the only science able to clarify all the disputes about the E5 guideline. Except for L. J. Wei as commentator and Professor Hsiung Chao, Director of the Division of biostatistics, NHRI, as host, six speakers were invited: James H.M. Hung at FDA, Professor W.J. Shih from University of Medicine and Dentistry, Sheng-Chung Chow from StatPlus Inc., Professor Masahiro Takeuchi at Kitasato University, Mey Wang at CDE, and Jen-pei Liu. Depite its size, the aim that this symposium wanted to achieve was large. It tried to be like the Kitasato-Harvard symposium. It not only provided an international forum in which

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[27] This group consists of Lee Pao-Jen of the DoH, Section Director Mao Pei-Ling from the CDE, two reviewers Wang Mey and Lee Jung-Jin on statistics and pharmaceutical kinetics.

regulators, scientists, and industry could meet, but the speakers were highly selected and the discussion was no doubt in the first rank of quality.[28]

In this symposium, two themes concerning bridging study, sample size and the evaluation of similarity, were discussed from Jen-pei Liu's E5 interpretation; based on these topics some strategies could be formed to keep as many clinical trials and as many local subjects for recipient states. From a statistical viewpoint, Liu thinks that a conclusion on whether a drug can bridge its trial data to a new region is made in the form of a two-step decision. The first step is to decide whether bridging studies are needed by evaluating the bridging evidence included in the Complete Clinical Data Package (CCDP), namely, bridging study justification. The second is to conduct proper bridging studies as defined by the ICH guideline providing clinical data on efficacy, safety, dosage and dose regimen in the new region, namely, studies that are statistically validated. Since the CDE has settled its interpretation on racial difference (see Chapter 5 and the part I of this chapter), they do not say much about bridging study justification. They focus more on what bridging should be done in order to provide necessary data for evaluating racial difference. Liu argues, because bridging studies are defined as "supplemental," it is almost impossible to reverse the result obtained from the original region; even if the result is completely opposite. Thus, two issues should be the concern of conducting bridging studies: optimal design and sample size for similarity with original regions, and the evaluation of similarity between the results of a bridging study in the new region and those of the trials in the original region.

In order to highlight their distinctions instead of similarities, in the rest of this section I will introduce three groups of arguments regarding the above concerns. The first is argued by Mey Wang of the CDE, who presents, more or less, the standpoint on current policy that features the minimum requirement of sample size for bridging studies. Since I have discussed intensively the CDE's E5 policy in previous chapters, here I shall focus only on her main point and the statistical methods offered to solve the problems created (Wang and Chern 2001).

Wang's argument has points concerning the nature of bridging study. First, as a study for evaluation but not an administrative requirement, the ethnic concerns should be defined completely either by "citizenship" or by "race." Thus, a full scale phase III study using local subjects is unnecessary and unscientific. Related to the first, the second point

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[28] Having experience of both the FDA and the MHLW, Professor Takeuchi Masahiro did not reserve his praise of the Taiwan's biostatistics. He said that Taiwan may not have an advanced pharmaceutical industry, yet its statistical research absolutely is one of the best in terms of its delicacy and well-thoughtness.

is related to the role that drug characteristics and indications play in the designing of bridging studies. From this practical perspective she proposes that the two fundamental elements can help regulators to decide the minimum sample size required for such studies.

Based on this idea, some statistical models are suggested to reduce the sample size. They do so by comparing to a full-reprititon of original trial. Using p-value distribution under alternative hypothesis, Wang proposed a rule with a flexible significance level to assess the required sample size needed to achieve a minimum tolerable power on the effect size of the observed original foreign pivotal. In this method a positive drug effect in Asian population is considered sufficient as sample size justification and its result is used as a factor to decide how many subjects should be used in bridging study only considering protection against type I error. After displaying several simulations, Wang claims that, in terms of significance level and power used in computing the required sample size, the one-sided alpha level could be relaxed with an upper bound of 10%. How many subjects can be eliminated from an equivalent full-scale repetition depends on the power that this trial is designed for. As for this value, it is deemed the sponsor's responsibility.

The second group of arguments contrasts the current policy by showing no convenient "bridges" that exist; even such a study requires an almost equally large recruitment to achieve meaningful results. Among the people who provided these arguments, Oliver Yoa-Pu Hu of the NDMC was the most notable. Hu argued that the Taiwanese population should be considered as sovereign in clinical trials, whose integrity has been preserved by the regulatory authority. In his opinion, Taiwan cannot be simply ignore or easily "downgrade" the requirements for local clinical trials. Using statistical model, these researchers tried to provide a working agendas for the CDE to practice this idea (Chow, Shao and Hu 2002). [29]

According to this study, they proposed a two-step strategy as to whether bridging studies are needed and they suggest the sample size that is required. The assumption behind this strategy is to treat the original region (e.g. the United States) and the new region (e.g., an Asian-Pacific state) equally, as they are the controlled group and a group to be tested in a clinical trial. If the given data can satisfy the reproducibility and sensitivity Index, an index concerning population differences and the probability of generalizability, there will be no need for bridging. Even so, it should be noted that the

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[29] Although Hu is not a statistician by training, he contributed to this paper the idea of applying reproducibility probability to bridging studies and a real case for analysis. For more statistical consideration on reproducibility probability, see Shao and Chow 2002.

probability of generalizability is a decreasing function of the sensitivity index and the value of sensitivity is usually unknown. This leaves regulators with room for adjustment based on policy needs, as they can set out how the requirement works: "An example of such a requirement is that the estimated reproducibility probability is higher than a percentage (which is *determined by a regulatory agent*, e.g., 90%) of the reproducibility probability for the original region. If the estimated reproducibility probability fails to meet regulatory requirement, then move to the next step to prepare for a bridging study"(emphasis mine).

If the given evidence cannot satisfy the reproducibility of sensitivity index, bridging studies are needed. The question then is what kind of bridging studies are required to meet the criteria of "similarity." Judged by a desired power for the bridging study[30] and sensitivity index selected by regulatory authority, the bridging studies have to be conducted with the necessary amount of samples. A series of numbers of sensitivity index, reproducibility probability, and the cases required can be obtained by a Bayesian approach. Using simulations, the authors showed the extremes for the sample size required. To just take one example, if the original trial is designed to compare a tested compound and a total of sixty patients (thirtty per treatment group) were recruited, formula, an acceptable bridng study may require up to sixty-eight local subject upon Hu's estimation. In short, in opposition to Wang's formula, Hu's proposal shows a high bar close to Japan's on bridging policy. In fact, Hu even suggests a small PK study, like the MHLW does, may be necessary to for provide information regarding the changes in population mean and standard deviation between regions.

The third group of arguments, led by Jen-pei Liu, shares Hu's argument by criticizing the current policy: "No quantitative method is applied to evaluate the risk of waiving bridging studies required to be conducted in Taiwan." Even so, he tries to work out a solution in the middle of the above two. He does so by mapping out the problems of bridging study consideration and sorting out the methodological repertory that the local agency can use to keep more studies and more local subjects.

The concept that Liu and his colleagues pick for arguing is "similarity." In brief, they argue that every bridging study has to be a meaningful study, namely, a study on the similarity of dose response, efficacy and safety between the new and original regions.[31] In the following I will summarize their points from three papers; two by Liu and Chow

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[30] This power is the reproducibility probability of this study, such as 60 or 70 pecent.

[31] Yet, please note that the use of the term "similarity" or "equivalence" does not mean that the authors misunderstand the ICH E5 guideline, in which it is stated that the safety and efficacy profile resulted from the trial in the new region has to be "*not substantially different* from that derived in the original region" (section 3.2.2, emphasis mine).

Hsien-Chung (Liu and Chow 2002) and one by Liu with Hueymin Hsueh and James J. Chen (Liu, Hsueh and Chen 2002).[32] Unlike Wang and Hu's emphases on the drug effect, basically Liu provides pure statistical thinking where he tries to set the criteria for a valid bridging study (non-inferiority, superiority, equivalence, for example).

About the necessity of bridging study, Liu and Chow do not differ much from Hu.[33] What Liu and Chow spend more effort on was a comparison of bridging studies and studies done in original region, arguing how many subjects were necessary to achieve a meaningful study. Although they do not give evaluation or comparison of the methods for estimating the number of subjects required,[34] some attempts are made by another paper (Liu, Hsueh and Chen 2002). In order to complicate the operation by adding the variables of dose response, safety and efficacy that Chow, Shao and Hu fail to do, this paper provides two strategies for estimating the necessary sample size. One is to consider an imaginative clinical trial consisting of the original trial and bridging study, assuming that it uses a target population stratified by ethnic factors (north American and Asian Pacific, for example). The other is to apply a hierarchical model, which considers together the treatment effect of the tested compound, the cases recruited in original regions, and the acceptance limit in a new region, to evaluate the sample size required for the analysis of bridging study.

Of course, the above strategies are far to complicated to discuss in detail. In his latest paper (Liu 2003), Liu simulates more strategies, looking at whether a balance can exist between the possible similarity and the objective of minimizing duplication of

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[32] In a presentation at the 2001 Kitasato-Harvard Symposium, for example, Liu reviewed methodological issues in the evaluation of bridging study, some of which were developed into a paper with Shein-Chung Chow titled "Bridging studies in clinical development." The most recent paper was published in Drug Information Journal in 2003.

[33] The only thing Liu and Chow add is a quantified approach to a five-point evaluating system for ethnic sensitivity developed from the U.S. Drug Master File. Based on these data, Liu and Chow claim an instrument consisting of three domains to determine the degree to which ethnic factors matter and thus the necessity of bridging studies can be determined. The first domain includes the critical properties of the compound. The second domain and third domain, each consists of the intrinsic and extrinsic factors discussed in the ICH E5 guideline. Within each domain, a scoring scheme can be designed to characterize the degree of the impact on efficacy, safety, dose, and dose regimen. For example, a possible scoring scheme could be a 5-point system such as 1 for no, 2 for mild, 3 for moderate, 4 for strong, and 5 for complete. An algorithm can then be developed to provide a summary index for an overall assessment of the impact on the efficacy, safety, dosage, and dose regimen of the study medicine. In practice, the database of these compounds can be divided into two data sets, namely, a training set and a validation set. Based on the summary indices computed from the medicine in the training set, a threshold can be determined to classify these medicines into two groups. One group consists of medicines that are insensitive to ethnic factors and hence do not require bridging studies. The other group contains medicines that are ethnic sensitive and hence require bridging studies.

[34] They are the two studies, or so-called between-study analysis, and different methods of population similarity, consistency among studies, hierarchical model and Bayesian approach are reviewed.

clinical data. It is not an easy task and the results do not please drug sponsors. Although in some approaches the sample size pursued is not as large as that calculated by Hu's formula, but they are still quite huge. After paralleling six strategies with four approaches to interpret similarity (for details, see 92S-94S), Liu addresses two conclusions. First, reproducing statistically significant results in this new region also requires a larger sample size than the original region. The reduction of sample size will inevitably sacrifice its validity. Second, using the empirical Bayesian approach for bridging studies, the result achieved is overwhelmingly dominated by the result from the origin region. It is supplemental to the result of the origin and can hardly reverse it. All these seem to display a standpoint that once the frame of bridging exists, a substantial amount of patients have to be recruited.

I have reviewed the three groups of arguments that try both to make communications with global industry on the one hand and to "save" more bridging studies for the state on the other. Although they have different standpoints, they share much in terms of intentions. Let me use two analogies, one secular and one philosophical, to summarize this strategy. To use the analogy of bargaining, the CDE's policy is the bottom price a seller offers to attract buyers to ask. Yet, contrast this policy with Hu's argument that insists on the highest price for the bargaining. Liu's summary, in this sense, presents a seemingly sympathetic third party voice (scientist) that offers an analytical overview of the problems and persuades buyers to compromise somehow with the sellers.

This intention will be clearer if we use Imre Lakatos' research program from the philosophy of science, my second analogy. Considering the CDE's bridging study policy as a research program, these arguments function like an "extended belt," which works to protect the core of the program, the theory and assumptions by which the formulas and interpretations are formed; in addition, it formulates possible ways along which the program can be stretched. The core of this research program, as I have described repeatedly, is to save the state from world.

To sum up. Using the guideline on multiple center studies, the CDE had survived its voicing by providing interpretations to save bridging studies. Not only making it a workable agenda, these statistical strategies provide a necessary repertory for other regulatory authorities to deal with foreign clinical data. Like the MHLW does with genomics, the CDE owns statistics that was contingently nurtured in the United States and which can serve both as a tool and a channel between Taiwan and the ICH experts. As we will see, its role became more crucial as global drug development rises. In the next section, I will describe how these statisticians responded to this project by making a

transition from bridging studies to the multi-state platform.

Seeing State in Bio-Globalization: Making Bridging Studies Global

In Chapter 6 I have discussed how global drug development became a strong paradigm backed up by Japan, and how it claims it will replace "imperfect" bridging studies soon. Thus, it is crucial that the CDE responded to this trend. The field I am looking at is the 2003 APEC statistical symposium held on November 15, but it should be located in a broader context. As a key technologie in clinical trials that earns increasing attention, biostatistics has become a much-discussed topic in Asia. And this trend made it much siutable for the MHRI and the CDE to host again this symposium.[35]

Of course, bridging studies were still its main mission, as written in its objective: "since statistical methodology plays an important role on the design and analysis for evaluation of the bridging evidence, we feel that necessity of holding the 2003 SSMEB (APEC statistical symposium) before the APEC meeting."

Table 7.3 Speakers and Paper Presented at the 2003 APEC Statistical Symposium.

Name	Position/Affiliation	Title of presentation
Chao A. Hsiung*	Director, division of biostatistics and bioinformatics, MHRI	Opening remarks
Oliver Yoa-Pu Hu	Department of Research and Development, National Defense Medical Center, Taiwan	Bridging study in Taiwan
Gordon Lan	Aventis pharmaceuticals, Inc., USA	The use of prior information in drug development
Weichung Shih	University of Medicine Dentistry of New Jersey, USA	Evaluation of clinical trials for cross-country drug development: three scenarios

[35] There was no statistical symposium in 2002. Since the APEC 2002 meeting was held in Tokyo, the MHLW hosted another side meeting under the series of the Drug Information Association Conference on Pharmaceutical evolution in Asia (DIA in Asia) at the University of Tokyo on September 18 and 19, dealing with the possibilities to achieve regional harmonization.

Chin-Fu Hsiao	NHRI, Taiwan	A group sequential approach to evaluation of bridging studies
Mey Wang	CDE, Taiwan	Clinical relevance of ethnic factor: a simulation study
Jen-pei Liu	Professor, National Cheng Kung University and NHRI, Taiwan	A comparison of statistical methods for evaluation bridging studies
Sue-Jane Wang**	FDA, USA	Cross trial statistical inference: bridging vs. non-inferiority scenarios
H. M. James Hung***	FDA, USA	Statistical issues with design and analysis of bridging clinical trials
Masahiro Takeuchi Fumiaki Takahashi	Kitasato University, Japan	Variance components in mixed effects models in bridging studies

* Originally Liang Kung-Yee, vice president of the MHRI and professor at Johns Hopkins University, was arranged as the speaker.

**because of a snowstorm on the East Coast, her presentation was postponed to November 17 and rearranged at the MHRI..

*** because of a snowstorm in the East Coast, his slides were read and commented on by Weichung Shih.

Source: *Proceedings of the 2003 Symposium on Statistical Methodology for Evaluation of Bridging Study.*

The speakers are almost the same as the first meeting except for some new faces, such as Sue-Jane Wang from the FDA and Chin-Fu Hsiao from the NHRI (table 7.3). When watching their interactions, I felt that these speakers had formed an intimate community through these activities, and the field, as Liu Jen-pei describes, is "well attended and discussion was intensive but constructive" (Liu 2004).

However, this intimate atmosphere does not mean that they agreed with each other. In Chapter 6 I have reviewed Takeuchi Masahiro's presentation, which addresses a genomic project on global drug development. Apparently, it is an agenda distinct from bridging studies. However, even researchers who insist on bridging studies have different strategies to respond to global drug development. In the following I will introduce three strategies presented at this symposium, which I will call "group sequential," "weighted/discounted," and "multi-center/hierarchical; these represent the cutting-edge ideas for this transition.

The first strategy was the group sequential method proposed by Hsiao Chin-Fu and his colleagues. It is not a new idea, as it had been previously applied to the assessment of grouped subject outcomes at periodic intervals. Using the approach of simultaneous drug development, namely, "synchronized" trials, the group sequential method facilitates a practical approach that allows a timely gap between the original trial and the new regional trial. This approach therefore has three key points when applied to a bridging study. First, the inclusion of patients from the new region as a part of the recruitment of the whole study for the submission to the original region; that is, the bridging study is considered a sub-study of a "whole" trial. Second, it allows the new region to join the whole trial as a group, thus the bridging study should be a group sequence that enrolls patients from the new region subsequently to the original region. Third, because the new and original regions are treated equally as group sequences, the bridging study should be conducted in the same way as the study in the original region using the same protocol except for the order of region and the order of patients' enrollment. The data generated is thus internally valid.

The sequential method is conducted by following steps. At beginning, the statistical method should be fully specified in advance of the availability of information on treatment outcomes and subject treatment assignments. Because the primary objective of this trial is for submission to the original region, most of the type I error rate measurement should be spent on the interim analysis based on the results from the original region. The interim analysis is performed when the recruitment of patients in the original region is completed. After the interim analysis, the recruitment of the patients in the new region, or the so-called "bridging study," starts. As a sub-study under the group sequential scheme, the study in the new region should be pre-specified to have the same protocol, with the same inclusion/exclusion criteria, the same study design, the same controls, the same doses, the same method of evaluation and the same efficacy/safety endpoints. Only after the second recruitment is completed can the final analysis be performed with the newly added data. If the interim analysis and the final one show similar results, that is, a similar significance level to meet the requirement of crossing the boundary values, then the results of the new region can be declared to have similarity to the original region.

The main concern about this approach is the sample size. In order to cross the boundary to terminate the recruitment of cases, a substantial number of samples are required for both the original region as well as the new one. This approach adjusts the sample size required by comparing the original trial (interim analysis) and the final one

(complete analysis), making the sample size a dynamic sum of cases in the original and the new region. In other words, though "additional", the study conducted in the new region, that is, the bridging study, in fact plays a more crucial role than before. This is because it can be equally as important as the study in the original region. On the other hand, although this approach "downgrades" the influences of the study in the original region, this approach leaves two manually adjustable preset factors, namely, the total information of the original region and the conditional power adjustment factor. These determine the necessary sample size. In short, the sample size in the new region is no longer a decision made by one party. It is affected by, first, the conditional power given to the interim results and this is related to the treatment effect of the tested product. Second, the required boundary for the final analysis can also affect the sample size required. Both are negotiable.

The second strategy can be called "the weighted/discounted approach." It was proposed by Gordon Lan and is derived from the traditional Z-test method. It is argued that while conducting a clinical trial, which is supposedly a study in the new region or the "bridging study," the prior information obtained from the study in the original region will hugely affect the partition of sample space of the new study. For example, it would increase the type I error from the standard 0.025 to 0.30. This effect will be the same, in this case, when using different approaches like traditional hypothesis testing or Bayesian argument. Approaches are thus applied to correct the drift of the value of Z or the type I error in order to maintain its power.

Like Hsiao's strategy, Lan assumes a trial that consists of the new study (bridging study) and a prior study, making them two "stages" in a global drug development. Thus, the Z value of this trial can be basically presented as the sum of the Z values of the two independent studies. Because the conditions of the trials in the original and new regions are different, their Z values have to be re-adjusted or "weighted" in order to achieve a satisfactory result. In contrast, a discounted factor is taken into account when considering the sample size required. Unlike the strategy one introduced previously, the discounted factor is defined as the degree by which the amount of samples used in the replication of a full trial can be deducted. Apparently, the more samples that are deducted, the more the type I error increases.

However, it is not a zero-sum game, because what is lost in sample size may be recovered in the weight factor. Thus, the choice of weighted and discounted factors depends on "the degree of belief in variability of treatment effects between regions." Related to this are many non-statistical issues such as product characteristics, disease area

and status, PD/PK and dose response data, therapeutic dose and effects, quality and strength of evidence from the body of knowledge in the clinical data package, pharmacological effects in a foreign region with a comparable population to the new region, experience with other members of the same drug class in the new region, intrinsic factors and extrinsic factors of the population (see table 4.7) that the drug hope to marketed in.

Many may suggest that this approach does not solve the question. However, I would say that under the new situation of global drug development, the novelty of this approach resides in the attempt to reduce the scientific question back to that "non-scientific" one. Putting aside the "pure" statistical concerns, this approach implies that the solution for the bridging studies under the scheme of global drug development can be found only in the "non-statistical" issues, which are negotiable. It is a reality that Taiwan cannot provide as many cases as before for global drug development, thus, it is necessary to make a return to non-regulation so that new rules can start to be determined.

As in a statistical framework, Lan's idea of "weighted/discounted" factors is much clearer in Shih Wei-Chung's named "multi-center/ hierarchical," which marks the third strategy I want to introduce in this section. It is an approach that confirms the need for global drug development, and has possible advantages for Asian-Pacific countries. Shih pointed out that, under the frame of bridging studies, no real equality can be achieved, because in reality every country wants to have as many samples as possible in each trial. Thus, no matter how close the bridging studies are to the original study, if the bridging study is done retrospectively, they just cannot be considered equal. Shih suggests: "Now is the time for Asia-Pacific countries to persuade the international companies to accept this strategy (global drug development) and this is what the revised E5 guideline should also address." According to Shih, global drug development is another name for multi-national or multi-center trials. Thus, his method is to construct a multi-national trial in which each participating country is considered to be a part of a "bridging study" while the drug sponsor, viewing the whole, sees it as a global trial.

The problem with this approach will be to decide what a fair share for every nation is. Shih persuades us that it is no more problematic to define a nation than to define a center; however, the definition of a nation seems to be the key concept that needs more explanation. Except for considering a nation as a collection of centers or an administrative body including sites of clinical trials, Shih insists that a nation preserves a necessary specific effect that has to be taken into consideration. On the other side, what we take for granted as a "nation" is also problematic. Taking the United States as an

example, he claims that in fact every state has its own policy toward new drugs; no drug so far is allowed to be marketed through out the whole country. Thus, a multi-state policy should be applied to the U.S. so that its heterogeneous nature can be protected. To address the above concerns, Shih proposed a hierarchical or multiple-level statistical frame, inserting more levels, such as nation/state and region, between the clinical trial centers and the world.

Under this frame, a bridging-study, like a global drug trial, is conducted though an application of the hierarchical Bayesian model. Clinical trials being performed in the centers of a nation/state (supposedly "bridging studies") are compared with what has already been completed in other places (the prior information). Like other approaches, there are factors that determine the posterior distribution of study in the new region, such as the relevance of the observed data, the prior information and the induced priors that gives weight to the prior information. Basically it is safe to consider this model a more complicated structured system in which data obtained from the different regions (or centers/states/nations) are given different weights when incorporating the new data. It is clear that the sample size required in new region has a rough positive correlation with the centers involved before as well as the variability of the observed data, but how to obtain this size is a complex and hard to evaluate.

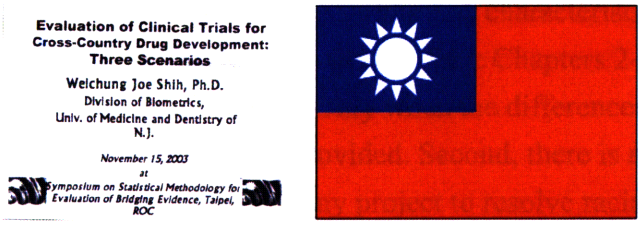
We do not yet know the importance of the nation or state. So far this experimental approach shows only a weighed evaluation system, though complicated, such that a bridging study can be done as a multi-center trial. For this, at very end of his presentation, Shih proposed a nation/center reaction (Rx) effect, which is more related to the local data observed than to the "overall" reaction. Because the nation specific effect is a total evaluation considering all factors that can produce local differences, it can thus only be pursued by empirical studies. Up to this point, it was not clear what Shih wants to save under his scheme of global drug development. He tries to preserve the nation, the basic unit for doing bridging studies.

Shih does so by pointing out two issues concerning the characteristics of a nation/state. First, he wants to preserve the state as a country. For example, in the case of the United States, Shih challenges its homogeneity on drug approval. According to him, only a few states would allow FDA approved drugs to be marketed immediately. In this sense, the U.S. has already been practicing multi-national trials and fails to make its "centralized" approval the final one. Thus, Shih believes that his approach is correct in that "combines" data from different regions, improving each nation/state's ability to estimate while preserving their uniqueness. Second and more importantly, Shih wants to save nations whose markets are too small to bargain for a trial that recruits a fair number

of patients from their citizens. Although bridging studies promises the nation a temporary "protection" for its citizens' bodies and health, it will soon be replaced by global drug development, in which only big nations/markets are selected for attention. Thus, he insists national reaction plays a more important role in his approach. He does not hide its administrative goal: since "[t]here won't be a 'global registration'; hence, nation/region-specific Rx effects (assuming these to be properly estimated) are more relevant than the 'overall' Rx effect."

I have introduced these strategies and despite the differences in methodologies and abstractions, their goals are consistent, namely, to restore as many as possible clinical trials, to extend the life of bridging studies and to preserve Taiwan's presence in global drug development. These strategies convincingly show the ability of bridging studies to extend its use from bilateral relationships to a global network. They are scientific and can be used anywhere that appreciates bridging studies. Above all, they match well the CDE's vision of "regionalizing" bridging studies. Unlike the MHLW's worldview that consists of distinct genomic populations, the CDE's one is a multi-layered network; on each level every state is linked to others by bridging. They bridge clinical data, bridging reviews, and they bridge markets and vision, all based on the real and vitally alive statehood.

Fig. 7.1. Title slide of Shih's presentation (left), on Which Two ROC National Flags (larger image is shown on the right) Are at Lower Corners.



Source: Shih's slide presentation in the 2003 APEC Statistical Symposium.

Only with this understanding can we see the Taiwan state in the globalization. I remember one scene when Shih Wei-Chung started his slide show, in which he displays two national flags of the ROC (Taiwan) waving at the corners (fig. 7.1), everyone in the audience laughed except foreigners. They did not do this because of its unrelatedness or because it was out of context. They laughed because they know the implicit meaning of this symposium and Shih did not hide this true intention, he made his homeland visible.

In fact, one more semiotic footnote can be added about this flag. As an emblem of a decaying authoritarian regime, the Republic of China (ROC), only a few people sincerely relate to this "blue sky-white sun-red ground" totem as Taiwan's national flag. Nonetheless, in the global context the message Shih hopes to deliver is well taken. No matter how many names Taiwan is forced to call itself;[36] its robust statehood should be preserved. Here an over-simplified Shakespearean answer seems not to be proper to this complicated problem that if Taiwan had any other name than the ROC, it would not be living as it is now. Instead, I want to call attention to the fact that in Taiwan's case, the quarrels over its names usually cover up the real needs of the people living on this island. The name of the Taiwan state may not be important, but the Taiwanese know very well what a proper identification of its *de facto* status can bring to them in terms of globalization. To be seen is just the first step in their efforts.

CONCLUDING REMARKS: LIMITED SCIENCE, STRETCHED CONNECTIONS

Echoing some general arguments in the fields of STS and cultural studies, three conclusions can be drawn from this chapter, and I will introduce them one by one. Concerning the difference between the CDE and the MHLW, the first conclusion that can be easily ascertained from the philosophy of science is that bridging studies and global drug development can be considered two research programs within the same paradigm of drug regulation.

From this viewpoint, both projects share similarities characteristic of Thomas Kuhn's classical definition of normal science (Kuhn 1962: Chapters 2-4). First of all, they have a worldview called "racial difference." Only when the differences are real for these scholars can methods and solutions can be provided. Second, there is a "puzzle" or guiding problem called "bridging studies." Any project to resolve racial differences has to refer to either the E5 or E9 guideline. Through the rules and tools of statistics, it is possible to produce paradigmatic knowledge.

Even under their shared paradigm, bridging studies and global drug development are research programs that compete with each other (Lakatos 1970). Chapter 6 and this chapter have described the theoretical interactions between them. While Japan presumes the essential uniqueness of the Japanese race as its core, Taiwan, as I have described,

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[36] According to an unofficial sourse, the Taiwanese government has used at least twenty-nine names for its country in different international organizations and countries across the world.

made its basis the existence of the state. Thus, the roles bridging studies play in each program are different. In Taiwan's program, bridging is a "positive heuristic," as it directs scientists toward fruitful avenues of enquiry. However, when Japan's program started using global drug development as a positive heuristic, bridging studies became a "negative heuristic" that would delay the move toward the avenues of simultaneous global clinical trials. Even so, both retained the term "bridging study" in their programs because it had been defined in the E5 guideline.

This thesis has no intention to identifying which program will finally win, since no result can be recognized until after the competition is complete, and paradigmatic shifts should be invisible. Even so, with regard to the world of the ICH that we are studying, the solution can be reached through a revision of the ICH guidelines and standards. After all, a theoretical competition between bridging studies and global drug development might not happen in the real world. Backed up by its huge market, it is doubtless that Japan's program will be easier to write into the guideline if the FDA does not intervene. Nonetheless, Taiwan is different. No matter how excellent a program it constructs, it has no ability to modify guidelines; it is always acted upon. Therefore, in reality, the two research programs move in parallel; sometimes they might meet, but most of the time each follows its own track. While Japan is pressured by the bridging approach in negotiations with the FDA, Taiwan worries about the disappearance of the state's integrity. Using the existing tools, Taiwan has to find a solution before the problem is settled.

From this observation we depart from a non-historical, non-anthropological comparison of two schools of thought and enter into an overall appreciation of voice and voicing in the world of proprietary drugs via science and society. Obviously, Japan and Taiwan have different concerns and paths for developing dialogues and conversations with the global. I have discussed Japan's part in Chapters 4 and 6, and I explained the making of Taiwan's voice in Chapter 5. Now I think this interdisciplinary, international investigation can be completed with a discussion of voicing.

Let me start again with subaltern studies. In Chapter 5 I discussed some issues concerning the representation of voices raised by Ranajit Guha. In addition, my own unexpected involvement in the writing project of Taiwan's voicing strategy represents a unique anthropological experience in which the ethnographer's voice and the voices of the observed have synthesized somehow and are presented in a unique form—this dissertation—in order to evoke circulations of ethnographic actions through reading. In view of the scientific material used in this chapter, most of which is not intended to be

read in this field, my second conclusion is a meta-analytical reflection of this chapter that brings in some arguments from Gayatri Chakreavorty Spivak's reading on early subaltern studies (Spivak 1988).

First of all, although Guha claims the voice of the subaltern is an independent and autonomous one, Spivak reveals its use in tracking the "successful cognitive failures" of previous historiographies of the history of colonial India (6-7). In the process, however, early subaltern studies failed to engage the discursive context in which the heterogeneous nature of Indian peasants' voices had to disappear into a single voice, articulated as if from a single agency, in order to forge an effective practice. Agreeing with this observation but not pursuing it further in the deconstructionist direction, I would like to turn this slipperiness of discourse into an ethnographic question of voicing. Instead of asking whether a "Taiwan consciousness" exists ontologically, this chapter tries to explore how voicing is possible through the logical (science), discursive (ICH and capitalism in a restricted sense), and social (global politics) mechanisms of networking that form our conception of the world of proprietary drugs. Thus while Spivak gives a theoretical answer about subaltern consciousness as a discursive existence strategically adhering to the essentialist notion of consciousness (15), I seek this existence by an analytical evaluation of the dynamic relationship of Taiwan's voices with the global in all its limitations and possibilities. The generalization of this thesis is thus not a theory of consciousness as subaltern studies is said to offer; what I want to contribute is an ethnographic understanding of voicing, the way to appreciate such voice and its dynamics in the modern world.

At the beginning of this chapter I evaluated Taiwan's *fasheng* status; I will do the same here from three perspectives. The first is about the right to revise ICH guidelines. I discussed in Chapter 6 how Japan's resistance to bridging studies is based on its unilateral interpretation of the E5 guideline. However, this situation cannot occur with Taiwan. Every attempt to argue for the similarity between clinical trials done in secondary and primary regions presumes that a meaningful bridging study should in some way be an exploratory trial. However, from global industry's viewpoint, bridging studies can only be confirmatory trials "intended to provide firm evidence in support of claims" (E9 guideline: 4). Second, considering the discursive field of the ICH, Japan would not readily accept bridging studies, since it hopes to have enough Japanese subjects in every trial. Even the United States, which respects the spirit of science, would show a negative attitude to this approach, because it is an "Asian problem." Indeed, in the near future, the FDA will still be the primary reviewer, making bridging studies unnecessary. Once this happens, it is very likely that the FDA will insist on full clinical trials, or at least

substantial trials on local subjects, for all applications. As Shih Wei-Chung's presentation points out, an "FDA" idea that suggests a large amount of local subjects for either bridging studies or global trials is not practical for small countries like Taiwan. The third and last aspect concerns responses from other Asian countries. Although the CDE's proposal of "regionalizing bridging"seems convincing, Singapore insists on its project, and the ASEAN countries remain cold toward Taiwan. One principle investigator shared with me somewhat cynical comment on bridging studies: "It is a bad game created by Japan. And now only its former colonies [Taiwan and Korea] follow. You ask whether it is useful for other Asian countries, and my answer will be a simple NO."

It seems likely that the CDE's attempt will not go well. However, echoing Spivak's reading of subaltern studies, I do not want to be pessimistic. I have two points to make here. First, as a voice that can be continuously heard, the CDE's bridging study proposal has earned responses in the discussions among ICH regions. As Spivak would say, it is a typical use of subaltern voices to displace the discursive field (1988: 9). In fact, she gives a good example of this effect by analyzing the use of rumor in subaltern studies (21-26). As both a verbal expression and a communicative tool among Indian peasants, rumors worked by accumulating social weight so that the colonizers start to report them and put them in written form for discussion. We see the same effect in the bridging study project. Although it is not formal in the sense that it cannot be recorded or accepted as part of the discursive achievements of the ICH and its voicing channel is scattered, its fragments have infiltrated discourses within the ICH, especially in the context of the E5 guideline and the relations between Japan and the other members.

Second, Taiwan's voicing ability might not be improving, as we read, but it is not declining either. Pointing out the heterogeneity of subalterns, Spivak reminds scholars that women, who have presented a vague, faceless, and fragmented figure in previous studies, should be considered in this discipline as a starting point for demystifying the discourse of subaltern studies, in which "the continuity of community or history is produced on the dissimulation of her discontinuity, on the repeated emptying of her meaning as instrument" (1988: 31). Reading her point into my ethnography, I will say that the CDE's continuous voicing constitutes an existence that is persistently challenging the superficial harmony created by the ICH and by global political organizations such as the WHO.[37]

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[37] I thank Professor Joe Dumit for providing this point. In fact, in his unpusblished work "Symptomic, Ill and Structually Damned" (1998), Dumit points out the discursive skills (such as the use of new media and scientific language) used by emerging social movements around illnesses that are ignored by current medical practice. As a "non-state" in global politics, Taiwan's voicing stragey shares this approach. More

Even so, the problem of voicing agency will remain, which leads to the third and last conclusion of this chapter. In this chapter I treat the CDE and Taiwan exchangeably, as if they refer to a single entity that makes a single voice. Yes, it is true that if possible the CDE would like to use the name "Taiwan," but neither the CDE nor the Taiwanese state is the agency that produces this voice in the context of the ICH. In this ethnography Taiwan or the CDE is a writerly agency that cannot exist without others, such as the FDA, the MHLW, and many of the individuals mentioned in this thesis. Echoing Stephen Tyler's notion of postmodern ethnography (1986), what we can conceive are voices and voices alone. This distinction is crucial, because once Taiwan is recognized as a state or is invited to attend the ICH as such, this *fasheng* may disappear or change. This chapter precisely shows this distinction by analyzing the CDE's strategies for bridging studies. It is Taiwan's "absence" that stimulates the actions of *fasheng*. Instead of making a voice for this state alone, these *fasheng* strategies always relate Taiwan to other counties, and only voices that present it this way can be heard by the global. If subaltern studies wanted to seek missing voices in the making of India's colonial past, this thesis hopes to achieve an ethnographic understanding of Taiwan's voice and *fasheng* through an appreciation of the history of brding studies, the ICH, Taiwan, East Asia, and the world of pharmaceuticals.

Here let me follow up on this voice. The 2004 APEC meeting was held in Seoul in November, and discussions on bridging occupied one section. What was new at this meeting was that APEC started inviting the ASEAN countries, looking for the possibility to make connections. For example, the CDE hosted an informal banquet for all the guests during the meeting. "Korea missed this chance to make friends and connections, but we will never let this happens to us," Chern Herng-Der said to me. Meanwhile, to many people's surprise, the CDE tried to sell the "Taiwan experience" to Japan and Korea. In a recent conversation, Chern confirmed this fact. "In fact, Japan asked us for help," he said. He recalled that during an earlier visit to Tokyo, Naito Chikayuki, now the senior consultant at the Pharmaceuticals and Medical Devices Evaluation Center (originally OPSR), had asked Chern to provide the CDE's bridging evaluation review documents, for he wanted to compare how close the Japanese were to other Asian people. In addition, the CDE director Chu Mong-Ling told me that in a regulatory affairs meeting held in Tokyo,

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discussions concerning Taiwan's voicing status in reference to Victor Turner's concept of liminality can be found in Chapter 8, part III.

the Korean FDA showed interest in Marie Lin's work on racial differences in Asia and asked Chu to send a copy (for more about this paper, see part II of Chapter 5). The CDE seems eager to voice, even to those who are unlikely to accept its agenda. Chern concluded enthusiastically, "If we can have Japan and Korea on our side, the network is large enough to bargain with the United States and Europe."

While making new connections, the CDE also attempts to strengthen existing networks. I heard from the GCG meeting in 2003 that APEC might be suggested as a regular member of the ICH-GCG. Ideally, if Taiwan can remain active and creative in APEC, it might be possible for it to attend the ICH through APEC.[38] Nonetheless, there are impediments to reaching these goals. More regional networks are formed, but Taiwan is excluded, which Chern, in a recent article (2005), called a "crisis." For example, ASEAN has decided to form a single drug market by 2005. Singapore and Thailand are proceeding with a free trade treaty with the United States in which pharmaceuticals are an important item for discussion. The PRC, meanwhile, is organizing a six-state network for harmonizing regulations on herbal medicines. None of these networks include Taiwan. If we read Chern's statement carefully, we can see that the crisis is not about Taiwan's being marginalized or ignored by the world, since it already is. The anxiety, instead, is whether its voice will be covered by these networks.

Even though no body knows the future of Taiwan as well as the CDE, it has no choice but to keep moving forward. Chern's remark nicely shows this desire: "It is a long journey for Taiwan and for me: the SRB [Strategic Review Board] meeting in 1997, the foundation of the CDE in 1998, its proposal for the APEC network on bridging studies in 1999, the ICH presentation in 2000, the interactions at ICH6 and ICH-GCG in 2003, and for now the participation of the LSIF [Life Science Innovation Forum]. Despite various pressures brought by the political reality, we walk high and shine. What we witness just reflects two proverbs: 'step by step with care' [*jibo ji kain*] and 'trails must be left after we walk' [*fan zoguo bi liuxia henji*]. I shall share with you these two proverbs for our future journey" (Chern 2005).

But I should save this for another ethnography.

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[38] In fact, the situation has become more complicated, since a newly founded network, LSIF, was later assigned to be the APEC representative for the ICH-GCG. Sponsored by PhRMA and dominated by the United States and Thailand, this forum was proposed in 2003 and attempted to replace the original APEC network. So far it is too early to estimate how this will affect the APEC network, and Taiwan has chosen to join this forum; however, whether Taiwan can keep active and gain delegacy at the GCG is still a question.

PART FOUR
The Interactive Transformation of State and Race: Taiwan and Japan

One day in late March 2005, when I was in the throes of the present work, I received a telephone call from Chern Herng-Der, the deputy director of Taiwan's Center for Drug Evaluation. After a bit of chitchat, he asked me whether I had heard about Lee Teng-Hui's new formulation, "new era Taiwanese" (*xin shidai Taiwanren*).

I hadn't. Of course, I was familiar the notion of "new Taiwanese" (*xin Taiwanren*), a phrase first used in the 1998 Taipei mayoral election 1998 by Lee, then the chairman of the KMT, to recommended its candidate Ma Ying-jeou, a so-called mainlander. Many saw the phrase "new Taiwanese" as an attempt to incorporate those who had immigrated to Taiwan fairly recently into the category of Taiwanese, previously used only to refer to the descendants of Han Chinese who had moved to Taiwan from China hundreds of years ago. Some political critics even believed that this shrewd linguistic innovation had been the decisive factor in Ma's eventual victory. Two presidential elections later, when the KMT eventually lost what had been a political monopoly over the island's government, "new Taiwanese" felt a bit shoddy. Lee was ignominiously dropped from the KMT roster by his successor and the racial concept "pure Chinese" replaced "new Taiwanese" as the ideology of the so-called nationalists, that is, the KMT and its returning allies People First Party and Chinese New Party.

Even so, I had no clue about what Chern would tell me. "That is because you are interested in racial differences and our attitude toward it," he replied. He told me that earlier that month he had been invited to attend the honorary degree ceremony of Taiwan Theological College and Seminary, where Lee Teng-Hui had received a doctor of divinity degree for his meritorious contributions toward Taiwan's democratization. Invited to say a few words, Lee delivered his recent thoughts on deliberate distortion of his phrase "new Taiwanese" and proposed a new locution. "For me, Lee said exactly what Taiwanese means, I mean, in terms of the ICH and of the E5 guideline." And Chern offered me some advice: "You should read his speech and write about it in your thesis."

Two weeks after the phone call I got a transcript of the speech from Chern. Published along with articles commenting the uproar surrounding the current KMT chairman's trip to the People's Republic of China (PRC), it is a beautifully written speech, clear and to the point. Abandoning all recourse to race, Lee clearly defined "new era Taiwanese" as those whose identity is based on a consciousness of democratic community. The obvious model is America: "We no longer need Taiwanese nationalism, not to mention fictitious Chinese nationalism. We can only imagine this identity in an organic society like America's, which is free, pluralistic, and open. [. . .] Our unity is based on a common belief in democracy, not on blood ties" (Lee 2005:61–62). Based neither on an essentialist notion of "Taiwanese race" nor on narrow patriotism, the idea of

a "new era Taiwanese" grew out of the awakening of Taiwan's subjectivity. I could almost hear the calls for a spiritual revolution.

I was familiar with the CDE's state-centric strategy and its political vision, which are consistent with my understanding of Lee's invention of this identity. But I fear that this discourse will not be able to escape misinterpretations emerging from racial politics. All nationalisms must be built around spiritual cores, but I wonder whether Lee can successfully build on the idea of new era Taiwanese. To be precise, I wonder whether people might worry that once Taiwan is independent it might rise up the tension in this area and give Japan an excuse to return to militant nationalism that proved so disastrous for it in the 1940s.

Taiwanese people, particularly those with anti-Japanese prejudices, often bemoan Lee's ambiguous connections with Japan. Lee was born and educated under Japanese colonialism. An outspoken critic of the discrimination that was rampant during this imperialist period, Lee has also pointed out important contributions the colonial government made to Taiwan. Moreover, he adores traditional Japanese culture and remains close to old Japanese friends, most of whom are right-wingers. These attributes and others have made Lee a controversial figure in both Taiwan and Japan. In Taiwan he is the leader who brought true democracy to Taiwan, as much as he is a champion of Taiwanese independence. In Japan he is praised as a foreigner who truly understands the Japanese spirit.

To understand Lee's relationship with Japanese culture, let us consider his thinking about the traditional thinking and behavior of the Japanese warrior, known as *bushido*. In his book *Bushido kaidai* [interpreting bushido: the meaning of noblesse oblige] (Lee 2003), Lee Teng-Hui recalled what he had learned from this tradition and expressed the hope that contemporary Japanese and Taiwanese might embrace once again the values they had forgotten. In his history of the idea of *bushido,* Lee explained that the author of an important book on the subject, Nitobe Inazo (1862–1933), a true "international man," had chosen to write his analysis of *bushido* in English. Nitobe had wanted to introduce what he considered the essence of Japanese culture to the foreign world at a time when Japan's identity was threatened by its growing involvement in the international community. Lee, too, is keenly alert to the significance of globalization. In an interview that appeared in the *Taipei Times* on January 25 2005, Lee said, "the stronger Japan becomes, the more helpful it is to regional stability in Asia. [. . .] Only when Japan normalizes as a country is it helpful for Taiwan." When Lee's book was originally published in Japanese in 2003, it soon became a bestseller and has since been reprinted

eight times. In a comment left on the Japanese website for Amazon.com, a reader even expressed the wish that Lee might become Japan's prime minister.

The Taiwanese edition aroused responses far from praises. Having claimed in the book that *bushido* could awaken Taiwan's "latent spirit," enabling it to cope with the difficulties it faced in global politics (*Xinlang Wang* [Sina News], January 5 2004), Lee turned his cultural argument into a political one only a month before the presidential election of 2004. He affirmed that Japan should stand firmly against the PRC; he supported Prime Minister Koizumi's decision to honor Japanese war dead by worshipping at the Yasukuni Shrine. Similarly, Lee recommended that Taiwan hold a plebiscite to determine its future and he encouraged the Taiwanese people to join a political demonstration to be held on February 28 to protest China's recent anti-Taiwanese legislation. "Don't be afraid of the PRC," he commented: "Taiwan, Japan, and the United States are the three powers in East Asia. If we are united, is there anyone we must fear?" (*Ziyu Shibao* [Liberty Times], February 18 2004).

Like his formulation "new Taiwanese," Lee's book failed to achieve what he had hoped, largely as a result of anti-Japanese and anti-Chinese emotions. A book that proposes to solve Taiwan's problems by adopting a Japanese spirit is not likely to make many converts in Taiwan, where opposing political parties occupy increasingly polarized positions vis-à-vis Japan. For example, in 2005 the new chairman of Taiwan's Solidarity Union Party, an organization for which Lee Teng-Hui's opinions are gospel, visited the Yasukuni Shrine to honor the twenty-eight thousand Taiwanese soldiers who died while fighting in the Japanese army, opening a new round of acrimonious political arguments.

I am not sure how to evaluate the concept of "new era Taiwanese," but I do know that in the current context of global politics, where the words "Japanese nationalism" and "Taiwanese independence" are taboo, the destinies of Taiwan and Japan are inextricably linked. In this sense, the ICH is a microcosm of global politics. Neither Japan's insistence on its racial uniqueness nor Taiwan's proposal based on its practical statehood matches the conventional scenarios approved by the United States and the PRC. These "odd" behaviors are the story I have told in this dissertation and Chern has indicated that I might extend my findings to a broader context.

Chapter 8
Cry to Be Normal: Govern-Mentality in Globalization

> To give a simple definition, it [i.e., healthy nationalism] is when a race or group of people who share a common destiny are aware that they share a common destiny and make every effort to enable the country to grow and prosper politically, economically, and culturally. It is when they have their own identity, or sense of self, in the world politically, economically, culturally, and otherwise and co-operate to contribute to that identity. Without this, there is no way that a nation will be able to stand on its own two feet.
>
> Nakasone Yasuhiro[1]
>
> The problem Taiwan faces today is not whether it should be independent or not, but how to make this state a normal country.
>
> Lee Teng-Hui[2]

PART I
ON GOVERN-MENTALITY

The Meaning of "Normal" and "Pathological" in Globalization

As mentioned in the introductory essay to this part, this chapter stands as a thematic elaboration of my observation about the debate over racial difference in the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). Although for some readers this chapter may feel like an aberration, for three reasons I am convinced of its necessity. As part of my effort to capture a particular moment when global capitalism was marching into Asia, I want to see whether what I learned about the ICH can be applied to a broader cultural and social picture of how Japan and Taiwan imagine themselves in the world. That is my first reason. My second reason is that the story told in previous chapters — the unbending insistence of Japan's Ministry of Health, Labor and Welfare (MHLW) on the racial uniqueness of

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[1] Nakasone Yasuhiro, *My Political Philosophy* (Tokyo: Liberal Democratic Party, 1987), quoted in Hood 1999: 6.

[2] Comments at the meet-the-author conference held on the occasion of the publication of *Xin shidai Taiwanren* (new era Taiwanese, Lee 2005) at the Grand Hotel, Taipei, May 1 2005.

the Japanese and the wish of Taiwan's Center for Drug Evaluation (CDE), often repeated, that Taiwan might achieve global visibility — provides insights into a cultural and social mentality. The third reason for this chapter is the need to convey some implications of this case study for global politics and nationalism. In my study, viewpoint has been treated as no less important than actions, so it would be difficult to summarize my findings about international negotiations over drug testing without an account of Japan and Taiwan's changing attitudes toward race and the state.

Nakasone Yasuhiro and Lee Teng-Hui, whose words are quoted above, share a number of traits. Both were in power at critical moments in their states' recent history, with Nakasone facing internationalization and Lee democratization. Despite their less than overwhelming mandates, both chose to confront these challenges, staking out clear agendas for the future of Japan and Taiwan. And the comments of both on national culture have led to confusion and controversy. Their comments have been very different, always in keeping with Japan's and Taiwan's behavior inside and outside of the ICH. Here I will briefly introduce their agendas and their shared concerns about the transformation of Japan and Taiwan in the era of globalization, and in the following section I will explain how my dissertation findings illuminate this topic.

As historian Christopher Hood has pointed out (1999), Nakasone Yasuhiro is famous for his seemingly contradictory beliefs in the value of internationalism and nationalism. From 1982 to 1987, he improved Japan's relations with neighboring countries, including the Soviet Union and the People's Republic of China (PRC). And he was the first Japanese prime minister since World War II to make a state visit to Korea. Nakasone also maintained close relations with United States President Ronald Reagan; indeed, a photograph from the 1980s that has a strong resonance for many Japanese shows Nakasone standing at the center of the group of G7 leaders — previously Japanese prime ministers tended to be found on the margins of the group (fig. 8.1, left).

Even so, Nakasone was also known for his nationalism. In 1985, for instance, he became the first Japanese prime minister to visit the controversial Yasukuni Shrine. Meanwhile, he initiated educational reforms that some considered nationalistic, such as the use of the emperor's song and the flag emblazoned with rising sun in official ceremonies. He also strongly believed that Japan should take greater responsibility for patrolling its own waters. In one infamous episode described in Chapter 4, Nakasone's nationalism crossed the line into what many considered outright racism: he proclaimed that Japan's brilliant successes had been won because it did not have ethnic minorities, like the United States. For this comment he was vilified both by the various non-Japanese

ethnic groups in Japan, particularly the sizeable Korean minority, and the United States.

Fig. 8.1. *Left,* Group Picture of World Leaders at the Williamsburg Summit, with Prime Minister Nakasone Standing between American President Reagan and United Kingdom Prime Minister Thatcher; *Right,* Cover of Lee Teng-Hui's *Xin shidai Taiwanren* (New Era Taiwanese)

Sources: Nakasone 1999, 214 (left); Lee 2005 (right).

What was Nakasone's real agenda for Japan's national identity? Many have commented on the prime minister's dual nature: he was, by turns, hawk and weathercock (*kazamidori*): the hawk was the nationalist who advocated such things as constitutional reform, increased defense spending, and support for the emperor; the weathercock was the great political opportunist. These descriptions appeared to annoy Nakasone. He once said: "When I first came onto the political scene the press took me to task for being a political opportunist or a hawk and wrote about me without realizing that I had progressive ideas" (quoted from Hood 1997). He wanted the public to know that although he had won his position by political strategy, this did not mean that he was a shortsighted politician or someone's puppet: his vision for Japan was clear and long-term.

What, then, were his progressive ideas? The core of Nakasone's vision for Japan was the racial concept of "healthy nationalism" (*kenzenna nashonarizumu*). Explained at a Liberal Democratic Party seminar in 1987, the essence of this concept was that the identity of the Japanese nation was based on the biological connections between every member of the polity, which ensured a common destiny. Describing Japan's wartime nationalism as "unhealthy," Nakasone hoped that a better understanding of Japan would improve relations with other countries. He routinely visited states involved in disputes with Japan, and he also set up the International Research Center for Japanese Studies, an institute located in Kyoto that facilitates foreign study in Japan, especially the work of foreign scholars who look at Japan's culture from an international perspective.

Nakasone also believed in cultural reform through education. He often repeated that "power must serve culture," and he believed that this was a key to facing globalization. While it would take longer than one generation to accomplish, only cultural reforms would bring further political change, including the revision of Japan's constitution. The healthy nationalism Nakasone had in mind depended on the coexistence of internationalization and the formation of national identity. The more Japan was exposed to the world, the more tightly it would cling to its national integrity. The solution was to remain in touch with that national character while acquainting one's fellow countrymen and the rest of the world with it.

Preserving Japan's national identity in the era of globalization, according to Nakasone, means sailing the ship of state on an international voyage. The world changes as Japan changes its relation to the world. Up to the beginning of the twentieth century, Japan had dramatically opened its ports to the rest of the world in two different periods; the late twentieth century, said Nakasone, marked the "third opening" and he declared that "the path that Japan follows internationally will determine her destiny." The leaders of Japan, he insisted, "must be sure at all times to explain to its people where the ship of state is on its international voyage and what the prevailing weather conditions are. [. . .] At the same time, they must secure co-operation and alleviate international unease by telling the world clearly where Japan is heading" (Nakasone 1999: 219).

Lee Teng-Hui came to power in the late 1980s. An agricultural economist, he followed a wandering career path, from technocrat to chairman of the Kuomintang (Chinese Nationalist Party KMT), and finally president of Taiwan. Unlike his authoritarian predecessor, Chiang Kai-shek's son Chiang Ching-kuo, who had served as unelected president for life, Lee was Taiwan-born and, in due course, democratically elected: he remained in office from 1988 to 2000. During his presidency, Taiwan's political system was completely reformed and democratized. He put an end to the one-party dictatorship of the KMT. His prestige reached its peak during Taiwan's first direct presidential election in 1996, which Lee won with 55% of the vote. For his achievements, Lee was praised by news outlets worldwide as "Mr. Democracy."

Many who admire Lee's record of domestic reforms cannot accept Lee's approach to foreign relations, particularly his strong advocacy of Taiwanese independence and *de jure* statehood, clear contradictions of longstanding KMT policy. The KMT holds that the territory presently governed by the PRC, combined with Mongolia and Taiwan, make up a country called the Republic of China (ROC), whose legitimate government is the KMT. Though it seized control over Taiwan when it was surrendered by the Japanese in 1945

and lost control of all other lands four years later, the KMT regime has steadfastly refused to recognize either the PRC or the Mongolian People's Republic. Nonetheless, during his second term Lee Teng-Hui tried to distinguish Taiwan from the ROC, setting out to resume diplomatic relations with Mongolia and proposing a special state-to-state relationship with the PRC. In addition, Lee's attitude toward the United States and Japan is ambiguous. His education and his statements have suggested to many that he is politically allied with the United States and culturally with Japan. As chairman of the KMT, Lee was dogged by persistent suspicions that he secretly supported his political opposites and was intentionally sabotaging the party he was leading. The defeat of the KMT in the 2000 presidential election resulted in a disgraceful expulsion of Lee from the party.

Lee Teng-Hui's policy of "resisting China" has been considered racially essentialist since Taiwan cannot avoid being assimilated into the PRC unless its people develop a unified non-Chinese identity which, some argue, may be based on biological difference (e.g., Lin et al. 2001). Such Taiwanese nationalism is often criticized as calculating and discriminatory to those who believe that they are Han Chinese.[3] When people talk about "authentic" Taiwanese, they mean always the Holos, who make up a majority of Taiwan's population. Some have complained that by seeking to turn their history into the central trunk rather than an appendage, the Holos forced other ethnic groups into the margins. For example, it is said that the so-called mainlanders can be considered Taiwanese in Lee's nationalist scheme only if they accept the additional identity of "new Taiwanese." For all of these reasons, Lee is by turns vilified and praised, especially since becoming the guiding force behind the pro-independence Taiwan Solidarity Union.

Although Lee's political career looks complicated, his agenda has been rather consistent. Like Nakasone, Lee may be an opportunist, but his determination to make Taiwan a globally recognized democratic state has never wavered. According to *New Era Taiwanese,* Lee is determined to situate Taiwan's path to survival in an international

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[3] Here is provided the island's ethnic geography. Except for the aborigines, who are Austronesians, three of the four main ethnic groups in Taiwan, the Holos, the Hakkas, and the so-called mainlanders, are considered biologically alike (see Chern Herng-Der's interpretation on Lin et al 2001 in Chapter 5, Part 2). Though each has its own language, all can be called Han Chinese or *huaren.* The largest group, accounting for about 67% of the population, is the Holo, who are the descendants of migrants from nearby Fujian Province. Often they are simply referred to as Taiwanese. The Hakka, who make up around 15% of the population, have a long history of moving from place to place in China and Hakka communities are found in may places in south China today. They have a culture and language quite distinct from any other Chinese group. Mainlanders, a cultural hodgepodge, are the descendants of the soldiers and refugees who immigrated to Taiwan between 1948 and 1953, and they make up about 10% of the population. There has been so much intermarriage that these groups are all hard to delineate, especially in the case of the mainlanders. Usually, anyone whose patrilineal line has recent roots in mainland China is called a

context. Occupied over time by various groups and now a part of the Asian security network, Taiwan neither belongs to any other country nor can it be isolated from the rest of the world. This means that Taiwan's political status has to be determined by international trends. Since it has not yet been recognized by large international organizations, Taiwan must construct a statehood acceptable to the rest of the world, namely, democracy. This means extending the domestic reforms for which Lee was lauded and distinguishing Taiwan from the PRC by standing with the globe's democratic countries. The most important characteristic of Lee's vision is the "deracialization" of Taiwanese nationalism. Although Taiwan exhibits less ethnic diversity than the United States, it has chosen to imagine its statehood this way in order to avoid unnecessary factionalism. This idea is nicely echoed by the cover of Lee's book, which is simply a face of a baby of fairly minimal phenotypic distinctiveness that cannot register as having a specific group identity (fig. 8.1, right). The Taiwanese of the new era, according to this vision, are simply those who have commitments to a specific political entity.

Despite the differences in Lee's and Nakasone's strategies for dealing with globalization, both hoped for "normal" countries. For example, Nakasone claimed that Japanese lacked the important experience of drawing up a constitution. While the Meiji constitution was drawn up under orders from the emperor, Japan's current constitution was largely sketched by the Western powers during the postwar occupation of Japan (Nakasone 1999: 223). Taiwan is in a similar position: its constitution was drawn up with the government of all of China in mind. Modifying this document would, as Lee writes, "put an end to a fiction, reviving reality and truth and making us confront our situation. There exists only one truth: Taiwan is just what it is" (Lee 2005: 71). Both Lee and Nakasone feel that making Taiwan and Japan "normal" countries will involve recasting the image of the two entities in the world.

But their programs led to problems. Nakasone was aware that his nationalist arguments could easily be misunderstood (Nakasone 1999:219), and indeed many have lumped him with such right-wingers as Ishihara Shintaro and Ishikawa Akira (mentioned in Chapters 3 and 4), who have long demanded that Japan be allowed to chart its own course and fight its own wars. Similarly, although Lee's wish to cast Taiwan as a normal country implies soothing the military tensions across the Taiwan Straits through diplomatic negotiations, few world powers appreciate this idea. Those who assert Taiwan's political agency are demonized as "Taiwan independence fundamentalists" or

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waishengren, literally "outside the province person."

"troublemakers." The message is clear: "Do as you are told."

I do not want to make any moral judgments here about who should be responsible for this situation. Instead I would like to speak of the normal and the pathological. In his historical study of medical knowledge, Georges Canguilhem (1991) argued that the creation of standards about bodily conditions shaped our understanding of pathology. In the same manner, the modern world creates a grid that defines which state should be seen as normal and which as pathological. Still, Japan and Taiwan do look like normal states, and this created a gray area where problems arose. [4] This is the starting point of my ethnographic investigation.

Asian States and Govern-Mentality

Given Nakasone's and Lee's ambitions to "normalize" Japan and Taiwan, the importance of a conference devoted to establishing universal standards becomes clear. The ICH is no ordinary global meeting, but a primal one: it determines rules concerning what will be considered normal in drug regulation and what will not. It establishes standards for what is "normal." If these two states are trying to be normal, why can't they just simply accept these rules and become "normal"?

Our ethnographic journey started with a simple yet demanding mission: examining a debate among the members of the ICH over racial differences to gain insight into Japan's and Taiwan's efforts to advance their national projects in the nexus of capitalism, globalization, and the international pharmaceutical industry. However, over the course of long and intensive fieldwork in these places, I switched from studying health issues to focusing on the state. For Asian countries, the ICH is not a purely scientific forum, and explaining some of its actions requires the use of historiographic and anthropological theories. Specifically, explanations often depend on careful examination of what goes on in individual member states.

That is why I have presented both a story of two Asian states encountering the ICH and a parallel ethnographic investigation of how they present their distinctiveness while coping with globalization. Public health may be the main concern driving their negotiating postures at the ICH, but that is not all that determines their behavior.

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[4] As a further discussion, we know in Canguilhem's historical thesis it was the existence of pathological that helped scientists make sense of what the normal should be. In other words, what is at stake is not which part of the world is treated badly but the action to divide these parts by a set of medical knowledge that shapes our imagination and practice about body and life. Similarly, the present thesis challenges the norm of modern state by bringing up the "pathological" reactions of Japan and Taiwan when encountering globalization.

Throughout the discussion of racial difference we have seen innumerable interventions that have far less to do with science than with politics. While the practical goal of the ICH is consistently the elimination of redundant clinical trials, each state acts according to its needs. The process is dynamic and interactive. It is dynamic because the two states encountered the ICH in various situations and at different times. Even after long and exhausting negotiations by the expert working group, the implementation of the E5 guideline did not mark the end of this story, since Taiwan then seized the chance to speak for itself. In reviewing this story, we find that the discussion of racial difference is never a simple bilateral business negotiation. While the global pharmaceutical industry attempted to "capture" Japan in the bilateral Market-Oriented, Sector-Selected Discussion (MOSS) talks, Japan's Ministry of Health and Welfare (MHW) silently retreated to the global ICH. Although the E5 guideline includes two interpretations of clinical trials and racial difference, the CDE's bridging policy brought lights to this situation. It did so by showing that even when different parties were deadlocked over it, the guideline still worked. Of course, Taiwan's embrace of globalization has several goals. To overcome a lack of global recognition, it is trying to weave a broad web to link the global and the regional. Along with this development, new global actors, such as Singapore, join the game, ensuring that parallel historical and ethnographic inquiries can continue endlessly.

While tracing the vision of the state in this process, I need to distance my approach from two misleading interpretations of Asian states. In Chapter 4 I took on the view that these states simply practice "protectionism under the disguise of cultural essentialism" Because they view questions about drugs almost exclusively in terms of profits, the industry people I interviewed tended to interpret failed attempts to get Japan to waive all local trials as the predictable result of the country's refusal to relinquish protective tariffs. Japan's unique culture is considered nothing but an improper attitude toward business. What is wrong with this line of reasoning? Unwittingly it separates culture from modern institutions. Westerners can appreciate exotic customs and culture, but at the institutional level the Western-dominated industry does not enjoy cultural diversity. From its mechanical viewpoint, the world has only one standard and every institution should obey the same logic.

From this perspective, the process of E5 negotiation is typical of the vicious circle of "making and breaking" rules that I have described in Chapter 4. Japan seems to be the only state that dares to disobey the rules of globalization. Through the construction of cultural uniqueness, it casts itself as an exception to all rules, permitting others to depict it as the player that unilaterally ignores rules. In the case of the E5 guidelines, race is a

disguise: a competitive Japanese state is the goal. Since there is no way to escape from this cycle, the only solution was more rules (for example, the Q&A on the E5 guideline) or a greater emphasis on science, which would, it was hoped, force Japan to clarify every word of the rule. As this thesis shows, these attempts failed.

The second faulty interpretation of Asian states and the expansion of medical institutions relies on ideas about global hierarchy. As readers may have noticed, this topic is little discussed in the previous chapters. Even so, humanities researchers, particularly those who are acquainted with anthropology and cultural studies, tend to conceive of Asian countries and the ICH in terms of a hierarchy. In a study of the introduction of the remarkable new group of antidepressants called SSRIs (selective serotonin reuptake inhibitors) to Japan, Kalman Applbaum (2005) connected the truly global construction of depression with a huge growth in the treatment of depression. The various actors in Applbaum's study, from industry representative to researcher, borrow frames and theories from evolutionary globalism, which stands for progress and political, scientific, and moral enlightenment.

The problem with this fascinating approach is its unequal treatment of the agents involved. To construct a coherent narrative about this top-down expansion of marketing from the United States to non-Western regions, only those who can present this agenda are mentioned. Thus, in an ethnography of Japan, we hear few local voices and many foreign voices commenting on Japan. For example, in his section on clinical trials in Japan, Applbaum notes the harsh criticisms offered by foreign industry representatives but says nothing about local reactions to them. The same is true of his discussion of the pricing system, where the agent of the MHLW, the policy maker, is simply absent. In addition, this study commits the unpardonable sin of failing to mention the ethnographic potential of the ICH. Although Applbaum notes the role regulatory authorities play in the global expansion of the market, he merely casts the ICH as an instrument through which this capitalist wish is fulfilled. As the present thesis has demonstrated, the ethnographic pitfalls in this theoretical construction are sizable.

Applbaum's hierarchical insights could also be called the story of global governmentality. It is not necessary to provide a detailed review of Michel Foucault's famous study: my interest is in three characteristics Foucault assigns to governmentality (Foucault 1991:102–3). First, it is a specific and complex form of power exercised through various institutions and practices. Second, its institutional preeminence produces a series of governmental apparatuses and a whole complex of ideology. Third, this institutional production is itself gradually "governmentalized," performed in a more disciplined, regulated way. But does this description apply to intergovernmental

institutional development?

Akhil Gupta's *Postcolonial Developments* (1998) helps answer this question. In a critique of the discourse of underdevelopment, Gupta shows how being drawn into the global politico-economy — what he calls "global governmentality" — becomes a dilemma for the Indian state. In this study, the sovereignty of the nation-state depends on "the recognition of *other* nation-states, of other units that are different in their culture, history, and even 'temperament' but alike in their constitutive modality" (318). Sovereignty is not a solitary fact but a relation to the rest of the world presented as self-sufficiency. In other words, when non-Western countries are examined through the lens of "hierarchical governmentality," the assessment of their relationship with the global tends to be pessimistic. The state, according to Gupta as the nation's governance, fuses in the grandiose world web and conducts unambiguously the control form the governmentality on the world scale (314).

Although I do not reject this worldview completely, over the course of the present thesis I have presented some alternatives or exceptions in which the state was neither a neutral instrument that passively transformed global governmentality, nor a nexus of politico-economic apparatuses that served only capitalism. We have to be careful in extending Foucault's description of governmentality from the nation to the world. In my opinion, those who borrow this idea and consider the world as thoroughly hierarchical fails to address, first, the possible ideological conflicts between the state and the world. If Foucault is right in saying that "local" governmentality is the result of a complex of ideologies compatible with state apparatuses, we are compelled to ask whether the encounter between state governmentality and global governmentality yields conflicts. Also, such an approach fails to address the possible conflicts during the formation of global governmentality. If Foucault was right about the governmentalization of governmentality, i.e., the international governmentality has to be achieved by a formalized, regulated way, we have to ask in what governmentalized ways the global governmentality is formed, and in what ways local governmentalities work together.

Let me take Taiwan as a rather extreme challenge to this approach. As described in Chapter 1, Taiwan has been a de facto self-sufficient state since the end of World War II but has a truly awful diplomatic record. Thus, when Taiwan encounters globalization the results are rather complicated. For example, while the ICH is officially an intergovernmental organization dedicated to facilitating a single, global market, Taiwan sees it as a channel through which its governmentality can be secured. As I have shown, in order to be incorporated into this global governmentality, the CDE tries its best to make itself heard by the rest of the world. Instead of a weapon that strong powers can

wield to repress the weak in the name of globalization, the ICH may well serve the voiceless in their negotiations with the rule makers. The CDE's decision to adopt bridging studies can be said to please global industry; however we cannot forget that if no "global" standard existed, the Taiwanese government would have lost all tools of resistance to the pressure to give up its clinical trials. In global governmentality some states will be somehow "defaced," but Taiwan does not even have a nose yet.

In combining Foucauldian governmentality with ethnographic attention to local concerns and perspectives, I have developed an approach to statehood in the era of globalization that I refer to as "govern-mentality." I emphasize three points. First, echoing Nakasone and Lee's visions of making their states "normal," this chapter will treat these cultural agendas sympathetically. Unlike scholars of international relations, who exclude cultural factors from their evaluation of policy making, I consider them necessary parts that contribute to the integrity of a state. In other words, I will not judge whether these ideologies are fictitious; instead, taking together these ideological factors (i.e., Japanese racial uniqueness and Taiwanese state solidarity), I hope to offer an appraisal of how Japan and Taiwan think about survival in the globalizing world.

The second aspect of the state's govern-mentality has to do with the governmental construction of global governmentality. Race and the state, the two cornerstones of nationalism, are treated very differently in Taiwan's and Japan's governmentalities. Why?

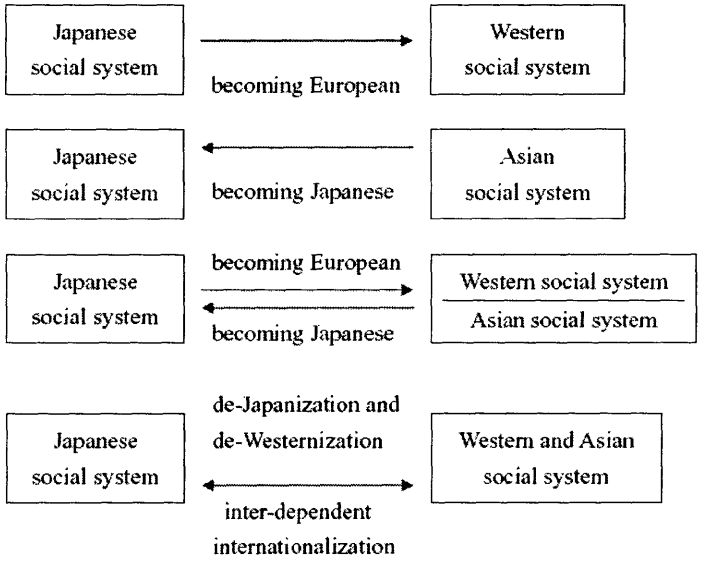
Third, I want to emphasize Japan's and Taiwan's different paths toward globalization. As Akhil Gupta points out, the notion of the nation is perpetually in flux; this is also true of the ICH. While I certainly accept that there are some essential differences between Japan and Taiwan concerning racial difference and the state, I would like to emphasize their divergent reactions to globalization. As we will see in the main body of this chapter, Japan presents a kind of "double helix" model, where its concerns about race and the state are always entangled. Meanwhile, isolated from and ignored by the world, Taiwan presents a territorial model. In domestic politics, Taiwan has to treat race as a prominent issue, but while facing the world it treats the state as its most important concern.

PART II
DOUBLE HELIX OF STATE AND RACE: JAPAN IN GLOBLIZATION

From Bilateral to Global: Two Modes of *Kokusaika*

In this part I trace Japan's transformation via two seemingly divergent concepts, internationalization (*kokusaika*) and race (*minzoku*).[5] While these Japanese terms were created to translate Western words, their meaning has since become subtly but unmistakably specific to Japan. I mentioned in Chapter 1 that *minzoku* refers to a group identified by shared biological characteristics and cultural values; it can be translated as *ethnicity, people,* or *nation* (see Chapter 1). And the meaning of *kokusaika* and *minzoku* has changed with time, making it difficult to discuss them in English.

Fig. 8.2. Four Dynamics of Japan's *Kokusaika*



Source: Adapted from Hoshino 1994, fig. 1-4.

Describing the Japanese people's feverish excitement about their country's growing role in global affairs, Sawada Akio declared in 1990 that it left many "unable to sleep at night" (1). Though the term *kokusaika* was only rarely used before the end of World War II, this does not mean that there was no contact between Japan and the rest of the world before then. Reviewing Japan's relationship with other countries, Hoshino Akiyoshi laid out four periods, each of which has a specific dynamic of interaction, as shown in figure 8.2 (1994: 23–25). My understanding is that these dynamics imply two modes of *kokusaika* that emerged after the long period of Japan's isolation. It originally conveyed bilateral interactions and later came to refer to participation in global affairs.

[5] For a brief review of different definitions of *kokusaika,* see Sawada and Kadowaki 1990:48–64.

The bilateral mode consisted of three dynamics up to the beginning of postwar period. An early dynamic was "becoming European" (*saioka*). Japan treated Western Europe, whose agents frequently visited Japan on mercantile and diplomatic vessels, as the very embodiment of modernity. The second dynamic of *kokusaika* presented it as "becoming Japanese" (*nihonka*). By the 1930s much had been done to transform Japan into a modern state, so when it offered the idea of a "greater East Asian economic sphere" as the ideological justification for a massive imperialist adventure, the rulers of Japan imagined that there could hardly be anything more modern than their industrialized and economically thriving state.

The third dynamic, which might be called dominant-subordinate *kokusaika* or parallel *kokusaika,* can be understood as a combination of the first two dynamics. It presents a unidirectional diffusion of cultural and political influence from Europe or the United States to Japan and from Japan to other Asian countries. This dynamic can be traced from the first postwar appearance of *kokusaika,* which, according to Kitamura Kazuyuki (1990), was in an article entitled "Internationalization of Domestic Policy" that appeared in *Nihon Keizai Shinbun* (Japanese economic news) on November 8, 1961:

> The economies of every country in the world are now closely related to each other, so domestic policy must take into account foreign policy issues. [. . .] In the past, when those charged with shaping foreign policy made critical comments about domestic policy, this was seen as intervening in internal affairs — such comments could not be accepted. But the recent tendency — reflecting broadly shared thinking — is to think of domestic policy as connected to international negotiations. [. . .] The point that attracts our attention is that when it comes to economic policy *the boundary between the domestic and the international becomes attenuated.* (quoted from Kitamura 1990: 29, emphasis mine)

The above quotation conveys the connection between economics and *kokusaika.* It was economic issues that first convinced the Japanese that putting an end to the embargo on foreign trade was inevitable (29–30) and initially the term *kokusaika* was used exclusively in the field of economics. It did not show up in major newspapers until the early 1970s, by which time the Japanese were well on their way to full internationalization. The Japanese government both led the actions and promoted the term *kokusaika.* In 1955 Japan joined the General Agreement on Tariffs and Trade; in 1963 it lifted the restrictions on imports from its member states; and in 1964 it eliminated controls over currency flow to eight International Monetary Foundation member states. In that same year, Japan joined the Organisation for Economic Co-operation and Development and arranged to reduce its tariffs. Over the ensuing years a series of

government studies appeared: *An Economic Plan for the Fifth Decade of the Showa Period* (1967), *Energy Problems in the Age of Internationalism* (1969), and *A New Plan for the Development of Economic Society* (1970). Taken as a whole, these identified the steps Japan would have to take to enter the world economy. And so the Western world gradually infiltrated every aspect of Japanese life.

Let us take a closer look at this dynamic. It is built upon a hierarchical world system, with Europe and America at the center and East Asia at the periphery. In this picture, Japan is not part of Asia and stands somewhere between the West and the East, a crucial node in the flow of influence from the center to the periphery. Of course, some view this system as problematic, but that is not the point I want to discuss here.[6] What I want to point out is the bilateral nature of this worldview. As the use of *kokusaika* in the above quotation of *Nihon Keizai Shinbun* suggests, Japan saw itself as a nation apart, fundamentally different from both Asia and the West. Ignoring interactions among other countries, the models in fig. 8.2. show only what Japan learned from the West and what Japan taught to other Asian countries. This is a "Japan-centric" world. The familiar — and racially charged — image is that of a boiled egg, its perfectly spherical and impervious Japanese yolk surrounded by the foreign white (Hoshino 1994: 14).

Putting aide the "Asian side" of *kokusaika,* namely Japan's relationship with other Asian countries, many Japanese viewed the Western part of *kokusaika* as a threat, the possibility of rich material rewards for surrendering the purity of one's culture.[7] For example, occupying the conservative position, Sawada Akio said that "the trade friction (due to the blame of protectionism), after all, is the result of a cultural problem. Internationalization means changing our traditional customs, in other words, our culture; we absolutely cannot accept this kind of internationalization" (1990: 4). But Japan cannot resist change forever.

In Chapter 4 I described an instance of the sort of bilateral negotiations between the United States and Japan that can emerge from this understanding, and the Japanese did not like the setting of communication. Still, for different reasons, some experts on Japan, such as Karel G. van Wolferen, have failed to come to terms with the Japanese worldview. Wolferen stated that Japan's refusal to open its markets to the world while taking full

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[6] Critics of the dominant-subordinate discourse appeared in the early 1970s, but only really attracted public attention in the late 1980s when Japan's bubble economy was teetering and its ODA policy was in question. A typical criticism is Toba Kinichiro's *The Japanese Who Have Two Faces* (1973).

[7] Apparently, influences from other Asian countries were not taken into consideration, since Japanese assumed that those countries on the receiving end of the flow of influence from Japan would have no reciprocal effect on Japan.

advantage of other countries' open markets was simply unfair (1986: 299). He accused Japan of cultural relativism and described the so-called understanding between Japan and the West as a form of bargaining. In the Japanese language, he explained, the term "understanding" (*wakaru*) refers to acceptance or tolerance: "You show true understanding of people or things by accepting them the way they are if you are not strong enough to challenge them. If you have strength, the other party will show understanding by a certain degree of adaptation to your wishes" (300).

Hoshino (1994) basically admitted this observation, but he did not admit that Japan's approach to negotiation led inevitably to a zero-sum outcome. He presented a structured process: the more contact there is between two cultures, the more complex their encounter becomes (11). The only way for Japan to survive in a globalized world, according to Hoshino, is to approach what he called "enforced internationalization" (*shikatanashi kokusaika*) warily and very calculatingly. This supports my previous observation about the quick resolution of the issue of foreign clinical data at the MOSS negotiations. (Recall that while the construction of Japanese race was challenged during these talks, the MHW eventually chose to retreat.)

However, the above dynamic was not what Hoshino wanted to see. The fourth dynamic of *kokusaika* (fig. 8.2, boxes at the bottom), which he called interdependency, differs from previous models by portraying a harmonious world to which the West and Japan contribute equally. This can be well-explained by Japan's attitude toward a multilateral relationship to the world. As Hoshino explained, this dynamic insists on fair and equal relations among states and on a degree of flexibility about one's own traditions and those of others. For example, Western societies must respect some Asian values, while Japan must make some changes in the name of internationalism. This does not mean that Japan has to open its markets or change its cultural values. Although Hoshino spoke of the need for interdisciplinary research on *kokusaika* and expressed concern about the negative influence of Japan's xenophobic society, the whole point of the research was to prevent deeper foreign infiltration of Japan so that its social system would suffer no changes (11).[8]

For Japan, *kokusaika* is still a process of bargaining; as Hoshino pointed out, Japan "acts as a member of the international community, and the Japanese social system, which clings to its characteristics, engages in some exchanges with other states" (11). This is a

[8] Hoshino reported on two projects conducted by Japan's Asia University between 1990 and 1992. The first project was meant to assess Japan's achievements since the introduction of *kokusaika,* while the second was to study potential future problems.

sort of ecological worldview: the world resembles an ecosystem in which every nation-state has its own niche. Harmony is achieved by preserving each one as a distinct "species." Only from this viewpoint can we understand the MHW's attitude toward racial difference in the ICH. While Western experts believe that the differences among human beings are essentially cultural and not biological, the MHW experts never even viewed this as a possibility.

In fact, underlying the interdependent dynamic is a unilateral attempt to preserve Japan's integrity while becoming part of a globalizing world. This is consistent with Nakasone's sailing metaphor and with the first project on *kokusaika* conducted by the Professors World Peace Academy, Japan.[9] The goal of this interdisciplinary study was to formulate an integrated strategy for Japan in the era of globalization. Over two thousand scholars contributed, from the fields of civilization, religion, politics, national security, economics, technological innovation, and education. Their results were presented at the International Conference on World Peace in 1978, which was attended by fifty-nine scholars from twelve Asia-Pacific countries, and were subsequently published in a 700-page report entitled *Japan and the International Era.*

The report is centrally concerned with determining Japan's "national goal" in the global era, and the analogy of sailing turns up in the preface: "Based on these studies and experiences [we hope] to draft at least a precise admiralty map to ensure the *Nihonmaru* [Japanese ship of state] safe sailing and then to draft precise guidelines for it" (PWPA-Japan 1979: 70). The report set the goal of restoring Japan's national essence, which had almost been lost as a result of rapid economic development. "As Japan's traditional educational system decayed," wrote the report's authors, "the racial spirit also declined. Japanese were no longer proud to be citizens of an independent nation-state. Instead they directed their efforts to industrial and technological development; economic growth became their goal" (70–71).

Factors that might deflect the great Japanese ship of state from its course included external pressures (*gaiatu*) and internal pressures (*naiatu*). To be truly independent, Japan had to consider its strategic position in global politics and international relations. At the same time, it had to protect its citizens from poverty and infirmity. But in addition to concerns about politics and the economy, policymakers were quite concerned about national consciousness and hoped to cultivate reflections on the beauty of the Japanese

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[9] The Professors World Peace Academy was founded in Seoul in 1973 by 168 Japanese and Korean professors and researchers under the supervision of the Holy Spirit Association for the Unification of World Christianity. The Japanese branch of the Professors World Peace Academy was founded in 1974 by Professor Matsushita Masatoshi, the former president of Rikkyo University. He is also the leader of the International Era and Japan Project.

and of Japanese traditions. This did not mean a return to imperialism, the report clarified, but the revival of an ethical code that could unify Japanese society, "rebuilding a racial ethics in response to the international community" (648–49).

This ideological view helps us understand the MHLW's post-E5 strategy. In spite of external pressures from foreign companies and internal pressure from patients' groups, it rejected a proposed bridging study and insisted on global drug development. As I repeatedly argue in the present thesis, global drug development must not be misinterpreted as one more kind of Japanese protectionism: if we want to understand Japan's actions on the international stage, we had better study the cultural and social roots of Japan's *kokusaika.*

Immigrants and *Minzoku:* Multiethnic Japan

This section deals with the changing idea of *minzoku.* I will point out challenges brought by *kokusaika* that pushed Japan to ponder the meaning of its nation. For this purpose, I will treat *minzoku* as a verbal reflection of the Japanese self-image, the sum of citizenship, race, culture, and spirit, and a working reference for coming changes.

Unlike the prewar and interwar periods, after World War II there were countless public discussions of the nature of the Japanese *minzoku.*[10] Tsukishima Kenzo (2000) pointed out that during the Meiji and Taisho periods the image of the simple *Meiji no hito* (Meiji person) captured Japan as a modern nation. But Japan's defeat and the following occupation started an inevitable institutional change, engaging anthropologists, philosophers, historians, literati, economists, psychologists, linguists, psychiatrists, and even entrepreneurs and businessmen (309–37).

Within a comparative study of Japan's postwar society, language, mentality, and culture, Tsukishima singled out for attention the burgeoning material contributed by ordinary persons' international experiences, such as overseas trips and foreign study. But such records do not deal directly with what the Japanese are and individual self-portraits are both fragmentary and desultory (2000: 332). The divergence of academic and popular discourses is my starting point. The transformation of the Japanese *minzoku* was not initiated by academic pursuits; instead, it was achieved by the accumulation of interactions between the Japanese people and the outside world.[11] As we will see in the

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[10] In his huge, well-documented book (1998), Oguma Eiji criticizes the cultural construction of Japanese *minzoku* before the coming of *kokusaika.* It did so by tracing the relationship of Japan with "non-Japanese" territories, such as Okinawa, Hokkaido, Formosa (Taiwan), and Chosen (Korea).

[11] For example, in his study on the discourses on what is Japan and the Japanese, Oguma Eiji points out that to consider Japan as a nation state made up by a single race is not a native concept (1995). For example,

rest of this section, the construction of a homogenous *minzoku* is continuously challenged by the new situations brought by exposure to the foreign world.

Under the bilateral mode of *kokusaika, minzoku* occupies a crucial position. In a famous book, Wagatsuma Hiroshi and Yoneyama Toshinao (1967) pinpointed the different understandings of *minzoku* held by Japan and the United States. When the Japanese picture Americans, they see only white people, much as they see a homogenous Japanese *minzoku.* On the other hand, the image they associated with the claim "We are all Americans" was a heterogeneous assortment of ethnic groups (146–47). Divergent American and Japanese conceptions of race resulted in a misunderstanding when representatives of the two countries discussed racial difference during the MOSS negotiation. The MHW thought that the United States would appreciate its commitment to protecting its people's health; this is clear from a comment made by Naito Chikayuki, the E5 expert. As discussed in Chapter 4, Naito not only divided racial difference into intrinsic and extrinsic factors, which corresponded to the categories of *jinshu* and *shudan,* he explained this difference by comparing Japanese and Caucasians, assuming the homogeneity of each population. Proposing a bridging study involves just such an assumption. Although Western scientists claimed that mathematical algorithms can translate the clinical data derived from a study of one race to another, the very need for bridging is a result not of racial differences among populations, but of territorial differences.

The meaning of *minzoku* shifts readily from citizenship, to race, to culture. Think of how the term is used in discussions of discrimination against *buraku*, Korean-Japanese, Ainu, and immigrants from former colonies.[12] After Japan signed a Convention on the Elimination of All Forms of Racial Discrimination (CERD) in 1963, it worked to make minority voices heard.[13] Even so, *kokusaika* played the leading role in making this problem visible, not always in a positive way. For example, as social activist Tanaka Hiroshi (1991) pointed out, Japanese law does not recognize ethnic schools (*minzoku gakko*) as part of its formal educational system; graduates of the Tokyo Kangoku

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it was harshly rebutted by the government declarations in the wartime. It was not consolidated until the postwar period after the Japanese Empire was forced to forsake all its colonies. For detail, see Oguma 1995, Chapters 16 and 17.

12 Discrimination against members of the *buraku* group — descendants of those who belonged to despised occupational categories — is the oldest form of racial discrimination in Japan, dating back to the Meiji period. According to a government survey, there were about 1.2 million *buraku* people living in 4,442 *buraku* communities nationwide; other sources estimate that the number of communities is roughly six thousand and the total number of *buraku* men and women surpassed three million.

13 For a brief introduction to and analysis of the CERD, see Shin 1997.

Gakuyen high school for Korean Japanese, for instance, are not qualified to take the university entrance examination. Revealingly, the recent *kokusaika* policy encouraging foreign students to attend college in Japan means that if a Korean boy or girl comes to Japan with his or her businessman father and spends the final year of high school at an ethnic school in Tokyo, he or she is ineligible to attend college in Japan, whereas classmates who remained in Seoul are eligible (164–66).

The direct effects of *kokusaika* have forced Japan to clarify its ambiguous ideas about *minzoku.* When many foreign workers immigrated to Japan in the 1980s and early 1990s, they contributed to what sociologist John Lie calls "the Second Opening of Japan" (Lie 2004). *Newsweek* magazine has predicted that by 2030 Japan will be a major destination for immigrants (fig. 8.3). Already urban Japanese see foreigners everywhere: they prepare food and wait tables at cafes and restaurants; they work on countless construction sites; they stand in line at the supermarket. And many of these foreigners are of Japanese descent.

Fig. 8.3. *Left,* Cover of *Newsweek* Magazine's Special Issue, "2030: Japan, a Great Immigrant Nation"; *Right,* Page from the Special Issue Showing a Brazilian Taxi Driver in Tokyo Awaiting a Fare

Source: *Newsweek* (Japanese edition), August 6, 2003.

Japan is no longer a static nation. People come and go. Due to Japan's low birth rate, if its labor force is to be maintained, the United Nations has estimated that Japan will have to accept 610,000 immigrants annually. Japanese may not embrace these newcomers, but their long-term recession has forced them to accept them. Figures from 2003 show that there are 1.78 million foreign laborers working in Japan, half of whom work in occupations considered unappealing by Japanese. Another phenomenon is that of "non-Japanese Japanese," citizens whose attitudes differ from those of traditional Japanese because of long periods spent abroad. Many emigrants have recently returned

from abroad; for example, now there are 33,000 Brazilian-Japanese living in Japan. And while some who are conventionally thought of as foreign, such as Japanese-born Taiwanese and Koreans, have been granted Japanese citizenship, few view them as authentic Japanese. These recent changes have undermined traditional ideas of what the *minzoku* is.

A recent case suggests how complicated the situation has become. Since 1996 a sign reading "Japanese Only" has hung outside a public bath in Otaru (Lazio 2000).[14] The bath is privately owned and the owner claims that the sign was placed to accommodate Japanese guests who do not want to share a bathtub with a foreigner. On November 1, 2000, a Caucasian male who is a naturalized Japanese citizen came to that bath with documents proving his nationality, hoping to use the facilities — he was turned away. The owner explained his concern that Japanese guests would leave because of the white man's "foreign appearance." Local authorities tried to bring the bath house into agreement with government policies requiring equal treatment of all Japanese citizens, but in vain. "The irony," the report comments, "is that in Otaru the bathhouses that reject foreigners are the most popular" (10).

If *kokusaika* calls attention to the Japan's changing demographic landscape, it has also created an increasingly visible group that throws into question the boundaries created by the concept of a Japanese *minzoku.* Somewhat surprisingly, Japan has a fairly long history of multiethnic marriages. Some emigrants to the United States and Brazil, as well as those who participated in the imperialist expansion into Manchuria and East Asia in the first three decades of the twentieth century, married local people, complicating Japan's biological complexion.[15] Between World War II and the Vietnam War, many American soldiers mated with Japanese women.[16] The number of marriages between men from Japan and women from the PRC or Southeast Asia and between Japanese

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[14] The group that issued a report on this situation, Issho, is a Japan-based, nonprofit, nongovernmental organization established in 1992. The goal of Issho (the word means "together") is the achievement of a truly multiethnic Japan, and the group monitors issues related to human diversity, language, culture, and coexistence worldwide, striving to facilitate a greater recognition and understanding of these issues, both in Japan and abroad.

[15] According to statistics collected by the Ministry of Foreign Affairs, by the end of World War II there were 4,258 Japanese emigrants residing in North America, 91,063 in Central and South America, 180,534 in Manchuria, and 25,740 in South East Asia (Tanaka 1991. 189). Although this does not tell us how much intermarriage took place at the time, it gives us some sense of the scale and breadth of Japanese emigration.

[16] According to Murphy-Shigematsu (2001), more than 80,000 Japanese-American couples have come to the United States since 1945, and the number of orphans abandoned as a result of Japanese-American reproduction has been significant. The stationing of troops in Japan led to the birth of many children fathered by Americans both in and out of marriage. This phenomenon is referred to in Japan as the *konketsuji boomu.*

women and Western men has been increasing since the 1970s. According to statistics collected by the MHW, in 1990 there are 25,626 cases of international marriage in Japan, a 350% increase over 1980; the number has exceeded 25,000 each year since then. By 1994 international marriages comprised approximately 3.5% of all marriages in Japan. In 1997 these numbers reaches 28,251 and 3.6%, accounting for one in every twenty-eight marriages. In some metropolitan areas, such as greater Tokyo, this number is as high as one in fourteen.[17] Still, it remains difficult to assess this trend with any degree of precision because the Japanese government has no intention of identifying its citizens by ethnicity.

Given unflattering labels, such as *ainoko* (built-up child), *konketsuji* (mixed blood), *hafu* (a transliteration of the English word *half,* meaning half-Japanese), and, more recently, *daburu* ("double") and *kokusaiji* (international child), these multiethnic people are trying to find an identity and a voice. Stephen Murphy-Shigematsu, a scholar and the daughter of Japanese and American parents, described some of the challenges (2001):

> A person who is thought to look like a Japanese is assumed to be Japanese. [. . .] [T]hose who can pass as majority Japanese are encouraged and permitted to do so because their phenotype enables the majority to regard them as if they were majority Japanese. Those whose phenotype is considered non-Japanese are still seen as different and not Japanese. [. . .] Those who do not look like a Japanese are not only assumed to be foreign but are also expected to act like a foreigner.

So what is the "in-between"? Thanks to *kokusaika,* his situation is better than in the past. Although he will not blend into mainstream Japanese society any time soon, the stories of these individuals are becoming widely known both in Japan and abroad. They are exploding *minzoku* from within.

By considering the impact of *kokusaika,* we get an idea of the "breakdown" of *minzoku.* Toyota Yukio (1994) has explained that there is no absolute definition of *minzoku.* Instead, it should be identified by its four components: culture (*bunka*), nationality (*kokuseki*), descent (*shujji*), and abidance (*kyojyu*) (fig. 8.4). As I pointed out at the beginning of this section, these are overlapping components. However, *kokusaika* complicates this situation. Some Japanese do not live in Japan and some foreigners have Japanese nationality. Even the question of culture is problematic. To take language as an example,

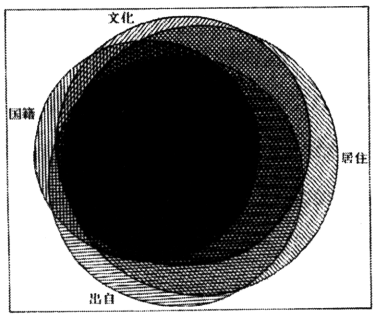
> What if someone not a Japanese by right of race [. . .] does manage to acquire some proficiency in the Japanese language? Well, in that case, the system

[17] According to a survey by the MHW, in 1987 only 1,010 children were registered as children of

literally makes no intellectual provision at all for his or her very existence. Such a person is a nonperson within the terms and definitions of Japanese social order. (quoted from Fallows 1986: 40)

Looking back to the 1980s, the period this quotation is taken from, one sees that language fluency was a conventional yet artificial boundary Japan applied to separate itself politely from the rest of the world. However, thanks to *kokusaika,* more and more Westerners now speak Japanese as fluently as do Japanese, and they are too obvious to be ignored (Morris-Suzuki 1998; Douglass and Roberts 2000; Lie 2004).

Fig. 8.4. Four Components of *Minzoku* (Clockwise from Top): Culture, Abidance, Descent, and Nationality



Source: Adapted from Toyota 1994: 206, fig. 6-1.

Toyota's hoped to solve this problem. Separating four components that determine Japanese *minzoku,* he claimed that there was more than one standard for assessing whether a person were authentically Japanese: all standards were applied and then depending on how the individual fared overall, he or she would be called Japanese. The more overlap there was between the regions, the darker the intersection became, the more Japanese she or he had to be. However, the shift in Japan's immigration and marriage patterns shows the inadequacy of this definition. Theoretically it is fine to call immigrants from overseas Japanese, but in practice Toyota's scheme fails to explain why those who look Japanese but have adopted foreign cultural attributes are treated as more authentically Japanese than those who fulfill every criterion but have blond hair and blue eyes. Worse, this scheme fails to deal with multiethnic populations, who would appear to be neither Japanese nor foreign.

Japanese-(Han) Chinese couples; by 2002 this number had risen to 38,927.

In the era of globalization, Japan's government may be able to switch its relationship with the world from a bilateral view contrasting self and other to a more integrated view of "Japan in the world," but the cultural image of *minzoku* is hard to change. Even in Toyota's approach, the "perfect" Japanese stands at one end of the scale and at the other stand those who have no relation with Japan at all. In between are subgroups such as "fairly Japanese" (*kanari nihonjin*) and "only a little Japanese" (*sukoshidake nihonjin*). But the swelling multiethnic population has produced a breakdown from within: their biological strangeness cannot be measured on Toyota's scale.

From Genetics to Genomics: Creating a Japanese Nation Suitable for Globalization

The previous sections suggest parallels with Japan's involvement in the ICH and the problems it encountered in presenting its views on racial difference. As I explained in Chapter 4, the MHW shifted from bilateral negotiations at the MOSS to multilateral negotiations at the ICH. This made sense for several reasons: not only was the issue a truly global question but the change of venue reflected the image of Japan as a *nihonmaru* sailing confidently in the ocean of globalization.

Still, the issue of racial difference challenged everything that the Japanese took for granted about race and was subjected to tremendous scrutiny. Since the MHW did not officially contest the Western belief in the basic unity of human beings, it was not going to be easy to construct an argument for Japanese exceptionalism. The process proved highly irritating and nobody liked it. As one European expert said to me, "You know, we were the ones who first proposed the issue of racial difference, yet it was Japan that turned it into an infamous problem and made solving it impossible. Unless they separate race from the state, there will be no solution to this problem. Every solution is a political one." His frustration is understandable, but really the problem is neither political nor commercial: it is a cultural problem. For Japan, race and the state are inseparable. The *nihonmaru* cannot sail under any flag but the *yamato tamashi* (Japanese soul), and the *minzoku* has to run up this flag.

And there is much to be learned from the debate that so frustrated both sides. It is clear that when the MHLW mentions the word *minzoku* it sincerely imagines a group of ideal Japanese men and women, culturally pure and biologically homogenous. This does not necessarily imply racist thinking, such as the superiority of the Japanese race to other Asian races, but when I asked an Organization for Pharmaceutical Safety and Research (OPSR) officer about multiethnic Japanese, whom the current E5 policy would by

definition fail to address, he was quite confounded by the question. "I have to admit that we did not think of them when making this guideline."

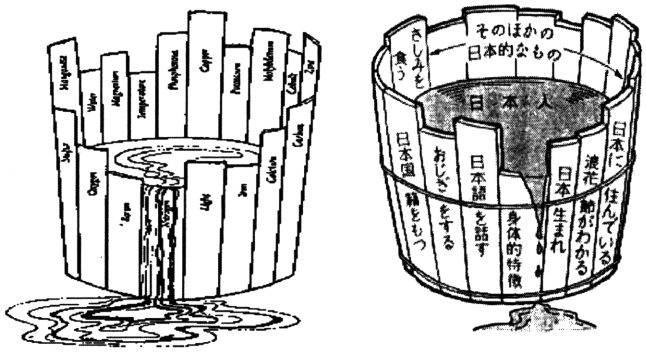
We also learned that in the discussion of racial difference the traditional criteria for defining a given *minzoku,* such as living in the same area, sharing a common culture and historical experience, and having a consciousness as a community, were irrelevant. In addition, although extrinsic factors were numerous and more complicated than intrinsic ones, they proved less important in determining membership in the Japanese race. The MHLW treated biological characteristics as the most basic features. This is strikingly different from academic discussions about ethnicity among Western humanities scholars, who tend to focus on the cultural and social aspects of ethnicity. But while the MHLW proved willing to sacrifice the spiritual components of its definition, and was willing to reduce social and cultural factors into variables, it would not budge on bodily characteristics.

The MHLW's approach to defining *minzoku* resembles the metaphor anthropologists Wagatsuma and Yoneyama (1967) borrowed from the German botanist Justus von Liebig (1803–73), who explained the essential nutrients needed by plants in terms of a barrel whose staves each stood for one type of nutrient — one missing or inadequate stave and the barrel was useless. For the two anthropologists, identifying a person as Japanese meant determining that all of the critical staves were in place (see fig. 8.6, right). Wagatsuma and Yoneyama identified the following criteria (from left to right, front row first): holding Japanese citizenship, following Japanese etiquette, speaking Japanese, having Japanese bodily characteristics, having been born in Japan, understanding *naniwabushi* (a traditional Japanese story), living in Japan, eating *sashimi* (sliced raw fish), and miscellaneous other Japanese traits. Although each of these criteria is essential, they are of varying importance. A glance at the illustration immediately reveals that the level of the water is only as high as the shortest stave, which corresponds to the most crucial qualification, in this case bodily characteristics. Physical appearance is the dominant factor leading others to consider a person Japanese.

Of course, according to Wagatsuma and Yoneyama (1967: 158), these biological characteristics can be explained by the theory of genetics: "The [above] argument about Japanese *minzoku* would run into serious problems if it failed to verify what its biological base was." To replace the ideal image of a perfect Japanese, they proposed a "pattern theory" based on the characteristics of the entire Japanese population, assigning it the term "genetic group" (*yidenshishudan*). This approach ranked the relative importance of characteristics by their significance in the gene pool, and the homogeneity of this pool

could be explained historically, by Japan's long isolation from other groups. All seemed to be perfect.

Fig. 8.5. *Left,* Von Liebig's Barrel, Representing Plant Growth Factors; *Right,* Wagatsuma and Yoneyama's Barrel Chart of Japanese Traits



Sources: *Organic Gardener's Composting,* chapter 2. http://www.soilandhealth.org/03sov/0302hsted/030202/03020202.html (left); Wagatsuma and Yoneyama 1967: 147.

However, if we compare Japan's changing conception of *minzoku* with Donna Haraway's three configurations of race, population, and the genome (1991: Chapter 6, see a brief summary in the table 4.1 of this thesis), their divergence become apparent. When Wagatsuma and Yoneyama apply population genetics to the problem of explaining the Japanese *minzoku,* they still stick to the old configuration of race. Rejecting the term *population* in favor of the more neutral — and more Japanese — term *group,* they failed to explain whether the boundary surrounding the *minzoku* was open or sealed. While they noted an increasing foreign influence on this gene pool (through interracial marriages, for instance), Wagatsuma and Yoneyama were confident of the "internal circulation" of genetic information, which was Japanese. "It is very subtle, like a Zen dialogue," they commented obscurely (158–59). In other words, nothing has changed: they were just using a new lexicon to talk about Japanese race.

Does this shed light on the MHLW's "scientific" problem at the ICH? The ICH deals with human beings in terms of populations, but this does not guarantee that all of the conference's experts are talking about the same thing. In an article on the unresolved debate between Robert Boyle and Thomas Hobbes on the existence of the vacuum, Daiwie Fu (1995) has shown why communication broke down. According to Fu, the

question was not who was more truly scientific or who was more objective — the real problem resided in an incommensurability between two proposals based on different configurations (or taxonomies) of nature. The E5 guidelines and bridging study illustrate just such an incommensurability. While the European Federation of Pharmaceutical Industries and Associations (EFPIA) and the Food and Drug Administration (FDA) thought they were dealing with questions related to races found in different populations, the MHLW cared only about the Japanese race and population. The former assumed a fixed race and a mobile, open population, while the latter assumed that both were fixed and could not change.

While Paul Gilroy (2000) may present genomics as the ultimate solution to the age-old problem of racial discrimination, as STS researchers we have to suspend judgment. The MHLW's move to genomics was, I have emphasized, a strategic move that did not match up with Haraway's time frame. In effect, what the MHLW proposed was nothing but a genomic version of "genetic group" or *yidenshishudan.* Although the group relied on the most advanced technology, this neither led to the new forums Haraway identified, such as the Human Genome Diversity Project, nor did it update old issues related to population, such as the shift in the frequency of certain traits in a genetic pool. Race — more exactly, *minzoku* — remains the core of this proposal.

Let me explain the above point via the HapMap Project. The HapMap is a catalog of common genetic variants that occur in human beings. It provides information about these variants, the places where they occur, and their distribution among different populations. Thus, it can be considered an extension of the Japan SNP project (mentioned in Chapter 6) to the global level.[18] Because of its previous achievements in genetic research, Japan has played an important role in this project. Unlike the controversial Human Genome Diversity Project, the HapMap looks ahead: its goal is the creation of a resource that can be used in future studies of health and disease.[19] Instead of collecting

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[18] The International HapMap Project is designed to provide information that researchers can use to link genetic variants to the risk for specific illnesses; it is hoped that this will lead to new methods of preventing, diagnosing, and treating disease.

[19] According to "Background on Ethical and Sampling Issues Raised by the International HapMap Project" (International HapMap Project's website), the purpose of the HapMap differs from the Human Genome Diversity Project. The latter is an anthropologically oriented effort proposed more than a decade ago that was designed to learn about human population history and the biological relationships among human populations. The point was "to see if, for example, the Irish are more closely related to the Spaniards or to the Swedes," according to the project website. A number of groups representing indigenous peoples were concerned that the project would exploit vulnerable individuals and populations. They also objected to the project's potential intrusion into cultural beliefs about population origins. Ultimately, and in large measure because of the criticisms, the Human Genome Diversity Project was never completed.

genetic material from small, isolated populations to show how races are different, the HapMap project aims at major populations to ensure the bio-products produced by those who rely on the HapMap findings suit those populations. Fine. But I would like to know what criteria have been used to designate certain populations as the racial standard of the future. The answer might be complicated for some, but not for the people of Japan: they know that those who care most about the survival of their race should be represented. The Japanese would fight to be chosen for this global project. The consequences are predictable. As the Japanese are one of only two races making up the Asian contingent in the HapMap study, research will be aimed at identifying genetic difference between the Japanese and other populations. The more we know, the more we know how different they are. New drugs have to be designed in accordance with these differences, as the information offered is the scientific standard for racial difference.

On the other hand, we cannot forget the ultimate goal of the Human Genome Project and the HapMap Project. Both use discrete populations to develop a range of individualized, customized medicines. The claim is that the HapMap "promises to accelerate medical research around the globe in many different ways. Not only will it lead to the identification of genes related to disease, it should help to pinpoint genes that influence how individuals react to various medications, discoveries that could improve drug design and lead to the development of diagnostic tools aimed at preventing adverse drug reactions" (International HapMap Project's website). In his argument for stemming new forms of eugenics in the age of genomics, Paul Rabinow said, "Perhaps some researchers should keep their data banks open to the possibility of looking for and discovering individual genetic variation" (1996: 127). If Rabinow is right, we are compelled to ask whether the trend toward individualized medicine will be the same in Japan and other parts of the world.

The answer is *yes* and *no. Yes,* because Japan has taken part in the Millennium Project, and this information is helpful in finding different genomic composition among individuals. Several diseases specific to Japan's aging society have been given first priority, and it is expected that in the near future more and more Japanese patient populations will be identified by genomic information. Even so, the answer is also *no,* because no such change would be possible without relying on the category of race. I have previously mentioned that the JSNP project is so expensive that no industry can afford it; even so, the Japanese government is willing to support it because it will help define the Japanese race. There is little likelihood that Japan will invest soon in any project that does not directly affect its own population.

Therefore, while moving toward genomics, Japan may not follow the path Haraway has predicted for the United States. Instead of developing a universal genome that describes all potential human beings, the Japanese genomic *yidenshishudan* will identify various clusters with similar genomic compositions. After all, the landscape of the Japanese *minzoku* overlaps with the territory of the Japanese state. As Wakatsuma and Yoneyama claim: "To preserve that which is of greatest concern, our *minzoku,* all sources of variation — identities, locations, and occupations — should be sacrificed to the concept of unity" (1967: 160). For *unity,* read *state.*

Although genomics is a promising source of solutions to current problems regarding the *minzoku* and hence a valuable tool for preserving the Japan state, it is far from guaranteeing the revival of the nation state. Perhaps Japan's engagement with globalization is ultimately driven by the determination to resist being "globalized" and "defaced" — all in the name of *minzoku.* Sawada (1990: 3) summed this up accurately fifteen years ago:

> In any debate about *kokusaika* it must be clearly stated from the outset that before the international must come the national, that is, *minzoku.* Therefore, before *kokusaika* the consciousness of the *minzoku* must be improved.

For Japan, the nation may never be distinguishable from race. In the era of globalization, it has chosen to construct its identity as a new nation-state in terms of Japanese genomics. Its govern-mentality has been endowed with the regulatory power needed to maintain this frame.

PART III
ETHNICITY AND THE STATE IN PARALLEL: TAIWAN AND GLOBALIZATION

Toward Democratization and Ethnic Controversies: The Taiwanese Experience Revisited

Taiwan's transformation over the course of its efforts to win a place at the table of nations has been an important theme in studies of Taiwan.[20] Even so, the state

[20] Since the mid-1980s, many have asked how the country's peaceful revolution took place. A series of works, from Robert Wade's *Governing the Market* (1995) to Thomas Gold's *State and Society in the Taiwan Miracle* (1986) and Stephane Corcuff's edited volume *Memories of the Future: National Identity Issues and the Search for a New Taiwan* (2002) have examined the process of democratization and political development; in addition, a special issue of the *American Journal for Chinese Studies* devoted to these

transformation I will outline here will be set in two contexts derived from my observations of Taiwan at the ICH. One context is that of race. In contrast to the MHLW's hesitation to accept foreign clinical data, the CDE has shown a more open attitude to racial difference. Might this be revealing of a more widespread Taiwanese attitude toward race? The other context in which I situate Taiwan's transformation is state sovereignty. While the CDE's E5 policy implies a consistent strategy to make Taiwan visible to the world, this does not necessarily imply a determination to build the nation.

In my study, race and sovereignty belong to a larger concern about the "normal" and "pathological" situation of nation-states. Having dealt with Japan's wish to be a "normal" country in the previous part, I would like to return to Nakasone Yasuhiro's view on Japan as an introduction to my discussion of Taiwan. The term "ordinary nation" is often used to describe the role Japan hopes to play in world politics, but this should not be taken either as a conventional expression of Japanese modesty or a sign for the revival of military nationalism. Like Nakasone, many Japanese are concerned that Japan is not yet a sovereign state. As a "semi-sovereign state" (*hanshuken kokka*), it has been economically threatened by the United States and for a long time it did not occupy a political role in the international community commensurate with its economic power.

The same was true of Taiwan in the 1980s. After its seat at the United Nations was taken by the PRC in 1972, Taiwan's political relations with other states began to wither away. Increasingly isolated, even Taiwan's formal name, the Republic of China, was confusing for most people. Its stated ambition of reclaiming mainland China could only be treated as a joke: it earned no support from the United States once relations with the People's Republic had been normalized and certainly was no threat to its Communist neighbor.

Like Japan in the late 1980s, Taiwan gradually revealed the role it wanted to play in the world. Beginning in 1976, President Chiang Ching-Kuo, the son of Generalissimo Chiang Kai-Shek, took steps that indirectly contributed to Taiwan's liberalization and democratization. In 1987, Chiang put an end to the state of martial law that had existed since 1949. According to his eventual successor, Lee Teng-Hui, Chiang realized that the KMT, a political entity grafted violently onto Taiwan in the wake of Communist victory in China, would never replace the PRC; without Chiang's policy of indigenization (*bentuhua*), the KMT would have been doomed. Chiang made a point of traveling to different areas in Taiwan, presenting himself as close to the people. Not long before his

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issues will be published in 2005.

death, Chiang made the ultimate ethnic claim: "Having lived here for over forty years, I am Taiwanese too [*wo ye shi Taiwanren*]" (Lee 1987).

Chiang died in 1988. His proposals for political reform were followed by Lee Teng-Hui, the first Taiwan-born chairman of the KMT and president of the Republic of China. Chiang's professed Taiwanese identity looked less convincing once Lee took office, since he was, by any standards, a "real" Taiwanese. Here I feel obliged to briefly describe the ethnic politics in Taiwan. Taiwan has three major groups: Holo, Hakka, and mainlanders (*waishengren*). Although mainlanders are the smallest, they long monopolized prominent positions as government officials, bureaucrats, intellectuals, military officers, and, less prominently, soldiers. They are generally considered more "Chinese" than other groups and thus better suited to the task of leading the "Republic of China." But while he is an educated man and an intellectual by any standard, Lee Teng-Hui does not belong to this group and his leadership has been strongly criticized by Nationalists. When he proved a highly popular leader, they grew even more concerned that his evident preoccupation with specifically Taiwanese affairs might divert the KMT from its primary mission — defeating the PRC.

Let us take a step backward to reconsider what Chiang Ching-Kuo meant when he said "I am Taiwanese too." As ambiguous as the English translation, Chiang's Chinese sentence could well have meant that he was *both* Chinese *and* Taiwanese. Some might think this statement is meaningless, since according to the KMT's logic all Taiwanese are Chinese. But if we are to appreciate the nuance of this sentence we must consider its political context. Given that he was officially the leader of the ROC and claimed sovereignty over a far larger area than Taiwan's 14,000 square miles, why mention Taiwan in particular here? Perhaps he wanted to avoid the vague, unrealistic claim that "we are all Chinese." Such a claim would not help the KMT win any support and could conceivably provide an excuse for the PRC to "liberate" the last territory that the KMT controlled. Chiang's statement served two functions, providing a bridge between the KMT and the people of Taiwan and separating the Republic of China from the People's Republic of China. But since Chiang never made these implications explicit, terms such as "citizenship" (*shimin*), "nationality" (*guoji*), "ethnicity" (*zuchun*), and "race" (*jongzu*) were all touchy issues for Taiwan on the way to democratization.

The controversy over ethnicity and nationality is clearest in Taiwan's elections. Since 1994 Taiwan has held national or local elections almost every year (table 8.1). Since candidates are allowed to campaign for sixty days prior to any election, it is safe to say that over the past decade elections have been a regular topic of discussion for many Taiwanese.

Table 8.1. Elections Held in Taiwan, 1994–2005

Year	Elections	Scale[21]
1994	Taiwan's first direct gubernatorial election	Local
	Taipei's first direct mayoral election	Local
	Kaohsiung's first direct mayoral election	Local
	Election of Taipei city councilors	Local
	Election of Kaohsiung city councilors	Local
	Election of Taiwan's provincial assembly	Local
1995	Election of legislators	National
1996	First direct presidential election	National
	Election of national assembly members	National
1997	Election of county magistrates and provincial municipality mayors	Local
1998	Election of legislators	National
	Election of Taipei mayor	Local
	Election of Kaohsiung mayor	Local
	Election of Taipei city councilors	Local
	Election of Kaohsiung city councilors	Local
	Election of county and city council members	Local
	Election of township magistrates	Local
2000	Taiwan's second direct presidential election	National
2001	Election of legislators	National
	Election of county magistrates and provincial mayors	Local
2002	Election of Taipei city mayor	Local
	Election of Kaohsiung city mayor	Local
	Election of Taipei city councilors	Local
	Election of Kaohsiung city councilors	Local
	Election of county and city council members	Local
	Election of township magistrates	Local
2004	Taiwan's third direct presidential election	National
	Election of legislators	National
2005	Election of national assembly members	National
	Election of Taipei mayor	Local
	Election of Kaohsiung mayor	Local
	Election of county magistrates and provincial mayors	Local

Source: Election Study Center, National Chengchi University, http://www2.nccu.edu.tw/~s00/.

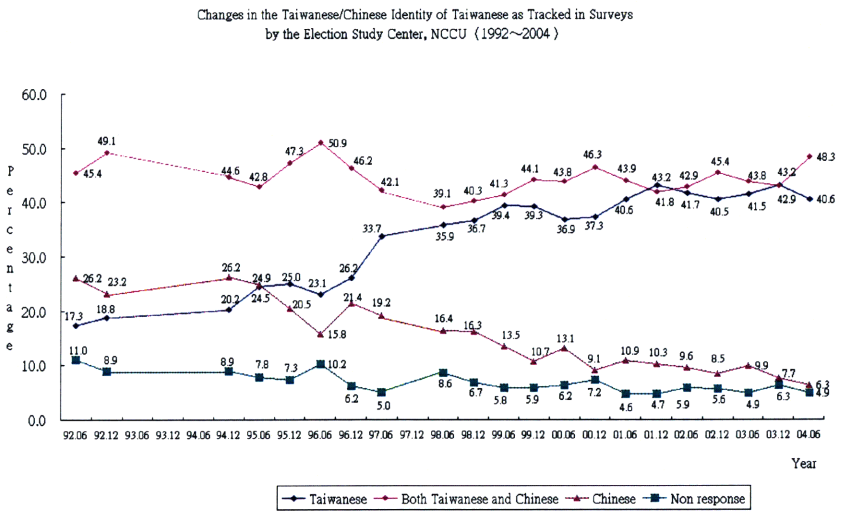
[21] Officially the term national refers to the City of Taipei, and the City of Kaohsiung, and the Taiwan-Fujian Region (which is all of Taiwan except for the two biggest cities). Local is just one of the three. But in reality there is almost no difference, since Taiwan-Fujian Province accounts for over 95% of Taiwan's land, and Taipei and Kaohsiung host over one-sixth of Taiwan's total population. Although the relevant posts are of very different importance and power, there is no difference between local and national elections in terms of their effectiveness as a topic for discussion among Taiwanese.

Whether on television or the radio, candidates and issues are ceaselessly discussed and candidates appear again and again on hugely popular television talk shows. In southern Taiwan housewives and retirees are exposed to the torrent of political talk throughout the daytime as well. As the critic Chen Sheng (2004) commented, the Taiwanese have been largely "kidnapped" by these media.

Taiwan's mass media constructs an intensive discursive matrix on which the elections mark periodical festivals; discussions of race and national identity serve to fill in the intervals. This network has a connection to the real world; the result of every election feeds back into people's thoughts about themselves and the future of their country. Businesses are created to serve people's craving for information: polling companies, companies that run election campaigns, public relations companies, political analysts, and, of course, talk shows.

Though it remains somewhat ambiguous, the people of Taiwan evidently are shifting their identification from "Chinese" to "Taiwanese" or "both Chinese and Taiwanese." As shown in figure 8.6, identifying as Taiwanese has risen dramatically from 17.3% in 1992 to 40.6% in 2004. Meanwhile, the percentage identifying themselves as Chinese has declined from 26.2% to 6.3%. Still, fifteen years after Chiang's declaration, almost half of the inhabitants of Taiwan have not settled on a clear identity.

Fig. 8.6. Changes in Taiwanese/Chinese Identity, 1992–2004



Source: Election Study Center, National Chengchi University, http://www2.nccu.edu.tw/~s00/eng/data/Political%20Attitude02.htm.

Of course, the conventional explanation of this trend is that ethnic politics is being used to manipulate the populace; candidates rely on emotional slogans, appealing to ethnic identity, national identity, or nationalist politics to mobilize specific ethnic groups. According to this interpretation, repeated mobilizations have polarized the Taiwanese people into two opposed camps: the Holos seek clear-cut Taiwanese independence, while the mainlanders hope to merge with the PRC. But then why do nearly half of Taiwan's voters identify as "both Taiwanese and Chinese," as Chiang Ching-kuo did eighteen years ago?

If we apply Japan's experience of *kokusaika* to Taiwan, perhaps we can figure this out. As I have explained previously, Japan's *kokusaika* exposed existing racial problems and challenged the old definition of *minzoku.* During recent decades, the people of Taiwan have had increased exposure to foreign ignorance and curiosity about their country. These experiences, as Wang Horng-luen (2004) pointed out, have forced them to clarify their identity. Frequently mistaken for citizens of the PRC (the words *Republic of China* on a passport look a lot like *People's Republic of China*), Taiwanese have assumed a dual identity. Culturally they are *Huaren* (Han-Chinese), but politically they are *Taiwanren* (Taiwanese).

While Taiwan has enjoyed remarkable political stability during a period of democratization, tensions about race do occasionally burst out as open quarrels, especially during election campaigns. While mobilizing their supporters, candidates link their positions to specific ethnic groups. So far, this domestic political divisiveness has not led Taiwan to deviate from its course in the realm of international politics.

Taiwan, *Quo Vadis*? A Reading of the 2004 Presidential Election

The 2004 presidential election marked the climax of a long debate over race and state.[22] Led by the KMT chairman Lien Chan and the People First Party chairman James Soong, Pan-Blue lost to the incumbent president and vice president, Chen Shui-bian and Annette Lu, by a mere 29,518 votes out of nearly 14 million. The 0.228% margin was surely a disappointing loss and led to a week of protests that climaxed with a protest attended by 450,000 people demanding a recount. As with the 2000 United States

[22] Pan-Blue was a coalition made up of the KMT and its two offshoots, the People First Party and the Chinese New Party. Basically their political attitude toward the PRC was conciliatory. Pan-Green was a coalition made up of the ruling Democratic People's Party and the Taiwan Solidarity Union, an offshoot of the KMT devoted to promoting Taiwan's values and the right to self-determination.

presidential election, the debate will never be resolved. Among other claims, the protesters accused Chen of using dirty tricks to influence the election.[23] My interest in all this is how racial metaphors were deployed over the course of the campaign.

It was Lien Chan who opened the quarrel on race. During a pre-election visit to the United States in 2002, Lien was interviewed in Washington, D.C., by some Taiwanese journalists. While his exact words remain in dispute, all agree that during the interview Lien expressed pride in being a pure Chinese. And in a public speech at the National Press Club which was published later under the title "Taiwan and the KMT, *Quo Vadis*?" Lien (2002) repudiated the "Taiwanese versus mainlander" construction in favor of the larger Chinese category, noting that "no matter what those who agitate for Taiwan independence tell you, the fact remains that more than 98% of the people on Taiwan are ethnically Chinese, speak one or another Chinese dialect, and remain indelibly stamped by Chinese culture" (2). For him, this racial fact implied a need for political unification. Since all Taiwanese are Chinese, Taiwan should be a part of a unified China (the Republic of China, Lien insists). Overlooking the multiethnic nature of the PRC (the state officially claims fifty-five ethnic groups), Lien argued that ethnic and linguistic affinities, along with existing connections between the PRC and Taiwan, militated for a revival of the unspoken agreement the two parties reached in 1992: "One China, interpreted differently by each side," an arrangement that did nothing to alleviate the problems caused by the ambiguity of Taiwan's political status.

Chen Shui-Bian, president of Taiwan since 2000, differs from Lien Chan in many ways. Born and raised in a rural town in southern Taiwan, Chen has always emphasized his Taiwanese identity. Speaking to Holos, Chen is fond of making racist claims that Taiwan has to belong exclusively to the Taiwanese. When visiting Hakka towns, he likes to claim that although his family has resided in Taiwan for one hundred years, he is related to Hakkas as well. "My home town is the Hakka town Shao-An; I am a Hakka," Chen once confirmed. Yeh Chu-Lan, the former chairwoman of Taiwan's Council for Hakka Affairs, once said, "We Hakkas always treasure the bonds within our group; for this reason, we must support our Hakka candidate, Chen Shui-Bian" (*Taiwan Ribao* [Taiwan Daily], December 8, 2003). When meeting mainlanders, Chen emphasizes his ties with mainland China. Chen might, for instance, speak of his family's ancestral home in Fujian Province, expressing the hope that some day he might go for a visit (*Dongsen*

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[23] These accusations include the following: Chen faked an attempted assassination just one day prior to the election; Chen was involved in fraudulent voting; Chen used the faked assassination to heighten national security, which kept Pan-Blue supporters from voting. For details, see *Bulletgate* (KMT 2004).

Xinwenwang [ET Online News], April 25, 2002). Despite all of these conflicting claims, Chen does not hesitate to advocate a united Taiwanese polity. "Like America," he has said, "Taiwan is an immigrant country. [. . .] We came here at different times, for different reasons, but we all love the place where we live. Taiwan is the place that links us; everyone who loves Taiwan is Taiwanese" (ibid.). In this passage, Taiwanese identity floats unmoored from a racial quality to a cultural identity, finally anchoring on patriotism.

Although neither Chen nor Lien has explicitly linked Taiwan's political future to its racial base, they like to accuse each other of racially-based nationalism. For example, since Lien contends that the preponderance of Han Chinese in Taiwan necessitates setting aside ambitions for national sovereignty for the sake of an uncertain unification, he is criticized for "Greater Chinese nationalism" (*da Zhongguo zhuyi*). Among Chen's weak points is his vulnerability to being attacked as a "Holo-centric Taiwanese nationalist" (*Fulaosawen zhuyi zhe*). In short, while Lien's racial plan is criticized for its political implications, Chen's practical plan is liable to attacks for its racist implications.

Fig. 8.7. *Left,* a Poster Indicating That a Vote for Candidate Number 1 Is a Vote for a "Taiwanese Person" (Below the Number 1 is the Word *Taiwanren* in the Traditional Chinese Characters Used in Taiwan), While a Vote for Candidate Number 2 Is a Vote for a "Chinese Person" (Below the Number 2 is the Word *Zhongguoren* in the Simplified Chinese Characters Used in the PRC); *Right,* a Pan-Blue Campaign Advertisement That Compares Chen Shui-Bian's "Dictatorship" with That of Hitler

Sources: KMT 2004:16 (left); *Lianhe Bao* [Unity News], March 12, 2004 (right).

As the campaign heated up, things took on an increasingly racist tone. It was suggested by some of Chen's supporters that he was the Taiwanese candidate and Lien was the Chinese (read, Communist) candidate (fig. 8.7, left). Some from the Pan-Blue camp took off their gloves and drew up a full-page newspaper advertisement whose headline — "Get rid of the president — end A Bian's [i.e., Chen Shui-Bian's] dictatorship" — accompanied a photograph of Adolf Hitler, accusing him of being not a peacemaker but a dictator (fig. 8.8, right). The accompanying text reads, in part, "Only a dictator equates himself and his country. A Bian thinks he is a symbol of democracy, but he is hostile to those who oppose him, treating them like enemies."

Upon the publication of this advertisement, Taiwan's Jewish community promptly condemned it for implying that Chen planned to "cleanse" Taiwan by sending all mainlanders to mainland China. Rumors spread. Some said, "Chen considers us 'Chinese pigs' and will sink us in the Taiwan Straits if he wins." KMT spokesman Justin Chou's remarkable comment that the advertisement "only tried to emphasize a certain aspect of A Bian's personality" did not placate the Jewish critics. Ephraim Einhorn, Taiwan's only rabbi, called on the KMT to apologize, saying he was "shocked and disturbed" that Chen could be compared to a man who had ordered the murder of six million Jews. He said, "I am sick to my innermost being. It's a terrible thing to have done" (*Taipei News,* March 13 2004).

In another racist gambit, a KMT spokesman named Tsai Chen-Yuan claimed that of all the candidates to run in a Taiwanese presidential election, only Lien was a "pure Taiwanese" (*ET Online News,* June 19, 2003). He reasoned that since Sun Yat-Sen (who founded the Republic of China), Lee Teng-Hui and Chen Shui-Bian (the first and second Taiwan-born presidents of the ROC) were all originally Hakkas, and Chiang Kai-Shek and his son Chiang Ching-kuo were born in southern China, Lien was the only one of the bunch who had been born into an authentically Taiwanese Holo family and hence was the only candidate qualified to serve as Taiwan's president.[24] Though insulting, this was hardly the worst part of Tsai's comments. To the Hakka community in Shao-An, home town of both Lee Teng-Hui and Chen Shui-Bian, Tsai applied the pejorative label "shabby Hakkas" (*ao ke*).

Naturally Chen responded to the attacks from the Pan-Blue camp. He asked Lien in public debate on February 21 to clarify what he meant by "pure Chinese." Tactically assuming Lien's Chinese nationalism and his unwillingness to answer this question, Chen misleadingly suggested the alternative category "pure Taiwanese" in an attempt to get

[24] Lien liked to say that his family was among Taiwan's oldest. One of his television advertisements

Lien to admit that he was a "pro-PRC" Chinese. Rejecting this accusation, Lien called this question "a new McCarthyism" and declared that he had never been to the PRC. Chen coldly replied that there was little doubt that the PRC would embrace any candidate who called himself "pure Chinese" (PBS on-line broadcasting at http://www.pts.org.tw/~web01/debates/).

The outcome of the election pleased no one. Elected by the slenderest majority, Chen saw his mandate slip even lower during the demonstrations mounted by the Pan-Blue camp in front of the presidential palace. Both sides were blamed for "tearing Taiwan apart with their racist accusations" (*zuchunsirie*). Those who hoped for reconciliation turned to bodily metaphors to counter all of the racist slogans tossed about during the campaigns. A group of students in Taipei collected the tears of ten thousand men and women to "wash away" all discrimination and injustice. A local artist announced a four-year project for world peace called "Actions of Blood Mixing": inspired by the election, he planned to collect blood samples from ten thousand people in ten places around the world, starting with racially divided Taiwan (*Dongsen Xinwenwang,* April 24, 2004). He said, "I hope that everyone will embrace each other by mixing blood. We are all one family. We want no more war, no more hatred, and we will only bleed more if we resist mixing our blood"

The foregoing passage might lead some readers to worry about Taiwan's future. Indeed, looking at local events, many wonder whether Taiwan can uphold its democratic integrity while entering the global sphere and they fear that it may fall apart because of conflicts among ethnic groups. But when we move shift the scale from the domestic to the international, we will find that a totally different image of Taiwan and a different set of questions emerge. They may be important, but race and ethnicity belong to the vulgar realm of domestic politics. At the global level, Taiwan is relevant to one question alone: that of the state.

If so, why has the issue of ethnic identity continuously dominated Taiwan's public sphere in every election? The answer may be an understanding on the island's ethnic politics in practice. Race is indeed an issue that mobilizes voters, but it is not about to precipitate a crisis.[25] In many situations, these quarrels are nothing but a response to

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was set in his home town, Tainan, said to be one of the first Han Chinese settlements on the island.

[25] Over fifty years after the KMT immigrated to Taiwan, the distinctions among the various ethnic groups are blurring. The new generation of mainlanders, many of whom have one Taiwanese parent, live lives essentially indistinguishable from those of any other Taiwanese. And many of the Hakkas and Holos born and raised in Taiwan under the KMT regime speak Mandarin as their first language and are as well versed in Chinese history as any mainlander. The old ethnic differences have been replaced by regional and

emotional electioneering rhetoric. As an editorial in *Yi Zhokan* (the Next Magazine) pointed out after the election, "Our world is built from empty language. [. . .] The same language, the same world. But from the point where this world is conceived lives develop along quite different lines" (May 27, 2004).

Moving onto the global scene, political analysts have pointed out many external threats to Taiwan's future, and there is no space specifically for ethnic politics. The thorniest threat lies to the west: the PRC. Although it employs the racial slogan "Chinese do not beat Chinese" (*Zhongguoren bu da Zhongguoren*) to support its proposal of acquisition, the increasing military threat proves that Beijing's ultimate goal is to grab this land even if that means destroying all of its political institutions. The United States hopes that Taiwan will remain an ambiguous entity, not at all influenced by the PRC. A Taiwanese government friendly to America can balance the expansion of communist power in the western Pacific region. For the Taiwanese government, any attempt to clarify its status would be interpreted as a move in the direction of independence, and this violation of the political picture drawn by the two powers would reinforce the global consensus that Taiwan is a troublemaker.

This reminds us that the CDE, the state, rather than the question of race, functions as both the motor and the vehicle in the creation of a voice. In Chapter 5 I showed that in order to make a bridging study workable the CDE introduced a paper asserting the existence of a Taiwanese race distinct from the Han Chinese to shore up its claim that Asian races are biologically similar. And in Chapter 7 I mentioned that at the 2003 APEC statistical symposium Professor Shih intentionally included the national flag of the ROC in his presentation. What sort of nationalism do these different events signify?

I remember a conversation I had with a Taiwanese official from the Department of Health after last year's presidential election. I raised the subject of nationalism. "Nationalism? Using that word is a luxury!" she cynically replied. A longtime observer of Taiwan's campaign to join the World Health Organization, she is keenly aware of how difficult the PRC makes it for Taiwan to be seen and heard. She told me, "There will be no nationalism if we cannot survive in this world as a state." Ignoring the discursive context that social scientists have constructed so that Taiwanese nationality is inextricably bound up with race and nationalism, this official thinks of statehood simply and empirically in terms of being seen and fitting into the global network. Through this vision I see an intermediate matrix between the individual and the world, which I call practical statehood. From a global perspective, the existence of a practical state is legitimized by

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class differences.

its ability to render visible a certain population by regulating its relations with other populations. In the case of the ICH, the CDE projects this kind of statehood in two ways. The bridging study allows it to relate the Taiwanese racially to other Asians. And its take on Asian regulatory authorities permits it to distinguish Taiwan from other entities.

Only from this perspective can we grasp Taiwan's real relation to nationalism and state building. Conventional sources of legitimacy — Benedict Anderson's "imagined community" and Pierre Bourdieu's powerful bureaucracy — do not apply to Taiwan. Nor is political autonomy the issue, since Taiwan has enjoyed that for more than a half century. The problem is that unlawful repression has deprived it of political rights in the world. This is a tricky situation. Clearly, any nationalistic attempt to change Taiwan's status — whether by achieving the full status of a nation-state or by becoming a special territory under the control of the PRC — is not favored by a majority of the population. But the people do not seem to favor the status quo either, since globalization has brought home to everyone the disadvantages of international political isolation. This is the reason why the CDE's efforts are appreciated by all of the people I interviewed, no matter their political preference.

Performative Statehood in a Global Panorama: The Welcoming Banquet at the 2003 APEC Meeting

Taiwan's failure to gain formal recognition as a state means that we must think of it in a new way, that is, as an entity whose statehood exists performatively. In Chapters 5 and 7 I described Taiwan's appearance on the global stage. The voice that I examined there first emerged from various individuals and in time became a unified and institutional voice. Even so, when we talk about voices, the question of agency is fraught, since a voice cannot be recognized alone.

Performativity, a concept the cultural anthropologist Victor Turner developed in his study of liminality (1969), is indebted to Arnold Van Gennep's concept of rites of passage. According to Turner, liminal entities exist between structures: they are "neither here nor there; they are betwixt and between the positions assigned and arrayed by law, custom, convention, and ceremonial" (95). Taiwan is such a liminal entity, trapped between the Cold War and the New World Order (for a historical study of a population control program, see Kuo 2002); its statehood was assumed and defended by the United States during the former but is now despised and rejected thanks to the dawning of the latter. But is this true statehood? Turner suggested another sort of grouping, a society "unstructured or rudimentarily structured [with] a relatively undifferentiated

communitatus, community, or even communion of equal individuals who submit together to the general authority of the ritual elders" (Turner 1969: 96). Apparently, the world of proprietary drugs is a *communitatus.* The ICH is trying to give it a structure but it is not yet stable. Only at this inchoate moment does Taiwan's statehood perform, and this performative statehood cannot to be easily transferred to other fields.

Taiwanese statehood, which I consider in the context of the discussions of E5 guideline on racial difference, can only be seen during rehearsed performances on a global stage. These performances take place at welcoming receptions, cultural nights, and city tours. Ancillary to the conference's main activities, these activities are important rituals that create connections between host and participant. Since Taiwan has been denied access to the formal channels through which interstate connections are made, it places special emphasis on these ancillary events, another place where its voice can be heard.

I observed the welcoming banquet for the 2003 Asia-Pacific Economic Cooperation meeting on Bridging Study (the APEC meeting hereafter) held in Taipei on November 17, 2003. This banquet, along with the cocktail reception that preceded it, reminded me of Yoshimi Shunya's description (1992) of world exhibitions and the display of modernity. Originating in the nineteenth century, these great expositions served as both platforms for the flow of capital and displays of empire in the process of modernization. In the APEC microcosm of the global and the local, I was both a participant and an observer. As representatives of industry, government authorities, and scientists greeted one another, exchanged cards, and traded information, I observed their interactions, occasionally joining a conversation as a researcher or a local helper.

I started with participants from the FDA and Europe. The former, few in number, occupied the center of the hall, attracting people like a magnet. Some people from a European company haled an EFPIA official, chatting in their own language until I briefly joined their conversation on the pharmaceutical industry in Southeast Asia, which they viewed as a new market to be conquered. Compared to the Western participants I had been observing, the Japanese and Koreans seemed reluctant to step out of their circles. Some Japanese bureaucrats and professors briefly exchanged ideas with colleagues and their Taiwanese branch mangers, while others discussed domestic issues in Japanese. One Japan Pharmaceutical Manufacturers Association (JPMA) representative I knew recognized me, but he only nodded politely without saying anything. From his serious demeanor, it was hard to believe that just a few months earlier he had treated me to dinner at a restaurant in Tokyo, joking to the waitress that the two of us were going to drink

ourselves to death. Spotting some Southeast Asians off by themselves, I could not help thinking that they looked lost and helpless. An exception was John Lim, the director of Singapore's Centre for Drug Evaluation, who moved from group to group like a busy bee.

I looked back at the group from Taiwan. The locals certainly made up an absolute majority, but they were hardly taking the lead on this occasion. While the leading officials of the CDE and some Bureau of Pharmaceutical Affairs (BPA) officials greeted people around the reception hall, the rest formed immobile and impermeable circles against the wall. Roughly grouped by affiliation, most spoke in Taiwanese or Mandarin about their current work. I noted few interactions between the Taiwan-born FDA statisticians and local scientists, who had all participated in a special meeting just the day before.[26] Some research fellows of the BPA reached out, chatting with participants they had met elsewhere, but most simply stood mutely, looking as though they were waiting for instructions. When I passed by, I overheard one or two complaints about the purpose of this "international" meeting.

At such modern "panoramas" one sees the two faces of a state in the throes of globalization. In a scientific meeting one face shows the opinions and arguments presented by high officials and technocrats. The more important they are in their fields, the more attention they attract to their state. The other face shows the state in general. Its visibility coincides with its power in the world. This key permits us to explain the behavior of the different groups I surveyed at the reception — with the exception of the Taiwanese. Although hosting the meeting implied that the CDE had achieved a certain visibility, this did not mean that all of the Taiwanese men and women standing around the lobby understood what was going on. Their apparent disorientation bespoke Taiwan's long isolation from the world and revealed a conceptual gap in the crafting of Taiwan's statehood. While the government strives to attract the world's attention, most of its people simply take it for granted. The international aspect of this statehood, unlike that of Singapore, exists only at the governmental level and is restricted to certain fields.

The performative nature of Taiwan's statehood was well captured later, during the banquet proper. When Japan held a world exhibition in 1877, Yoshimi pointed out (1992), it was based on the European imperialist model and presented visualizations of the lands Japan then occupied. In 1970, nearly a century later, a rather different Japan mounted an exhibition in Osaka (Chapter 6). No longer a panoramic translation of the host's subjective worldview, the 1970 fair was a celebration of capitalism, advertising dreams of

[26] It is the 2003 APEC Statistical Meeting. For more about the meaning of this meeting and the people

the future. Though the United States seems to have lost interest in world exhibitions (the latest one was held in New Orleans in 1984), developing Asia is still fond of them — the Brisbane Expo in 1988, Tsukuba Expo in 1985, Daejeon Expo in 1993, Aichi Expo in 2005, and Shanghai Expo in 2010. They are the best way to propagate a state by celebrating its participation in the world. Although nowadays the host country cannot be the main focus that former empires were, it still seizes the opportunity to promote itself to the world.

The logic of organizing a global conference is driven by similar concerns. In Chapter 5 I conveyed how difficult it is for a "nonstate" like Taiwan to host such a meeting, so I am interested in how Taiwan makes the best of such events. While the guests ate, a local band performed songs from around the world. From my distant seat, I could only make out the end of a song by the applause that followed, so it was with some surprise that I discovered that the event was in fact karaoke. As far back as the 1920s, Taiwanese businessmen held banquets in entertainment districts or hot springs sites and hired live bands (*nakasi*) to entertain their guests. After a couple of songs by professional singers, the host, and then every guest in turn, would contribute a song or two. There exists an ethnographic meaning in this activity. In a group, everyone is asked to "voice" him/herself by the pieces they choose and how they are performed. It is one of the ways Taiwanese make friends. Something like karaoke has, as a result, existed in Taiwan for a long time.

For some Westerners who had never been to East Asia, karaoke was clearly a novel experience, and many were immediate converts. A Swiss pharmaceutical representative chose a ballad from the Alps and an EFPIA representative went with a French chanson. As two Filipinos sang, I saw how this custom neatly served to bridge the local and the global. As a modest host, Taiwan yielded the stage to its international guests, much as it would do over the course of the conference. But as with the bridging study procedure, the setting was Taiwanese and people were asked to project their customs into peculiarly Taiwanese (or East Asian, anyway) settings. The localness can be operationally defined as a territory where an indigenous style is appreciated. This is the key to understanding Taiwan's approach to the bridging study as well. Without emphasizing its distinctness, the atmosphere conveyed the place people were visiting.

I was curious to see what the locals would do when their turn came. Then twenty people stepped onto the stage. The CDE's executive director, Chu Mong-Ling, announced the first song: "Story from a Small Town" (*Xiaocheng gushi*). It was an

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who attended it, see Chapter 7, part 2.

inspired choice, originally sung in the movie of the same name by the legendry singer Teresa Teng (1953–95), who was hugely popular throughout East Asia even after her sudden death. Although the movie was filmed in 1978 in a small, old-fashioned town in central Taiwan, there is nothing particularly Taiwanese about the song. Written by Huang Ho, the lyrics are as follows:

> There are many stories in a small town, full of joy and happiness;
> If you visit this place, you will reap rich rewards.
>
> Looks like a picture, sounds like a song,
> Here is included all of the truth, virtue, and beauty in life.
>
> Chatting, talking, small-town stories are really good.
> Please invite your friends to come, and we will treat them as our guests in our small town.

This simple song suggests a range of associations. At the simplest level, it is a sweet homage to the good old days. Insistently referred to not by name but by a vague description, the small town of the title is anyone's home town. The conference hosts, known as "Chinese Taipei" at the APEC meeting, also suffered from a sort of nominal amnesia. The song, which of course could not be understood by many of its foreign auditors, conveyed a welcome, a humility, and a decidedly accommodating attitude toward the question of Taiwanese sovereignty.

The song's most profound meaning appears only in retrospect, as we reflect on the context in which the Taiwanese contingent sang. The lyrics neatly echoed Taiwan's performative statehood that emerged in the process of networking. To borrow Roland Barthes's comment about the subway station in Tokyo (1983: 38–40), Taiwan's statehood can be understood as an empty spot in a complex nexus. It is a center without a name, through which enormous volumes of information travel every day. Its importance, if it has any, does not reside in the place itself but in the amount of information that goes through. Let us read the messages the song delivered bit by bit. The reason given at the outset for visiting the small town (i.e., Taiwan) is its many stories (i.e., information). This is followed by the gently seductive suggestion that only if you visit can you be rewarded. Then we are told how "useful" these stories are: they can induce a highly spiritual experience unavailable through other means, because they are stories shared by all precious guests. Thus, it is not enough for people just to come and hear; they must bring

friends to make their visit to this town meaningful.

At the 2003 APEC meeting the song suggested a "decentered" network of information with Taiwan at one of the nodes. Consider how people relate to their destination when they embark on a pilgrimage: for them it is a sacred place where people can congregate. Of course, this song explains the utility of fulfilling these needs and answering these questions, but it is not merely a question of making a pilgrimage to Taiwan. Taiwan is not a place of worship; no god dwells there. It is simply a meeting point and could be anywhere. But then, the value of the global network is not evenly distributed over all of its points. Like an oasis in a desert, the importance of the "small town" is assigned by its visitors, not by anything within. People visit not to admire a certain spiritual existence but to meet others, to hear their stories. All of the people assembled there share their stories — this is what I mean by *placedness.* Taiwan's performative statehood has to go along with this dynamic process.

The CDE had one more song for its guests. Would it be a Mandarin pop tune or a Taiwanese ballad? I was thrilled to hear the familiar prelude to "High Green Mountain." Again, the choice was inspired. The theme song to the movie *A Mount Ali Story* (1949), generally considered the first postwar Mandarin drama, it is among the few Mandarin songs that has achieved a crossover popularity among Holos and mainlanders. In addition, because the movie set its story among the Tsoas, an Austronesian tribe inhabiting southern Taiwan, this song is rich in local color, including an interlude sung in the Tsoa language. Many consider this a Taiwanese folksong honoring the island's small indigenous population. Rather than an image of a nation based on a uniform culture and ethnicity, it presents a mixed cultural identity which truthfully reflects Taiwan's current situation.

More importantly, this song delivered a political message: gently but clearly, it announced that Taiwan was not a part of the PRC. In this sense, the Austronesian tone is an alternative means of emphasizing Taiwan's non-Han character. Of course, Austronesians are not the majority on this island; in fact, they make up the smallest and weakest ethnic group. So we might consider the use of this song a cultural tactic revealing Taiwan's placedness. It should not be interpreted either as a cheap exploitation of Taiwanese "exotic" culture or a facile and nationalistic demonstration of the essential differences between Taiwan and the PRC. From an anthropological viewpoint, this song is a cultural window through which Taiwanese society can be appreciated. I was reminded of the lecture where I first heard about the CDE (for more about this lecture, see Chapter 5, Part 2). The first slide shown by speaker Chu Mong-Ling to illustrate

Taiwan's bridging policy was a close-up photograph of the face of an old Taiwanese aborigine (fig. 8.8). Later I learned that this slide is shown in many presentations made by the CDE; the surprise of seeing a definitely non-Han face and being told that this is a Taiwanese person never fails to arouse people's curiosity.

Fig. 8.8. Slide Entitled "Taiwan Formosa," Showing an Old Taiwanese Aborigine

Source: Chu Mong-Ling's slide presentation at National Yang-Ming University, March 22, 2003.

But as I watched CDE staff members doing their best to mimic the Tsoa ritual dance, I grew keenly aware of the limitations of this statehood. After all, the life and language of the Tsoas are still strange to these Han Chinese. Taiwan is not ready to "live out" the multiethnic or international characteristics it claims. As I had seen at the reception, few of those involved in the performance understood the meaning of this meeting and the role they were supposed to play in it. Thus, Taiwan's statehood is neither actual nor fictitious — it is performative and only performative. I was reminded of Clifford Geertz's comments about Balinese cockfighting (1973). Drawing on the insights of structuralism, Geertz conveyed the profound logic behind this performance through thick description. But as I continued to watch the performance of statehood, my thoughts also traveled in another direction. I wondered whether there might be no cultural logic at work at all; was it possible that this was nothing but a song and dance? Postponing the nihilistic conclusion that the nation is an empty concept, I would like to call performative statehood an intentional construction in the global era. Taiwanese nationalism, if we can find it, should reside solely in this intention. Unlike Japan's determination to make the rest of the world recognize its distinctive racial attributes, Taiwan simply wants to escape from its isolation. It may not be ready to launch itself as a nation, but the desire to be seen and heard is present in every Taiwanese man, woman, Holo, Hakka, mainlander, and Tsoa.

CONCLUDING REMARKS: TRACING THE STATE WITHIN GLOBALIZAITON

After reviewing Japan's and Taiwan's distinctive responses to globalization, it is time to return to the quotations from Nakasone Yasuhiro and Lee Teng-Hui cited at the beginning of this chapter. If we extract their comments about "normal countries" from their original contexts, the speakers sound strangely old-fashioned, stubborn conservatives in an era of globalization. Almost universally, foreigners reject the suggestion that Japan and Taiwan are not states. While distinctively East Asian, they look like any other country. People around the world use their products and treat the words *Taiwan* and *Japan* as they would *France* or *Brazil.* This argument obtains support by comparing the two states to regimes such as Iran, Cuba, or the Palestinian Authority, whose religious fundamentalism, retrograde ideology, and history of political struggle have divided them almost completely from the norm of the state. After all, Taiwan and Japan have almost everything that constitutes a state. Moreover, they are practicing democracy in one way or another.

Some read Nakasone and Lee as commenters on the development of nationalism in Asia. Assuming Japan and Taiwan to be normal states, these readers, such as cultural critics in Japan or political opposites in Taiwan, project their words onto a larger political project. The process can be understood as follows: along with increasing their economic power, Japan and Taiwan are trying to expand their political influence, which some consider out of proportion to their current status. For example, because Japan was defeated in World War II, its pursuit of a permanent seat on the Security Council of the United Nations strikes some as improper. Similarly, comments by Lee Teng-Hui and Chen Shui-Bian about Taiwanese independence are considered outrageous by those aligned with the PRC. These political projects are seen as dangerous because they create tensions among "normal" countries. Japan's ambition is read as a revival of military nationalism, and Taiwan's quasi-diplomatic maneuvers have earned it the name of troublemaker in the western Pacific.

Why are Nakasone and Lee unsatisfied with the current status of their counties? Why do Japan and Taiwan still want to be "normal countries," if not because of overweening nationalism? To grasp the instrumental aspect of the formation of the state, Pierre Bourdieu's pioneering works are of great importance. According to Bourdieu (1998: Chapter 3), the state emerges as the accumulation of a process of concentration of different capitals, such as the "capital of physical force or instruments of coercion (army,

police), economic capital, cultural or (better) informational capital, and symbolic capital" (41). This is a bureaucratic field that functions as both a central bank where various capitals are exchanged and cashed and a generator that exercises these capitals. Since it is so, the state possesses a territoriality: when entering a state, everything is interrelated in one way or another. More importantly, people take on a *habitus,* a set of internalized and largely unconscious responses to specific social interactions, that blinds them to the logic by which the state is actually run: they simply think of the state as a combination of universal apparatuses. Through this *reason of state,* legitimacy is acquired to exercise physical and symbolic violence (58). Of course, Foucault's notion of governmentality, which I discussed earlier in this chapter, is based on a similar view.

While these scholars did not extrapolate their arguments to a global level, they did not rule it out. As I explained earlier, Foucault noted the governmentalized process of state transformation. Unlike historical states that may emerge through contingent processes, Foucault wrote, modern states are transformed in a more regulated way (1991: 102). Echoing this point, I argued that as an effort to create a single market for proprietary drugs, the ICH could be understood as a global platform created as part of the process of governmentalization. From a different perspective, Bourdieu emphasized (1998: 59) the interesting relation between the monopoly of the state and the monopolization of the universal: "The relative unification and universalization associated with the emergence of the state has for counterpart the monopolization by the few of the universal resources that it produces and procures." This observation can be applied to the formation of the ICH discussed in Chapter 2. The FDA's practice was extended into the global realm through the ICH, an institution that turns local rules into universal standards. Capitalism, as expected, plays a critical role in promoting this process, as Bourdieu pointed out:

> The profit of universalization is undoubtedly one of the historical engines of the progress of the universal. This is because it favors the creation of universes where universal values are at least verbally recognized and wherein operates a circular process of mutual reinforcement of the strategies of universalization seeking to obtain the profits associated with conformity to universal rules and to the structures of those universes officially devoted to the universal. (60)

In the case of drugs, science provides the universal standard. Through guidelines, it erects a stage where industry can accumulate more profits while the states involved present themselves as modern and progressive. The success of the ICH in harmonizing drug regulations is, in this sense, an *opus operatum* that looks like a fait accompli.

This is my starting point for thinking about the national problems of Japan and Taiwan. I believe that they should be understood beyond their borders and should be traced by distinguishing the *modus operandi* from the conventional discourse of *opus operatum* (Bourdieu 1973). Thus, what Nakasone and Lee mean by "normal country" is "country that enjoys normal relations with the world." In previous chapters, I provided a thick ethnography describing the actions that the MHLW and the CDE performed inside and outside of the ICH; in the present chapter, the end of my story, I provide a comprehensive account of their actions in globalization. (Note that my study is not a substitute for regional studies, which are of great value.)

Working from Bourdieu's idea of the state as a bureaucratic field, Horng-luen Wang (table 1.1) insisted on an institutional approach to the nation-state that took into consideration its interactions with other states: analysis of the nation-state must not, he emphasized, be limited to the political field. In other words, there is no ontological base that can determine statehood; the state is always in an operational field defined in a dynamic process. This framework is extremely useful in mapping out the factors as they appear in the story of the ICH. My argument is: without an analytical review of this story, we cannot capture these two countries in a diachronic fashion.

Table 8.2. Analytical Frame for Japan's Interactions with the ICH

International-Political Field (Field I)	International-Nonpolitical Field (Field II)
1. MOSS negotiations 2. ICH	1. E5 EWG primary unity of human beings 2. E5 guidelines 3. Kitasato-Harvard symposium/genomics
National-Political Field (Field III)	National-Nonpolitical Field (Field IV)
1. MHLW 2. Drug regulations 3. Bridging study policy 4. Global drug development	1. Japanese *minzoku* (intrinsic/extrinsic factors) 2. Uniquely Japanese biological attributes

Let us discuss Japan first (table 8.2). I began with 1986, the year of the MOSS negotiations (Field I-1). At that bilateral meeting (Chapter 4, Part 1), the United States pressured Japan directly through a political channel, hoping to make the MHW change its policy on drug regulation (Fields III-1 and III-2). Although the MHW accepted some foreign clinical data, it shifted the venue from bilateral to international, that is, from the MOSS to the ICH (Field I-2), and brought the subject of racial difference to the table (Field II). But Japan's approach to racial difference was challenged at the E5 Expert Working Group (Chapter 4, Part 2) by the mainstream ideology that asserted the primary

unity of human beings (Field II-1). An attempt was made to force the MHW experts to correct their "misguided" thinking on the uniqueness of the Japanese race by accepting a guideline based on the ideology of unity, which was to be added to the local regulations. This attempt did not succeed; it led only to a compromise guideline (Field II-2) and a vague concept of bridging (Field III-3) that could be variously interpreted.

On the other hand, while resisting the pressure applied through the E5 guideline (Chapter 6, Part 1), the MHLW tried to preserve the integrity of the Japanese state by suggesting its own solution to the debate over racial difference (Chapter 6, Part 2). This attempt started with a domestic request for applications to develop drugs for international sale in accordance with MHLW suggestions (Field III-4). This method, which assumed the existence of different races in the areas represented at the ICH, was enhanced through the use of the genomic definition of race. The MHLW promoted this agenda at the Kitasato-Harvard symposium (Field II-3), hoping to revise the original guideline. However, so far this proposed solution has been studied by no more than a handful of Western experts and many technical problems must be overcome before it can serve as a workable agenda.

This sketchy review presents a picture of Japanese strategy in the wake of globalization. The first step in this transformation was a practical shift from the bilateral to the global. As I have explained in the present chapter, one goal of *kokusaika* is to render Japan's political sway comparable with its economic influence and to forge an inseparable relationship between the Japanese state and its *minzoku.* Thus, while the Western experts tried to distinguish race from citizenship by clarifying what the MHLW meant by race or by citizenship, they failed. For Japan, dealing with the state is the same as dealing with the *minzoku.* In other words, Field III and Field IV are in fact a single block called Japan. This was not merely a strategic resistance to economic competition, I argue, because even where *kokusaika* complicates the landscape of Japanese *minzoku* (Chapter 8, Part 2), Japan pursues its nationalist project by initiating new syntheses of biology and imagination, such as genomics and individual medicine. To sum up, Japan's transformation resembles what Michael Billig (1995: Chapter 4) called the making of "national identity in the world of nations." Thanks to an awareness of other states, he argued, this national identity is involved in a dynamic process of categorizing its people and its state in a world system. In the case of the ICH, the Japanese notion of "Japan versus all" or "inner versus outer" evolved into complicated categories, or, more accurately, a taxonomy concerning body and the state in globalization. Even so, the guidelines set up by the ICH did little to change Japan's national identity, which still occupies the highest position in this taxonomic system.

Taiwan is harder to sketch because it is not formally recognized as a state at the international level (table 8.3). My starting point was the mid-1980s, when drugs were first listed as a topic for discussion in United States-Taiwan trade negotiations (Chapter 5, Part 1). This period superficially resembles Japan's bilateral phase. Using this quasi-formal channel, the United States Trade Representative and the Pharmaceutical Research and Manufacturers of America pressured the DoH to waive all requirements for drug approvals (see list of trial requirements, Field III-2). Even so, unlike Japan, Taiwan had no way to shift the venue for negotiation since it lacked the ability to create a global forum. This situation did not change until Taiwan created CDE to deal with the technical requirements of clinical trials (Field IV-1), resisting American pressure by introducing a universal standard for the E5 guideline (Field II-1), which it connected to questions about racial difference (Field IV-2 and IV-3).

Table 8.3 Analytical Frame for Taiwan's Actions Concerning Drugs and the ICH

International-Political Field (Field I)	International-Nonpolitical Field (Field II)
1. United States-Taiwan trade negotiations 2. ICH-GCG	1. E5 guidelines 2. APEC network 3. Regional integration of regulatory authorities into a statistical symposium
National-Political Field (Field III)	National-Nonpolitical Field (Field IV)
1. DoH 2. Listing trial requirement 3. Bridging study evaluation	1. CDE 2. Asian race (intrinsic factors) 3. Taiwanese customs (extrinsic factors)

On the other hand, while adopting the bridging study evaluation (Field III-3), the CDE tried to use it to promote Taiwan's visibility as a state (Chapter 5, Part 2). First, by minimizing the differences between Taiwanese and other Asian groups (Fields IV-2 and IV-3), the CDE made its bridging study evaluation (Field III-3) a workable agenda (Chapter 7, Part 1). Because it held a strategic position in the ICH debate over racial difference, the CDE further promoted Taiwan by organizing a global forum to address this matter (Field II-2). Second, to maintain the voice of the bridging study and compete with other agendas — such as global drug development — the CDE proposed the regional integration of regulatory authorities and created a separate forum for promotion (Chapter 7, Part 2). If these strategies pan out, they will give Taiwan a long-term voice in more formal platforms on globalization, such as the ICH-Global Cooperation Group (Field I-2).

Taiwan's actions in the wake of globalization present quite a different path from Japan's. Denied the autonomy enjoyed by Japan, Taiwan thrusts itself into the limelight through cooperation with other states, such as the United States and Japan. Moreover, the statehood that the CDE presents is ambiguous. It is at variance with conventional thinking about ethnic controversies in domestic politics and challenges the truism that Taiwan should not be treated as a state. That is why I devoted a certain amount of space to considering ethnic tensions in Taiwan and their relation to democratization. As to Taiwan's nationalistic project, I have emphasized the role that internationalization plays. In Chapter 5 I reviewed Taiwan's gradual international isolation since 1972 and in the present chapter showed how ordinary people's accumulation of foreign experiences impinged on how they thought of themselves. As Billig points out (1995: 83), nationalism can arise from an awareness that "if 'our' nation is to be imagined in all its particularity, it must be imagined as a nation amongst other nations." Taiwanese people might not know how to achieve a "proper" representation of Taiwan, but their willingness to sacrifice their racial uniqueness to win normal statehood attests to their desires, a longing for the "normal country" Lee Teng-Hui invokes.

Still, I am not saying that these strategies have won for Taiwan a real statehood, although an incipient statehood sometimes appears on the horizon. Virtually no international organizations, governmental or nongovernmental, include the Republic of China on their rosters. Even when it is allowed to join, its membership is limited and distorted, as if to say, "This is not a state." Such is the case with the ICH. Even though Taiwan was invited to the ICH-GCG, this was strictly on the behalf of the APEC and under the unexceptionable name "Chinese Taipei." As Horng-luen Wang wrote (1999, 6–8), political scientists consider Taiwan a "political oddity" or a "challenging case." This does not mean that we cannot find a way to describe Taiwan's situation, and my suggestion is "performative statehood" (Chapter 8, Part 3).

We have seen the different strategies Japan and Taiwan used to pursue their national goals in the context of globalization. Can the two "abnormal" states cooperate, as anthropologist Victor Turner might suggest, so that "we have a loving union of the structurally damned pronouncing judgment on normative structure and providing alternative models for structure" (1982: 51)? While some politicians have begun to investigate possibilities, in a political world the chances are slim. Still, in the world of proprietary drugs such cooperation is more likely. In Chapters 6 and 7 I described the failure of Japan's efforts to position itself for global drug development and the fruitfulness of CDE's tactics in promoting discussions of racial differences: both fostered

an atmosphere where strategic alliances became possible. I have emphasized the effects of govern-mentality on the world of drugs — perhaps in the near future we will see approaches to international pharmaceutical regulations that may bear fruit in the political world.

Chapter 9
Epilogue: Ethnography of the World, Ethnography of the State

> Nationalism has been defined, in effect, as the striving to make culture and polity congruent, to endow a culture with its own political roof, and not more than one roof at that.
>
> Ernest Gellner[1]

> If we follow only one value, [. . .] no options can be chosen other than an "ultimate solution." [. . .] In other words, choosing an ultimate solution implies the confirmation of a particular value and viewpoint.
>
> Murakami Yoichiro[2]

> The shared imagination between anthropologist and informant that creates space beyond the immediate confines of the local is also what projects the traditional site-specific mise-en-scene of fieldwork outward toward other sites. [. . .] Complicity as a defining element of multi-sited research is both more generative and more ambiguous morally; it demands a mapping onto and entry of the ethnographic project into a broader context that is neither so morally nor so cognitively determined as it appeared in previous critiques of rapport.
>
> George Marcus[3]

PART I
THE USE OF (THIS) ETHNOGRAPHY

Anthropology as Cultural Critique

Like the present thesis, the quotations above are interdisciplinary: they do not fit easily into a given field. A renowned philosopher and social scientist, Ernest Gellner pours his insights into both social anthropology and political science. Murakami Yoichiro belongs to the first generation of historians of science in postwar Japan; his broad interest in philosophy enabled him to play a leading role in making Japanese science and technology studies a productive discipline. George Marcus, along with Michael Fischer, has obliged anthropologists to reconnect with the intellectual tradition of the social sciences and the humanities. Fortuitously, the backgrounds of these quite different

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1 Ernest Gellner, *Nations and Nationalism* (1983), p.43.
2 Murakami Yoichiro, *Anzengaku* [on security] (1998), p.234.
3 George Marcus, "The Uses of Complicity," in *Ethnography through Thick and Thin* (1998), p.123.

scholars mirror the membership of the ICH. Born to Czech parents and raised in Prague, Gellner has taught mainly in England. Murakami was educated at the University of Tokyo and taught there before moving to International Christian University, also in Tokyo. Educated in New England, Marcus teaches in Texas. These are the scholars who most influenced the present study.

It was only well after I had begun my fieldwork, when I had the crucial encounters with Andrew and Mike that I described in Chapter 1, that I began to develop the problematic into which the names of Gellner, Murakami, and Marcus fit so neatly. While their specific research programs differed from mine, my systematic observation of race, globalization, and the state at the ICH would have had very different premises and conclusions were it not for this trio.

If my project was to succeed as a cultural critique, it needed three things. First, I needed to shift my research object from a group of individuals to a collective entity, the state. Second, I would focus on non-Western culture. This would not be a superficial appreciation, but an examination of how this culture structures its practice in science and medicine and how these practices "crash" in the era of globalization. Third, this study would identify itself as an ethnography. Not merely a form or a methodological tool, this decision would affect the scale of my research and its moral concerns, addressing the ambiguous relationship between the observer and the observed.

Neither the MHLW's "ridiculous" criteria addressing Japanese race nor Hu's "maniacal" search for a proper nationality can be considered an exclusively personal problem or the problem of a special group, such as Asian immigrants. In the Japanese case, the government believed in a special national value, while in the Taiwanese case Hu wanted the world to see his homeland as it really was. Issues related to the state distinguished these two cases from other discussions of cultural conflicts and global diasporas; they should be viewed as general discussions about how the state is articulated in a global age. As Gellner points out, the state is an embodiment of nationalism that links culture and polity, and these "political roofs" cover the modern world. Of a pair of ethnographic maps, one drawn before and one after the age of nationalism, Gellner observed: "There is little shading; neat flat surfaces are clearly separated from each other, [. . .] we see an overwhelming part of political authority has been concentrated in the hands of one kind of institution, a reasonably large and well-centralized state" (1983: 139–40). His observation on the modern world helps to focus this thesis. As a political roof that frames people's lives and thinking, the state has appeared as a clear object for anthropological study.

This thesis is an ethnography of the state. Focusing on the state's behavior in the

context of globalization, it reveals that the state is neither a casual accumulation of various apparatuses nor the exquisite plot of controlling mechanisms evoked by so many social scientists. At the global level, the political roofs of Japan and Taiwan look quite different than they do in isolation. At the technical or institutional level, the state is sensitive and responsive to short-term changes in the world. It skillfully keeps a dynamic balance between domestic tensions and external pressures. The basic problem for Japan and Taiwan is the same. In the field of health care, the state is responsible for protecting its people's heath, so providing access to the latest medicines is of great importance. However, for the sake of public safety necessary measures have to be taken, and these administrative processes inevitably delay the introduction of potentially lifesaving drugs. Meanwhile, as a commodity, drugs are hugely lucrative. This induces foreign (drug producing) states to call for the opening of local markets and the acceleration of the administrative process for granting approval. Hence the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

On the other hand, the domestic industry of Japan is quite different from that of Taiwan. As a more advanced country, Japan encounters friction in its efforts to protect its domestic industry. In addition, its population is increasingly divided. Taiwan's problem is a relatively simple one of "accept our standard or no drugs will be imported." Inclined to petition for more stringent ICH guidelines for drug approval, if only to keep a hand in the process, Taiwan's experts are aware that if this standard is introduced too soon, it may curtail domestic industry. As I have shown in the present thesis, most of Japan and Taiwan's actions can be explained if we consider all of the above factors.

This thesis has taken into account the state's irrational behavior in globalization. Alongside its quick, predictable reactions, the state has long-term projects and national agendas that cannot be easily understood in terms of purely Machiavellian calculations. Others have failed to examine these factors but they are important in understanding the state's reactions: specifically, they help us avoid two kinds of mistakes. First, while discussing a technical standard for drug approval, some people, especially medical experts or officials, tend to consider it a scientific topic and ignore all other factors. They believe that only by rejecting what they consider nonscientific factors can an agreement be made. The other kind of mistake, which tends to crop up in regional studies, is made when a drug is considered purely as a commodity. Assuming an alienated, essentialized East Asia, scholars take into account cultural factors such as "protectionism" and "nationalism" but treat them as a stereotypical variable.

In previous chapters, I have identified individual weaknesses in interpreting the behavior of Japan and Taiwan; here I want to further, pointing out that these analytical assumptions are generally inapplicable to a globalizing world. We long ago left behind those days — the sixteenth and seventeenth centuries — when Asia was totally foreign to the Western world, and since the expiration of the nineteenth and twentieth centuries people are no longer isolated from science. We live in a world colonized by science and by Western modernity, the world that, according to Michael Fischer, calls for new tools and methods. In a discussion of how to teach anthropology to science students, Fischer points out (2003: 38) that there are "spaces in which disciplinary assumptions are always subject to question, where tools of analysis from different disciplines are brought together, sometimes smoothly, more often in a kind of practical creolized urgency to solve real-world problems."

Through an examination of the debate over racial difference and pharmaceuticals, this thesis concludes that the key to understanding the questions from Mike and Andrew in Chapter 1 resides in the distinctive long-term agendas adopted by Taiwan and Japan in the face of globalization. I acknowledge the cultural aspect of the state but object to labeling Japan protectionist before a careful consideration of its thinking. Similarly, I have bracketed certain political questions related to Taiwan, refusing to call it a part of the People's Republic of China (PRC) or call for its independence. These preliminary steps are not the ultimate answer to our inquiry but they provide the means to getting reliable answers. Rather than foregrounding an analytical frame based on out-of-date assumptions, my interpretive approach sheds us new lights on refreshing our understanding of the two states. I have relied on several methods. Besides collecting oral accounts from local informants, I have turned to archival materials as well as local interpretations. Given that this kind of multidisciplinary methodology is necessary for studying a civilized, modernized area such as East Asia, and is particularly useful in dealing with a well-archived international conference at the ICH, I am saddened that many researchers still rely on only one or two methods commonly used in their disciplines or academic practices.

In the course of my fieldwork I noticed a serious asymmetry of narrative production in terms of area and field. Let me explain. Although there is abundant material about Japan's attitude toward the E5 guideline, virtually no mention of it is made in studies published in English. In addition, although some scholars who have treated the subject try to address local voices in their narratives, they tend to inquire about only the immediate cultural impact of a certain scientific agenda or the cultural assumptions that affect such an agenda. In other words, they still think science is a *timeless artifact* and that attempts

to understand it proceed from outside, not from within. To make up for this, I have followed Dumit's example (2004) by adding three specific methods to my approach: ethnohistory or historical ethnography, archaeology of scientific practice, and a cross-cultural dialogue of knowledge and values.

Among these methods, the last is especially important for two reasons. First, the ICH provides a universal standard for drug approvals; the standard itself, as Murakami points out in the quotation at the beginning of this chapter, implies a certain set of values and attitudes. In the case of racial difference, the set of values includes a cultural logic that assumes the primary unity of human beings and a capitalist logic that smoothes out all bodily differences in order to maximize the scale of the market. Of course, Japan has its own values. However, as this thesis has shown, not all values are given a hearing in the scientific field. Thus, only through cross-cultural dialogue can we discover that which remains implicit during the process of negotiation before and in the ICH. Second, scholars tend to apply an Aristotelian dichotomy, seeing the West (the United States in many cases) as providing the form of a study (this might well mean the analytic framework) and non-Western areas (in this case, East Asia) as contributing the matter (issues and materials). Recognizing this situation, I have tried to make a truly cross-cultural dialogue possible. This means not only letting Asian states speak, but letting them speak in their way and from their own cultural context.

These concerns made defining the field for this study crucial. Where are the sites where one can study a global issue like drugs? How does one keep a narrative coherent while letting each local actor express her or his own opinion, when these may well be incommensurable in the Kuhnian sense? Even if this can be done, how is a dialogue among the actors set up? Marcus's idea of multisited ethnography (1998) helped me deal with these problems. And I decided that to capture a mobile issue like drugs I had to rely not on several sites but on an international or global site. A site where many states assemble, the ICH provides a chronological and synchronic reference for meetings and occasions held in specific places to address specific topics. Further, it is an ad hoc site formed for the very purpose of creating a universal standard. Unlike other international institutions, such as the United Nations, if the ICH fails to show progress it will cease to exist. Therefore, intrinsic tensions push for negotiations.

More importantly for me, as the author of this study and a Taiwan-born researcher, choosing a global field helps dodge the possible criticism of complicity in multisited ethnography. Although Marcus lists among the advantages of the multisited approach the creation of a new kind of complicity between the observer and the observed, in practice many are quick to ask why certain sites but not others are chosen for observation, why

certain issues but not others are listed for discussion. In this sense, the ICH was guaranteed to provide topics that *really* aroused global attention and reactions that *truly* had global impact. Thus, the topics and projects cited here were not selected by the author's personal preference or by any theoretical inspiration; they appeared as topics taken up by the ICH. This does not mean that I intended to overlook complicated relationships in my fieldwork (for example, see the concluding remark of Chapter 5), nor did I reject all ethical and moral concerns derived from the interactions with informants by claiming a return to an objective description. Instead, I turned these concerns into anthropological questions of voice and voicing. The ICH, in this sense, became an index for assessing a voice, recognizing such agencies as the state's and judging such occasions for voicing as symposiums and meetings. In other words, beyond analyzing the voices within the ICH, this thesis examines those voices that originate from outside but have effects on the discussion within.

Ethnography as a Moral Call in "Third Spaces"

In his article "The Third Spaces of Anthropology," Michael Fischer (2003) clearly pointed out that the anthropological voice should be considered along with a keen understanding of the modern world, as well as the role that anthropology can play in it. The challenge, he explained, to renewing the notions of the ethnographic and anthropological voice

> is not the disappearance of difference, of different cultures, or of ways of organizing society any more than it is not the disappearance of class, capital, unethical exchange, power, or gender relations. On the contrary, the challenge is that the interactions of various kinds of cultures becoming more complex and differentiated at the same time as new forms of globalization and modernization are bringing all parts of the earth into greater, uneven, polycentric interaction. (3)

Considering "the aspiration for cross-culturally comparative, socially grounded, linguistically and culturally attentive perspectives," an anthropological consideration of the voice "continues to be valuable amid the pressures to simply turn to statistical indices for all policies and judgments." The challenge for anthropology is "to develop translation and mediation tools for helping make visible the differences of interests, access, power, needs, desire, and philosophical perspective" (3).

In keeping with the above argument, I employ anthropology to identify the voice of the state with a carefully chosen space that is well defined by its boundaries and its moment. The ICH possesses all of the characteristics Fischer associates with "third

spaces," that is, zones where "new multicultural ethics are evolving out of demands that cultures attend to one another, and within technoscientific networks where the demands of the face of the other, history, and autobiographical figurations counter the reduction of all to the same" (3).

In Chapter 2 I have presented the world of proprietary drugs as such a technoscientific world. On the one hand, by providing us with medicines that regulate various bodily conditions and moods this world impinges profoundly on our everyday lives. On the other hand, as a highly technical and highly profitable sector, it is opaque to the public. Before the creation of the ICH that world clearly identified who could produce and who could afford these products; it also established rules affecting pharmaceutical innovation and production. Only with the advent of the ICH did the drug world's attempts to homogenize all bodies and its inner conflicts arising out of different ideas about health become visible. I have presented the ICH as the place where all of the tensions surrounding culture, race, and global capitalism imploded. Its birth took place at a critical moment in what Negri and Hardt call the formation of empire (2000), as a transnational hierarchy emerged out of capitalist logic.

The voice we are concerned about can be captured in such a space and is revealed in the interactions among cultures. Cultures on display at the ICH include the ethical culture related to drug use, the bureaucratic culture related to drug regulation, the expert culture discussing drugs' connection with race, and even the linguistic culture related to health and drugs. While the interactions among these distinctive cultures make possible the presentation of these voices, they also make such presentations almost impossible because these interactions are so complex. Since, as I have described in Chapter 1, the ICH has a clear structure and procedures for processing discussions and also has rules governing the accumulation of archived materials, we can differentiate institutional voices from individual ones and meaningful voices from background noise.

I situate the voice of the state in two different yet interrelated processes. One relates to its ontological existence: it traces the production of the state's voice, its circulation in various dialogic contexts, to the effects it brings to the attention of the ICH. The other process treats the voice as a representational subject: it traces how a voice can appear in a text, how this text can be recognized in the circulation of texts, and how this voice as a representation affects the creation of discourses concerning my topic (i.e., ethnography). Faced with this division between the two processes (which one might label modernist and postmodernist), many researchers tend to equate the two or distinguish them according to hackneyed generalizations — the former empirical and naïve, the latter abstract and

pedantic. For me, the two processes are equally important and separation is necessary. First, because the ICH is a discursive representation of the world of proprietary drugs that provides us with a manageable site we can observe more or less in its entirety, a stage where every action is clear and traceable (though this does not mean that we can ignore all who fail to speak for themselves at this site). Second, I have relied on Fischer's "voice one-two-three" frame (2003: Chapter 6) to describe institutional voices. Although Fischer neither described the standards he used to choose the texts at the center of his study, nor why the texts represent their authors, this thesis has to address this problem, because the ICH does not include every statement made at one of its meetings in the official record: specific regulations determine whose voice merits recording. No matter how many claims Taiwan's Center for Drug Evaluation (CDE) makes to the ICH, if it cannot make itself an instrument for voicing (for instance, via Asia-Pacific Economic Cooperation, or APEC), these statements will fade away without an echo.

The third and the last reason to situate the voice in two distinct processes is the correspondence between the locus of ethnography and its discursive specificity. As Fischer puts it (2003), as a discipline anthropology operates in the third spaces, while as a discourse anthropology *is* a third space.

> If anthropology was in part a creation of the colonial enterprise, its formations have increasingly been a third space between the desires of empire (of control) and the defense of the oppressed (of subaltern voices, interests, values, and perspectives), a third space of helping evolve new multicultural ethics, with translation and meditation tools for helping make visible the differences of interests, access, power, needs, desire, and philosophical perspective. (8)

As empires crumbled and colonial states won their independence, anthropology evolved into a more sophisticated space where "social formations challenged analysts to develop tools for analysis, not just slot development into categories of the past" (8). For me, the problem of narrative is that I am both actor and observer, an ethnographer trained in the West and an informant born in Asia. My ambiguous position prevents me from combining an ontological existence — for example, a *de facto* Taiwan — with its textual representation — a *de jure* one. It might not be necessary to turn this voice in a philosophical direction, such as Stephen Tyler's postmodern ethnography or a Derridean exercise in logocentrism, but we have to pay attention both to the form and to the content of this ethnography.

Considering first the ontological voice of the Japanese and Taiwanese states, we can list their components as autobiographical, biographical, and scientific (table 9.1).

Produced by the government, the voice of self-portrayal, or voice one, shows a state's basic attitude toward a topic, such as the acceptance of foreign clinical data. However, as an agent in the world, this voice has to interact with other state agents, thus creating a dialogic voice, or voice two. In our case, Japan ceaselessly explains to whoever will listen that racial difference should be taken into account in drug regulations. Meanwhile, Taiwan's dialogic voice addresses the pressure from the Pharmaceutical Research and Manufacturers of America (PhRMA) ro waive all local clinical trials. During the discussions that have ensued, both shored up their agendas by developing different scientific discourses, which amount to voice three. Using this analytical frame, I showed that to some extent the ontological voice was a mosaic of the three voices.

Table 9.1 Making the Ontological Voice of the State in Japan and Taiwan

	Japan	Taiwan
Instrument for voicing	MHLW, OPSR	DoH, CDE
Voice of self-portrayal (voice one)	Policies and Regulations	Policies and regulations
Dialogic voice (voice two)	Debates over racial difference	Debates over waivers of local trials
Scientific voice (voice three)	Global drug development project and genomics	Bridging study project and biostatistics

Table 9.2 The Narrative Technologies of Voicing Used by Japan and Taiwan

	Japan	Taiwan
Platform for voicing	ICH	APEC network
Channel of voicing	Kitasato-Harvard symposium	APEC statistical symposium
Archive of voicing	1. ICH proceedings 2. Kitasato-Harvard symposium proceedings	1. Drug Information Association (DIA) journals 2. Website proceedings
Postproduction of voicing	Interviews with ethnographer	Interviews with ethnographer

But the ontological voices are not fully present in the materials people use to construct their understanding of this issue. Japan's ability to present its cultural concerns is in doubt because as a public forum the ICH does not treat all parties to a discussion

equally. When the topic is the uniqueness of the Japanese race, for instance, Japanese representatives feel that other countries fail to take the topic seriously. Taiwan's problems are comparatively far more fundamental and severe: it is barred from presenting itself as a globally recognized polity.

While forming their ontological voices, Japan and Taiwan have created several ways to deal with their problems of representation. I have listed these narrative technologies of voicing in table 9.2. As a member of the ICH, Japan's voice is well documented and archived. Its narrative technologies are applied only when it is unhappy with the outcome of some negotiation. For example, because its agenda on global drug development did not get a proper airing at the Expert Working Group (EWG) during discussions of the E5 guideline, the Ministry of Health, Labor, and Welfare (MHLW) supported a new "channel" of communication, the Kitasato-Harvard symposium, and circulated there an English-language outline of its position — this was its alternative voice.

Taiwan's problem is much more complicated. Both because Taiwan is not an ICH member state and because it has long been politically isolated from the world as a sovereign state, Taiwan pursues a dual program of making a voice for Taiwan and making Taiwan a voice. Unlike Japan, racial difference is not Taiwan's main concern: it is a strategic point where individual voices converge and form an institutional voice. By exploiting narrative technologies (organizing series of conferences where it can speak out, encouraging often-cited journals to run special issues on Taiwanese themes), Taiwan produces a stronger voice. But how does it maintain such a voice? The answer is globalization. In its push for a regional bridging study, Taiwan fought for a place on the global map by situating its voice in broader networks. Of course, in many cases these narrative technologies are merely part of a political plot, but this does not apply to Taiwan's actions at the ICH. The ICH is not a conventional international organization and operates according to its own nonpolitical logic. At this point, Taiwan presents a silent example of how its existence in text is not an accessory of a factual statehood; by contrast, at the global level it is this textual existence that gives rise to the epistemological imagination of itself in the world.

For ethnographers, the most interesting voicing takes place in "postproduction." Here my Asian identity was both a help and a hindrance as I interviewed representatives of the MHLW and the CDE. Of course, different societies have different ways to approach experts and officials, yet everyone I met was excited about my project and their generous testimony betrayed the hope that I would present my conclusions from their perspective. Though many of them had published papers on some of the subjects of

greatest concern to them, these were in Chinese or Japanese: what could be better than conveying their convictions in a book or a dissertation written in English and bearing the endorsement of a prestigious institution like the Massachusetts Institute of Technology? Several times since I interviewed him, Naito Chikayuki of the Organization for Pharmaceutical Safety and Research (OPSR) has asked about my project, and Chern Herng-Der of the CDE, one of my local helpers and a key informant for the present thesis, pushed me to publish the section on Taiwan before submitting my dissertation. "You now know more than anyone else about how the E5 guideline is applied in Taiwan and Japan," he told me, "so you should write it down." They do not expect me to produce a text about their voices, but they evidently would like it if I did — this is what I call postproduction. They hope that the stories they tell me about the E5 guidelines will take the form, in my report, of a coherent voice clearly heard in the ICH.

This sets me an ethical challenge. First of all, should I trust their accounts? I have described this challenge in Chapter 5: some active Taiwanese informants told me a great deal about the field and eventually asked me to join their team. When I analyzed their country's embarrassing isolation and tried to know how these elite medical experts reacted to this unspoken trauma, they opened up my personal history as a Taiwanese, a licensed medical graduate, and a researcher of medicine in Taiwan. In Taiwan I enjoyed extraordinary access to almost everyone I thought could help me but, as I have written repeatedly, as far as I can tell they did not fabricate any facts and certainly they did not pressure me to write anything that they knew to be untrue. They showed me around the discursive fields — the APEC meetings, Drug Information Association (DIA) meetings, Kitasato-Harvard symposiums, even the ICH-Global Cooperation Group (GCG) meeting — allowing me to witness their achievements.

The more I learned, the more I understood their distinctive agendas. Of course, this is a familiar situation for ethnographers and this is where George Marcus encourages practitioners to adopt a multisited approach. This explains why the present thesis has become a large volume consisting of nine chapters. I have listened carefully to Japan as well as to Taiwan, and one of the results is that what one group said has to be confronted with what the other group said. Furthermore, the moral connotations of this narrative have been altered — often relaxed — by juxtaposing the two countries in a comparative framework. This framework is detached from national interests and focuses on the more strictly academic issue of a new methodology, namely, voice and voicing, in writing global cultures.

But I have yet to clarify a fundamental question concerning writing: why does the

author choose to write a certain text? This is, after all, a moral question that no one can avoid. Like those ethnographers who are willing to spend years living among strangers, I know that my goal was never the creation of a text isolated from other texts. The birth of ethnography was accompanied by the appearance of a host of ethical effects and moral evocations, what Michael Fischer calls (2003: Chapter 2) "emergent forms of life," which acknowledge an ethnographic datum, a social theoretic heuristic, and a philosophical stance.

I opened this dissertation by describing my seminal confrontations with an e-mail message and a Mexican shuttle driver. These fortuitous meetings invited me to assume the ethical responsibility of understanding and explaining a world that others could not understand. The state, in this sense, is a subject guiding us along this academic adventure, and it exercises a writerly agency over its outcome (an ethnographic text). Ernest Gellner said that nationalism cannot be a natural social unit without its own political shell, the state (1983: 140). I believe that every state deserves an ethnography.

Of course, such studies are common. The dramatic work of the weak and disenfranchised to gain a voice of their own should not lead us to the faulty conclusion that these people were utterly absent from previous discourses; but their depictions were consistently such as favored the dominant groups. The first step in providing a powerless group with a voice is to call attention to their unjust treatment. The creation of subaltern studies was not an academic curiosity: it was a moral effort to rehabilitate a distorted, ideology-driven understanding of history and nationalism. I would like to mention a recent example of an "affirmative movement" that played a leading role in connecting the state to globalization.

When the PRC passed an "anti-secession law" asserting the right to employ all measures, including "nonpeaceful" actions, to put an end to local (read, "Taiwanese") calls for self-determination, as many as one million Taiwanese citizens courageously took to the streets. Encouraged by the ruling Democratic Progressive Party (DPP) and more than five hundred nongovernmental and civic organizations, the people gathered on Ketagalan Boulevard in Taipei on March 26, 2005 to express their outrage (fig. 9.1, left).

The implications of the demonstration were clear. Although the people who marched on March 26 knew that they would not shake the PRC's determination to seize a territory it never controlled for so much as a single day (keeping in mind that the anti-secession law belonged to a body of domestic law), they lifted up a collective voice to decry this threat,[4] because otherwise the world would think that Taiwan had meekly

[4] In fact the demonstrators used a local term *chianshia,* which means something between "to voice"

bowed its head.[5] More importantly, Taiwanese realized that this bellicose law severely complicated regional security and the eyes of the world would be trained on them. The poster illustrated below (fig. 9.1, right), with its emphasis on voicing, makes this widespread conviction quite visible. Highlighting the objections to the anti-secession law raised by several world leaders, the poster asks, "Taiwan, what about your voice?" This approach closely resembles the strategy employed by the CDE in negotiations over E5 policy. As a "nonstate," Taiwan presents its voice by manifesting its desire to join the global mainstream.

Fig. 9.1. *Left,* Taiwanese Protesting the PRC's Anti-Secession Law on March 26, 2005; *Right,* A Poster Announcing the Demonstration: The Large Characters Read, "Taiwan, What About Your Voice?"

Sources: *Taiwan Zibao*, March 26 2005 (left); *Minzuheping hu Taiwan dalianmong* [alliance on protecting Taiwan by democracy and peace] (right).

Examples like this posed moral challenges for me throughout my fieldwork. While I feel a strong compulsion to document these states' efforts to present themselves to the world, their voices will never remain intact once they have interacted with others. Sometimes — in the case of Taiwan, for instance — even the action of voicing can be a factor in creating a voice. In the next part of this chapter I will argue that we cannot achieve an understanding of these two countries without listening to their voices; however, these voices are neither fixed, self-contained entities, nor are they meaningless, rhetorical constructions. Weaving between the real and the textual, their long-term goals for state development can only be seen in the changeable, dynamic process of interacting

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and "to argue against."

[5] When Taiwanese were polled after the passage of the anti-secession law, more than 50 percent of respondents said the Taiwanese government should increase its defense budget and hold a referendum to reject the law.

with the rest of the world. This is where world ethnography and state ethnography are produced.

PART II
JUXTAPOSING WORLDVIEWS AND ETHNOGRAPHIES

How the World of Proprietary Drugs Operates

I have tried to draft three ethnographies in the present study: the ethnography of the world of proprietary drugs and those of Japan and Taiwan, all three in terms of race and the state. As part of this trinitarian project I have tried to problematize two conventional thoughts concerning globalization.

The first is the idea that the nation-state, a casualty of globalization, is dying or dead. This bold declaration appears in the concluding chapter of Eric Hobsbawm's *Nations and Nationalism since 1780.* Hobsbawm asserted (1990: 182) that nations and nationalism were becoming irrelevant to "the new supranational restructuring of the globe." Indeed, when "race" has been proved a historical myth by science and the state has given way to global institutions, the notion of the nation-state became an odd combination of two seemingly irrelevant concepts: nation, which refers to a people sharing a common culture and heritage, and state, the government of a bounded territory. Although I will not try to dismantle Hobsbawm's assertion, anthropological attention should be paid to nation-states in fields related to health and policy: pharmaceuticals provide a link.

The second thought has to do with our understanding of the world. Since Immanuel Wallerstein's theory of world systems (1974, 1989), scholars have sought a unified formula, such as capitalism, to interpret how the world operates. Using a universal rule as a reference, they distinguish among local populations by their different responses to these global impacts (Lewellen 2003: Chapter 11). In Chapter 1 I pointed out the problem with this approach: a theory-oriented meditation does not satisfy our empirical curiosity about exactly what is going on in the world and how to make sense of it with a comprehensive interpretation. As the present investigation draws to a close, I will add another criticism. While capitalism plays a dominant role in the drug business, profit is not the only logic that drives it. Regulatory science, as I have shown in the present thesis, has a distinctive logic that is not necessarily consistent with capitalism. In other words, as Hardt and Negri pointed out in *Empire,* globality "should not be understood in terms of cultural, political,

or economic *homogenization.* Globalization, like localization, should be understood instead as a *regime* of the production of identity and difference, or really homogenization and heterogenization" (2000: 45; emphasis in original). The nation-state and the local should not monopolize the attention of ethnographers: the distinctive nature of the international entities merits separate ethnographies.

As readers may have guessed from its chapter arrangement, this thesis is an extension of George Marcus and Michael Fischer's notion (1986: Chapter 6) of "cross-cultural juxtaposition" as part of a cultural critique.[6] Based on the critical strategy of defamiliarization — "doing the unexpected, placing familiar subjects in unfamiliar, or even shocking, contexts" (137) — this methodology, which stems from a demystification of Euro-centric ideology, matches ethnography abroad with ethnography at home:

> Presumably, members of other societies, increasingly literate, will read ethnographic accounts that concern them, and will react not only to the manifest descriptions of their own societies, but also to the premises about our society that are embedded in the double vision of any ethnographic work. For their part, American readers might react negatively to the idealized and simplified accounts of societies abroad, and might require realistic ethnography at home, as well, for anthropological critiques to be persuasive. (163)

The present study deviates from this model in two ways. Here a non-American has examined a global moment related to both the United States and Asia. Rather than the familiar scene of the American ethnographer reflecting on her or his peculiar position as a writer, I have been quite concerned about making this non-American text acceptable to my American readers, who might be wary of a foreigner's take on America, before challenging the presumptions these readers may have about Japan and Taiwan.

And just as no one can speak for the United States, no one speaks for East Asia, so I have introduced a third state into the narrative. This project thus involves multiple references to other cultures triangulated with the primary juxtapositions. This is the "fully developed reciprocity of perspectives, involving two, and even multiple, cultural reference points in the writing of anthropological texts" that Marcus and Fischer mention as "a potential" (1986: 163–64). As the story of the debate over racial difference inside and outside the ICH comes to a close, I want to return to the worldviews examined in the previous pages one last time.

Americans are quite familiar with the world of proprietary drugs. They know this

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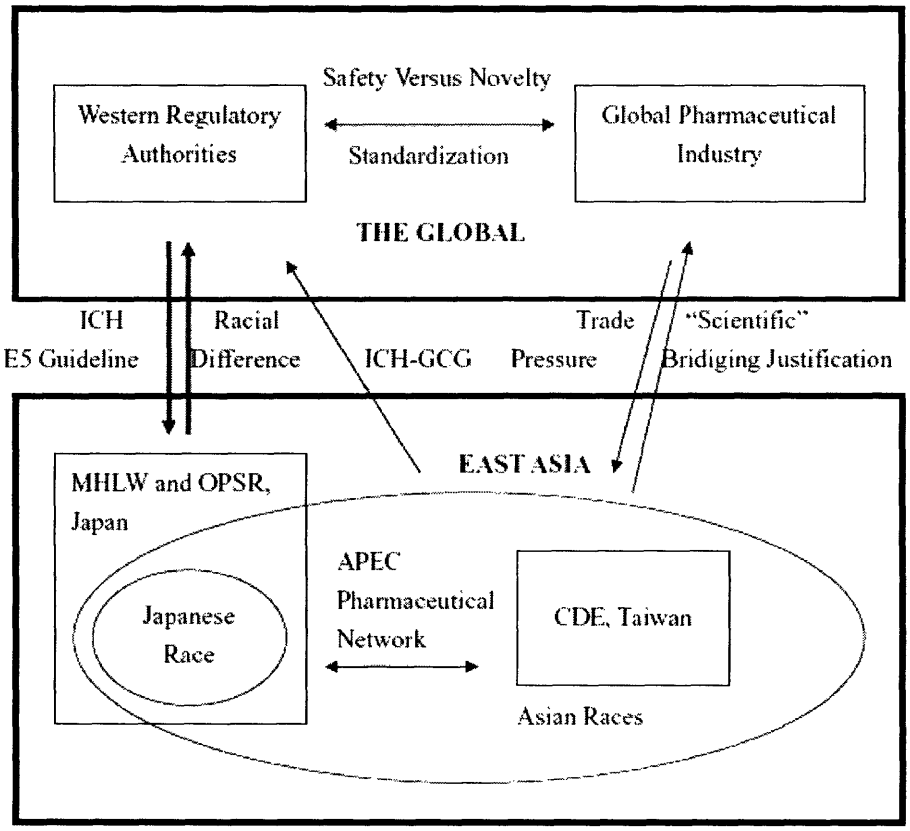
[6] Chapters 2 and 3 are about the world of proprietary drugs; Chapters 4, 6, and 8 are devoted to Japan;

world not only because they consume its products (and absorb countless advertisements about them) every day, but because, as an advanced technology, drugs require profit-driven calculations that match their ideas about capitalism. The world of proprietary drugs is a club whose membership is restricted to a handful of countries able to produce these drugs.

Fig. 9.2. Imposition of the World of Proprietary Drugs on East Asia Through Standardization



Key to signs: Solid ovals stand for races; solid boxes identify adminstrative territories, such as regulatory authorities or the pharmaceutical industry, and broader fields, such as regional markets or a zone of regulation. Arrows indicate the forces generated by subjects and objects.

As shown in fig. 9.2, this small yet highly influential world is governed by

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and Chapters 5, 7, and 8 are devoted to Taiwan.

regulatory authorities and the drug industry itself. Visible on the surface are tensions between the regulators and the manufacturers. But they are really the two sides of a single coin (for more details, see Chapter 2). Unlike conventional accounts hamstrung by the complicated connections among government, the academy, and industry, I have pointed out the underlying logic of standardization that constructs the rules of this world. Regulators can test only the drugs that achieve high standards (mainly efficacy and quality) and only thanks to these high standards can the industry promise its customers good health. Altogether this standard is beneficial for both regulators (keeping things simple) and industry (low competition), and it presents a high barrier to latecomers.

Treating Asia primarily as a new market, drug companies do not differentiate Asian states from Asian races. If a new market does not demand further trials and is too small to begin a process of bargaining, drug companies will call for unconditional surrender. But this could not succeed in Japan, a substantial market. In order to acquire this market, a common standard had to be negotiated. The ICH is a bold attempt to bring together regulators and industry representatives, including the MHLW and the Japan Pharmaceutical Manufacturers Association (JPMA), and is the main interface where global forces interact with East Asia.

Of course, we have witnessed the growing significance of international and transnational organizations. Like other global institutions, the ICH has its own procedures for discussion and a decision-making structure that both constrains and facilitates the activities of each member. In addition, both sides negotiate to come up with a standard. In my study, racial difference emerged in the ICH as a troublesome variable that complicated the desire of the global community to make a single world market for proprietary drugs. As the bold arrows between the upper and lower boxes of the figure above indicate, the first contact between the world of proprietary drugs and East Asia was limited to the ICH and to Japan, its sole Asian representative. Until that point, the ICH was a scientific forum with commercial goals.[7] Only when other members asked Japan to allow extrapolations of clinical data so that they could more easily enter that market did Japan's insistence on racial difference shake things up.

Moving back and forth between science and politics, the discussion of racial difference, described in Chapter 4, encountered a fundamental difference over race and the state. Treating them as utterly distinct concepts, the United States then tried to

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[7] It is thus an excellent anthropological site for the study of market. As Marcus and Fischer notice (1986: 93), although market is a global subject that ethnography ought to be able to take on, there are practical difficulties in constructing a multi-perspective account of a system or a major social drama that is encompassed by it.

substitute other Asian races for Japanese in clinical trials. Meanwhile, Europe recognized the state as an administrative organization integrating current regulations. Faced with strong resistance from the Japanese side, they shifted their focus from Japan to other Asian countries. This is how Taiwan won an appearance on the ICH map.

The CDE provided these experts with a model of how Asian race and state can be dealt with separately. Recognizing the difference between Asians and Caucasians, yet asserting the possiblilty of adjusting data from one trial group to suit the other, the CDE showed that a bridging study was not a fantasy. Moreover, it shifted the focus of the discussion of racial difference from "Japanese versus non-Japanese" to "Asians in the diversity of races," the approach favored by the West. To magnify this opinion, ICH experts not only attended activities organized by the CDE, such as the regional APEC meetings, they invited the latter organization to contribute its ideas to the founding of the ICH-GCG (hence the regular arrow from East Asia to the global in fig. 9.2). On the other hand, global industry never stopped pressuring the MHLW to clarify its position on foreign clinical data, but Japan proved unexpectedly determined. Its position has not been affected by Taiwan's approach to bridging studies, and thus far Japan has not approved any revision to the ICH guideline defining race. Despite all of its efforts, the world of proprietary drugs has failed in its attempts to use the ICH to crack open Japan's markets.

My sources for the preceding summary of conflicting worldviews were mostly Western businesspeople and experts. Consistently, they viewed Japan as a troublemaker and Taiwan as an intriguing actor in the drama of harmonization. Many had not noticed that over two decades of dealing with the local, the forces of globalization had silently undergone a transformation. Let me summarize three changes described in Chapter 6. First, forcing Japan to accept foreign clinical data is less important now: the patents on the drugs that companies were so determined to introduce have expired. Second, some Japanese drug companies have successfully entered the global market. Third, the introduction of the ICH guidelines to other Asian countries has paradoxically made selling drugs to those markets more difficult: places that never had any say over the actions of huge corporations acting on their soil now have a voice at the ICH and elsewhere.

Globalization is not a static force; as Hardt and Negri suggested (2000: 45), "The better framework, then, to designate the distinction between the global and the local might refer to different networks of flows and obstacles in which the local moment or perspective gives priority to the reterritorializing barriers or boundaries and the global moment privileges the mobility of deterritorializing flows." My study of Japan and

Taiwan is based on this suggestion. Instead of repeating the inaccurate metaphor of an "objective" boundary between the Western world and East Asia, in the following section I will show the ways that Japan and Taiwan situate themselves in the world. In spite of the steady flow of advanced drugs from the developed to the developing, from the West to the East, from the rich to the poor, the obstacles that the local throws up are not ill deployed and fragmented. The attempts to "reterritorialize boundaries" are in fact derived from a systematic perspective driven by concerns with cultural survival in the midst of globalization.

Race, State, and the Reason for the Nation-State: Two Ethnographies on East Asia

In Chapter 8 I described Japan and Taiwan by tracing the last two decades of their changing ideas of race and the state, two of the classical elements in the construction of a nation-state. In this section I will address their "govern-mentality" at a conceptual level, looking at how they construct ways to situate themselves and the world in a comprehensive framework.

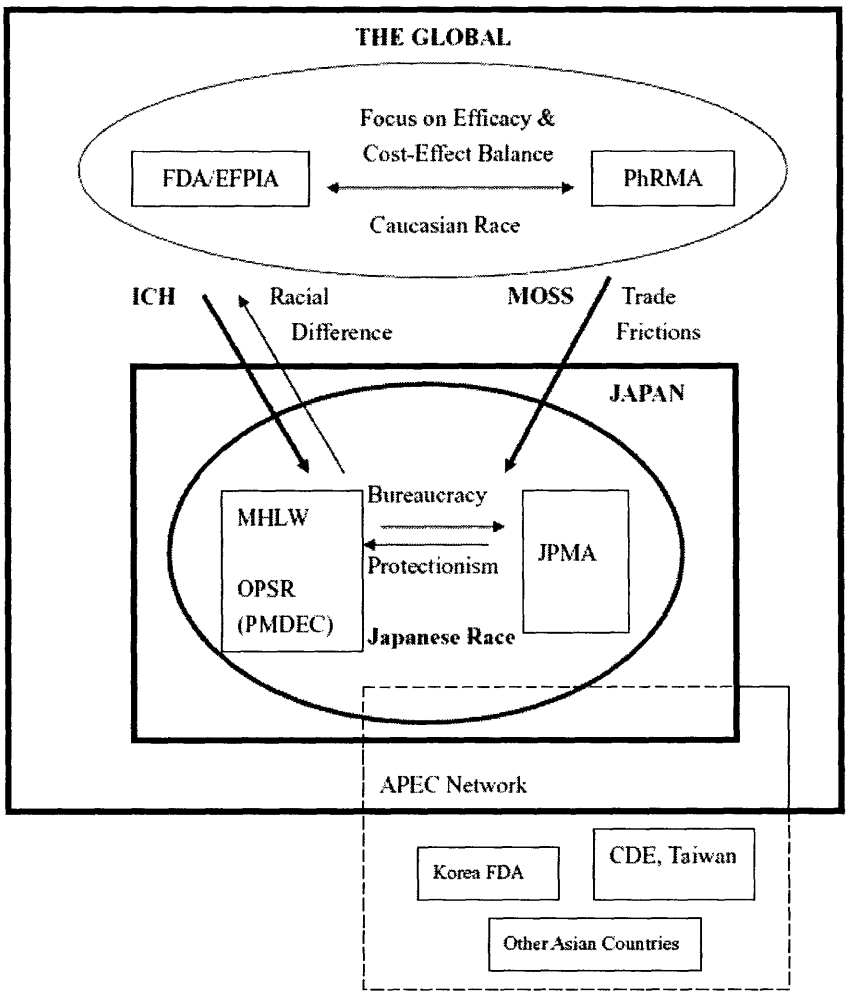
Let us begin with the worldview of Japan, which is illustrated in fig. 9.3. First of all, the inner box at the center of this world represents the Japanese state. In Chapter 3 I explained that, thanks to the nature of Japan's social institutions, pharmaceuticals operate through the collective trust of professionals (physicians and hospitals), institutions (drug makers and the JPMA), and ultimately the government (the MHLW and the OPSR).

In short, the Japanese pharmaceutical business is not run by a "high risk, high profit" discourse. Of course, as in other countries, Japanese makers have to produce products that are safe and useful and regulators have to protect the people's health. But the mechanism is unique. Japan's clinical trials, for example, are performed like a ritual whose credibility depends on various trusted entities (senior professors, teaching hospitals, reliable manufacturers) rather than on science. Furthermore, safety, rather than efficacy, is the regulators' first priority when they review a new product. To avoid harming a single patient in clinical trials, they reject the absolute measure of efficacy. Such practices are criticized by the West as backward and unscientific, but Japan's caution goes beyond culturally specific ideas about the body and death, attached as it is to strong feelings about the social basis for state intervention in public health. As the ultimate organization and political realization of the Japanese race, the government maintains its ruling legitimacy by protecting its people from all possible hazards.[8] To do

[8] As Murakami Yoichiro pointed out (Murakami and Ichinokawa 1999: 87–90), drug regulation could

this, it shares its drug regulation duties with several different domestic groups, which form a tight and closed system.

Fig. 9.3. The World of Proprietary Drugs from Japan's Viewpoint



Note: EFPIA: European Federation of Pharmaceutical Industries and Associations; FDA: Food and Drug Administration (USA); MOSS: U.S.-Japan Market-Oriented, Sector-Selected Discussion; PMDEC: Pharmaceuticals and Medical Devices Evaluation Center.

Key to signs: As in figure 9.2, solid boxes identify adminstrative territories, such as regulatory authorities or the pharmaceutical industry, broken boxes indicate

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not be handed over to professionals, because this would mean that the government had given up its responsibility to take care of its people. While Murakami feels that individuals should be responsible for many matters, drugs are too important to be left to civilians.

unstable entities or relationships, and arrows refer to the forces generated by subjects and objects.

Trying to look beyond the monolithic explanation called protectionism, we cannot ignore cultural and historical factors. While in the United States drug regulations became tough and competitive due to industry disasters, in Japan the direction of reform has been toward more constrictive and Japanese-centric regulations. These slow down the reviewing process, incorporating more people in order to avoid risks, and the Japanese government hesitates to extend to other states the social trust that permits its regulatory institutions to function.

But even Japan has to concede that it cannot survive in isolation from the rest of the world. As its economic power grew, Japan had no choice but to interact with other states in many ways. This was clearly acknowledged, as mentioned in Chapter 4, when Japan shifted from a bilateral MOSS negotiation with the United States to a multilateral negotion with the ICH. Political factors, such as the end of Cold War, also help explain this shift, but here I have emphasized Japan's ambivalent encounter with globalization as the boundary of the nation smashed into that of the state. While Japan represents itself as racially homogenous, this reflects neither the facts nor how individuals think about themselves. Racial homogeneity is purely a vision that contrasts Japan with the rest of the world.

Surrounding the box that represents Japan in fig. 9.3 is the world, a fictitious "other" at the center of debates between an agressive pharmacetuical industry and the Japanese state. Japan finds Western practices inappropriate because of drug makers' exclusive concern with the efficacy of their products, which are developed under a cost-efficient logic with virtually no consideration of nonwhites in clinical trials. More importantly, some fear that the full flowering of globalization will eradicate Japan. Juliette Chung has pointed out the crucial role eugenics played in shaping Japan's national ideology and identity (1999: 206–29). In Japan, Chung argued, Lamarckism was a cultural logic by which the individual body related to a greater national and racial body. To guarantee the survival of the national body, undesirable traits had to be removed. In this view, the world resembles an ecosystem: every race and state has its distinct niche. To avoid being eliminated by other states, Japan had to protect itself against hostile outsiders. This conception did not change even after Japan encountered globalization at a scientific, technology-oriented conference such as the ICH. Scholars like Murakami Yoichiro think that Japan must play a role in shaping the ICH's safety guidelines because the Japanese care more about health than others do (1998: 148, 153). Similarly, some

MHLW officials thought that through the ICH Japan could export its excellent products to more patients abroad. Even so, Japan's behavior in the ICH was more defensive than aggressive and rarely did it try to impose its standards on other ICH countries. Japan contended that global harmony had to be achieved without impinging on the uniqueness of any state or race.

Hence the proposal that representative populations from Japan, Europe, and the United States all be tracked in clinical trials. At the same time, Japan proposed moving to the frontier of genomics, where a new definition of race could replace the current global standards. Preaching the gospel of individualized medicine, it is sure for now that the integrity of the Japanese state will be preserved. Of course, on the surface Japan has sound, scientific grounds for this argument, because Japan can provide clinical data as the representative of the Asian region. However, when Western experts suggested considering data from other sources, the MHLW rejected the proposal, claiming that only ICH countries were relevant (see Chapter 6).

This resonates with Okamoto Koji's division of Japanese regional diplomacy into "Japan and Asia" and "Japan in Asia" (1998). At the ICH, the MHLW never considered Japan a part of Asia. As fig. 9.3 shows, the ICH is an international entity, but it includes only three countries and regions. The APEC network, shown as a broken box, is situated outside this entity. Hayashi Yoshikazu of the MHLW nicely explained this situation (2003). When talking about the future of the ICH in Asia, he preferred not to emphasize Japan's peculiar role as the first and only Asian country invited into this global conference; instead, speaking as an ICH member, he pointed out that the only channel for other Asian countries to address issues treated at the ICH was the GCG.

Let me sum up the above worldview. As globalization sweeps over East Asia, defacing all local traits, Japan's mission is to preserve its identity. Ideas about race provide the motivation for this campaign, and the state pursues the plan of action and benefits from it. Can this be a positive sign of the recurrence of Japan's nationalism? Murakami clearly states that a race-sensitive state does not necessarily mean a nationalist state. The state, he argues (1999: 91), is a collective agency representing various small communities and societies within its territory. Fundamentally speaking, the "Japanese race" does not have to have a biological reality in a strict sense; it is a social factor, a collective belief that binds these communities together. Furthermore, this collective vision is reinforced during its involvement in globalization.

Taiwan, as shown at the center of fig. 9.4, falls outside of the world of the ICH.[9] But the primary problem for this country, as I have mentioned, is embedded in the representational crisis of its nationality, which I have marked in the figure with broken lines. Although globalization has affected how the Taiwanese people imagine their nation, its identity at the global level remains unchanged, even after its remarkable economic growth. The embarrassing rituals Taiwan has to go through to participate in the WHO's annual World Health Assembly show just how difficult it might be to return to the world stage.

Unlike studies that address only interactions within the ICH or discussions of discrete topics, this thesis pays equal attention to how Taiwan presents its existence on this global stage. In Chapter 5 I provided a comprehensive account on how some individuals tried to create an institutional voice that would be heard by the entire world. The first of the factors that contributed to the development of this voice and the worldview it projects is the human factor, the medical technocrats with a clear memory of what they think of as the "golden age" of Taiwan's public health, when the country cooperated closely with international organizations. They are not bureaucrats who follow commands but nationalists with a larger mission — saving their country from a humiliating position. Reclaiming the golden past is not pure nostalgia since the technocrats hope to return some of Taiwan's vanished luster.

The second factor is the organizational restrictions circumscribing Taiwan's contact with the world. Since 1972 Taiwan's applications for membership have been rejected by every organization affiliated with the United Nations and other intergovernmental organizations. For historical reasons it has managed to retain its membership in two organizations, the World Trade Organization (WTO) and the regional APEC. Although there are still controversies about the name used for Taiwan at these organizations, they are among the few gateways by which it can communicate with the world.[10] As I noted earlier, the APEC is both a platform where the CDE can make itself heard and a channel to the ICH.[11]

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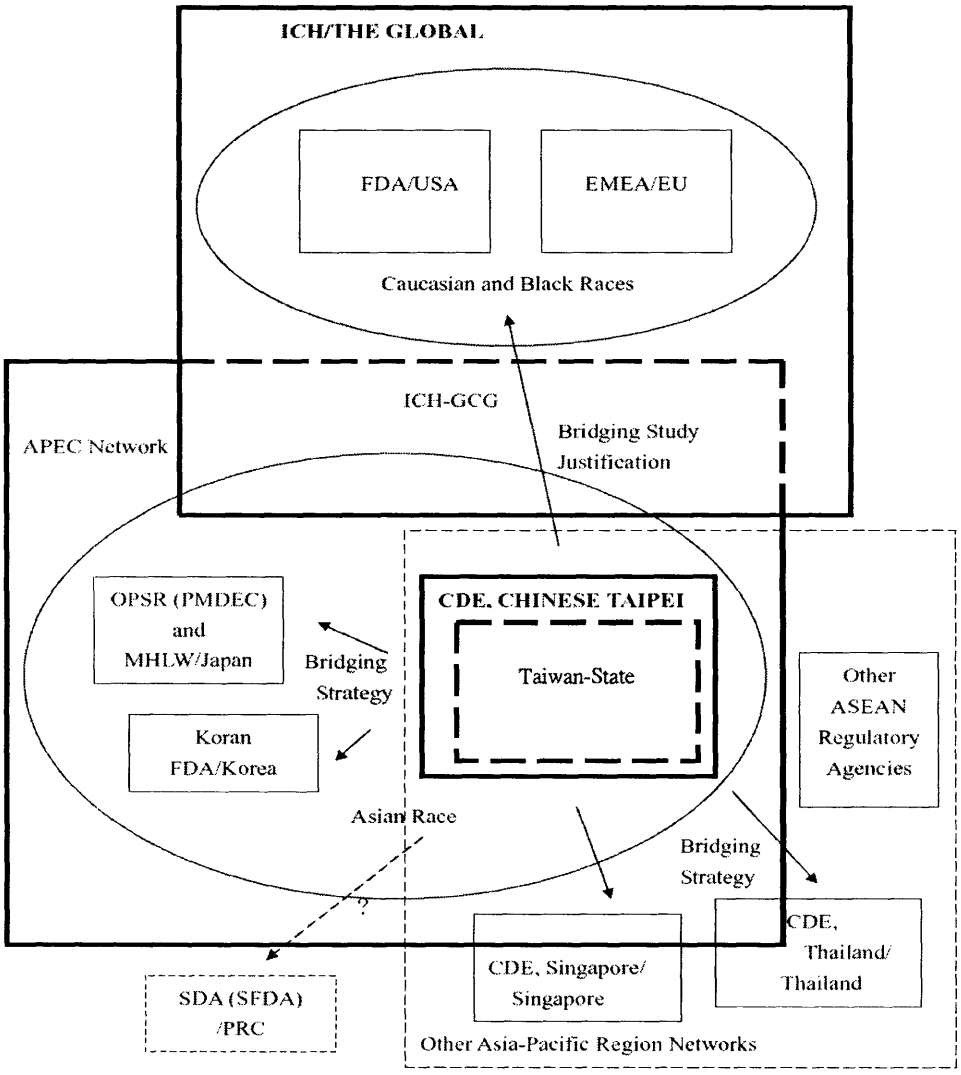
[9] I mentioned in Chapter 3 that Taiwan's vibrant economy allowed it to develop a sizable drug market, but it produces almost no innovative pharmaceuticals. As a result, industry does not play a part in Taiwan's relationships with the ICH.

[10] Taiwan is formally called "Chinese Taipei" at the APEC and in the World Trade Organization it has an even weirder name: "Separate Customs Territory of Taiwan, Penghu, Kinmen and Matsu."

[11] It is not necessary to make a list of comparison here between the WTO and the APEC. In short, the APEC has several advantages the WTO does not have to make Taiwan a global voice. First, it is a network operated on the basis of open regionalism and concerted unilateralism. Therefore, it is relatively easy to propose a new project for cooperation. Second, despite it is a regional organization, but because of the rising importance of East Asia, the APEC includes world powers such as the United States and Japan. Third, originated from Asian Development Bank, the APEC has Taiwan as one of its founders and a major

Fig. 9.4. The World of Pharmaceuticals from Taiwan's Viewpoint



Note: ASEAN: Association of South-East Asia Nations; EMEA: European Agency for the Evaluation of Medicinal Products; SDA: State Drug Administration; SFDA: State Food and Drug Administration.

Organizational restrictions have shaped Taiwan's worldview and its voice as much as have the technocrats who dream of returning Taiwan to its golden age. The existence of Taiwan's statehood is problematic, so it is identified either through its regulatory

supporter, thus Taiwan has more bargain power than does in the WTO.

authority, the CDE, or by the formal name it agreed to use at the APEC, "Chinese Taipei." Taiwan's main stage at the ICH is the Network of Pharmaceutical Regulatory Science-APEC Joint Research Project on Bridging Study. If we take a look at fig 9.4, we notice that by putting Taiwan as its operational center, this network was constructed by members committed to the bridging strategies Taiwan provides. Related to this, the members of this network are as active as they are able to practice these strategies. Hence only Japan and Korea are qualified and willing to serve as supporting members, sitting beside Taiwan. Some ASEAN countries, such as Singapore and Thailand, are barely visible at the margins of this network.

Here we should notice how Taiwan treats Japan within this network. Interestingly, Taiwan does not consider Japan as an ICH member. Since the MHLW has no interest in presenting other Asian countries' interests at the ICH, Taiwan would not expect it to provide access to the ICH. Also, the MHLW and the CDE have different opinions about the acceptance of foreign clinical data. Because the CDE follows the E5 guideline strictly, it believes that it can communicate directly with other ICH members without the mediation of the MHLW. According to this view, Japan remains significant but less significant for Taiwan than Korea.

Even so, Taiwan knows perfectly well that if the CDE ever fails to perform brilliantly, its existence can only be guaranteed by the discursive networks it creates. In Chapter 5 I showed how the CDE connected directly to the ICH via the APEC by attending GCG activities. The CDE restlessly made connections with other countries that might be interested in bridging studies and tried to establish a regulatory platform for the Asia-Pacific region (see fig. 9.4, lower right) — it even attempted to contact the mysterious PRC. This is a complicated world consisting of various networks; through them these medical technocrats successfully gave Taiwan an institutional voice and have tried their best to maintain its voicing ability. But these connections are fragile: the CDE could be replaced in the GCG at any time and its plans to "regionalize" bridging studies may well fail. This world cannot be stabilized unless Taiwan manages to convince the relevant organizations to make these networks permanent. And this Taiwan cannot do: its voice is far too weak.

Let me sum up Taiwan's worldview. Taiwan's voice has been created by a group of medical technocrats. By pursuing excellence in drug regulations, they not only skillfully resisted the PhRMA's demands that Taiwan's barriers to pharmaceutical imports be dropped, they crafted a scientific yet strategic bridging study that raised Taiwan's profile at the ICH. Since the world is an issue-oriented, dynamic nexus, Taiwan has to keep exploiting global trends to make more connections if it is to survive.

Now we have two East Asian worldviews. These are not just two different ways to conceive of the world, they help us understand the priorities of these two entities that go beyond mere politics. Furthermore, they indicate distinct social concerns or cultural values (perspectives) usually ignored by policy analysts. And they prove that the norm introduced by globalization does not ineluctably erase unique attributes. On the contrary, Japan's systematic resistance to the attempt to draft a universal human standard and Taiwan's fierce commitment to making its statehood visible demonstrate the need for an ethnography. As presented in this thesis, transnational institutions have not led to the decline of nation-states, but rather reinforce the prerogatives of such states. As long as these prerogatives are reiterated, it can be expected that the aspiration to achieve full nationhood will remain. In this sense, the debate over racial difference at the ICH is a technoscientific outgrowth of Nakasone Yasuhiro and Lee Teng-Hui's hope to that their countries might become "normal" in the era of globalization.

PART III
PARTIAL PERSPECTIVES AND MULTIPLE READERSHIPS

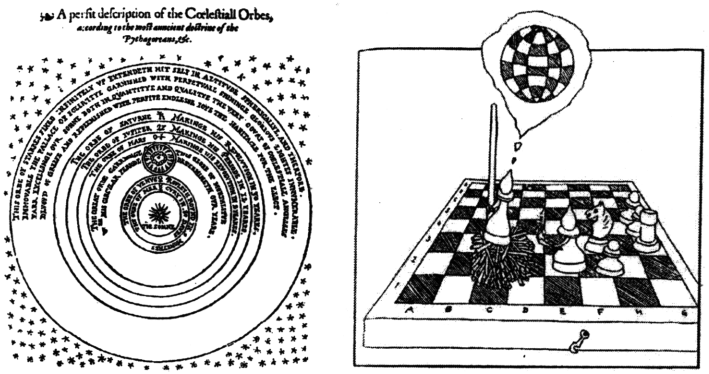
From Ethnographic Texts to the World of Texts

Finally, I will deal with the issue of the writing of cultures. This part serves as an explication of the first part of this chapter, where I briefly discussed the notion of voice and voicing, and of the questions I brought up in Chapter 1 concerning the reasons for writing the present thesis and the readership I expect.

In order to combine the three ethnographies on which my thesis draws, it is necessary to return to the analogy of the Aristotelian-Ptolemaic universe (fig. 1.2). In this cosmology, the state is like the lunar sphere in a cosmological model. When the United States becomes the point of observation for the rest of the world, the state (in this case, the U.S.) abruptly becomes unidentifiable because its domestic viewpoints more or less affect the way world thinks and acts. It is an "America-centric" view of world and the state many hold even when dealing with other states in the world. Only when the point of observation is moved to another planet (for example, East Asia) do ethnographers realize that the state is a lens shaping what they see. In the previous section I showed how such a lens works by tracing how Taiwan and Japan control their domestic territories and how they define their relationships with other countries. In keeping with the theoretical

demands of contemporary anthropology, my thesis presents three worlds from different viewpoints.

Fig. 9.5. Where Does the Truth of the Universe Rest? *Left,* The Copernican Universe; *Right,* Scientific and Cultural Revolutions, Then and Now.



Source: Rice College website devoted to Galileo. http://galileo.rice.edu/sci/theories/Copernican_system.html (left). Cartoon by Leven Abrahamian, in Fischer 2003: 337, Plate 29 (right).

One might ask which of these three is correct? During the scientific revolution the Copernican model finally prevailed over the Aristotelian-Ptolemaic one, but that kind of paradigm shift is not a possible outcome of the confrontation among perspectives that takes place at the ICH. While questioning the American worldview is an important aspect of my study, any essentialist assertion about the true nature of this worldview is dogmatic and dangerous. Rather, the scientific revolution should be a zone where scholars of science and technology studies can explore different ways to appreciate cultural practices, social mobilization, and epistemological reorganization through and about science (fig. 9.5). Similarly, I have used the debate over racial difference at the ICH as a window into the world of proprietary drugs. Mine is no Kuhnian thesis on the philosophy of science and I do not deal much with how paradigms compete each other; instead, it is a historical and ethnographic narrative investigating the dynamics at the interfaces between East Asia and the bio-global world. Access to these worldviews is available only through a sympathetic understanding of Japan's insistence on its racial uniqueness and Taiwan's struggle to achieve normal statehood.

If I am not about to make a final judgment on this cultural encounter, why compare these worldviews? In this final section, I will complete my ethnographic theory of voice and voicing by adding a set of metaphors of vision, emphasizing the spatial aspect of writerly agency. Vision is more ontological than voicing; it always presents a

phenomenon that has meaning only for the seer, whereas voicing is more relational. The three worldviews examined in my study are not incompatible: they can coexist because they are situated and offer only partial perspectives.

Of course, this is not original. Donna Haraway built her scientific projects on just this strategic argument (1991, Chapter 9). My take on globalization in East Asia closely resembles her critical review of feminist science. In a discussion of "situated knowledge," Haraway rejected two feminist attempts to essentialize women's experience in science. This experience was real and objective, she insisted, and the worldview it supported could not be interpreted as relativistic or totalizing.[12] Explicitly relativistic approaches fail to explain women's different worldviews among women with different experiences and cannot generalize this worldview. Totalizing approaches lose their objective ground while generalizing local experiences and make communication with other worldviews more difficult. As Haraway said,

> Relativism is the perfect mirror twin of totalization in the ideologies of objectivity; both deny the stakes in location, embodiment, and partial perspective; both make it impossible to see well. Relativism and totalization are both "god-tricks" promising vision from everywhere and nowhere equally and fully, common myths in rhetorics surrounding Science. But it is precisely in the politics and epistemology of partial perspectives that the possibility of sustained, rational, objective enquiry rests. (191)

My efforts to construct and juxtapose three different ethnographies are due in no small measure to this passage. I neither excoriate the West (the "objectivity" in Haraway's quotation) nor do I glorify non-Western regions (feminist science Haraway referred in her study). I neither dismiss universal modernity nor do I propose Asian alternatives. The moral of this thesis is: preserve the rhetorical symmetry between different worldviews. Although the worldview of the West is often portrayed as strong and invincible, it is not a universal truth but a local culture. In accordance with this narrative scheme, the worldviews of East Asia are somehow generalized (while, paradoxically, remaining partial) in order to be set into symmetric correspondence with the Western worldview.

I am not describing a cultural divide between East and West. I am not following the fashionable line that opposes the global to the local. By demystifying the political and

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[12] This is an important argument because it is the basis on which Haraway builds her epistemological agenda for feminist science. As she says, "Only [a] partial perspective promises objective vision" (1991: 190).

economic concerns raised in the name of science and public health, I have shown the temporal and cultural specificity of the logic behind the world of proprietary drugs. In the same manner, by analyzing the tactics and strategies that the MHLW and the CDE used at different times and in different situations, I describe the systematic, positioned rationalities of countries long considered socially passive, technically fragmented, and culturally superstitious. I make no claims for an objectively differentiated "Asian" culture totally incommensurable with the West. As Haraway writes of feminism, it "resists the politics of closure, finality, or, to borrow from Althusser, feminist objectivity resists 'simplification in the last instance'" (1991: 196). Whether global or local, here all worldviews are treated symmetrically — only "god-tricks" are forbidden.

The present thesis presents a world of texts based on no particular viewpoint; instead, it is a description, a story, told rather plainly. It casts the Asian states as its writerly agencies, but they function in my thesis merely as actors. The theme of this thesis is that which Bruno Latour has proposed for the ethnography of science (1993), namely, the connections and relationships formed by states facing a new situation called bio-globalization. Of course, this kind of narrative has a strong moral concern about being seen and understood in a particular way. Addressing the competition bound to arise among different visions, Haraway wrote, "Struggles over what will count as rational accounts of the world are struggles over *how* to see" (1991: 194; emphasis in original). My narrative includes not only reconstructions of new visions or worldviews; it demands that various technologies reconstruct the process of a creation that might have been erased by other visions.

Mostly, I am concerned about how such agencies and worldviews can appear in this world of text, namely, this thesis. This is where it departs from a purely philosophical investigation and where the auditory metaphors of voice and voicing are called upon. The world of text is a presentation of what Mikhail Bakhtin called *heteroglossia,* the interweaving of voices that meet to exchange ideas and opinions, which in turn generates new meanings and signs that are not predictable in their original dialogic contexts. Before comparing existing worldviews, I investigated how individual voices came into existence. Since not every state can speak a line or two at the ICH, I differentiated between two sets of technologies concerning the making of the voice. Moreover, Michael Fischer (2003) reminded us of the importance of comparing different voices

> as a form of critique by juxtaposition between cultural, moral, or social discourses, where the juxtaposition would recognize that these were socially situated, that they required further inquiry about their formation, efficacy, and place among

> contesting perspectives. Similarly, *Writing Culture* was an interdisciplinary effort to draw attention to the complex rhetorical forms that professionals adopt, both to encourage inquiry into the formation of expert cultures and to encourage experimentation with a wider range of disciplinary tools to heighten the multidimensionality of anthropological inquiry and analysis. (12)

In the present thesis, I have slighted neither traditional fieldwork nor traditional ethnography more generally. This is definitely not either a playful experiment or an empty, rhetorical construction. Rather, I champion the use of ethnography by emphasizing its moral content, just as the pioneers of this discipline did 150 years ago. By giving voices to the voiceless and juxtaposing them, ethnography can serve as a new form of metanarrative, like the grand theories of the nineteenth century (Fischer 2003: 40).

From the World of Texts to an Ethnography of Globalization

Because reception is always multiple, because I am presenting different (and contradictory) anthropological voices, my narrative has been focused on the global discursive fields surrounding the ICH and the different voices in the debate on racial difference. The juxtaposition of distinct worldviews involves readers in ethical issues tied to reading and writing.

Some have suggested to me that the ICH is so idiosyncratic that it cannot possibly provide the basis for generalization. Certainly, the discussions held at the ICH are highly technical, but this does not disqualify them from shedding new light on the state and globalization. Others have said that the ICH is too complicated for the sort of focus needed in a serious investigation. It is true that, like many global institutions, the ICH belongs to a particular domain; it is related to the fields of medical policy, public health, capitalism, globalization and regionalism, bodily politics, and many others. This very complexity is why I have limited my scope to a highly discrete issue and prepared my narrative with certain readers in mind.

The value of the present study can be judged only by the people for whom it was written. I have borne three kinds of readers in mind: cultural anthropologists who want to understand globalization and new ways to deal with it, regional researchers on East Asia, and analysts of medical policies. Certainly cultural anthropologists are my principal audience. Using the debate over racial difference as an example, the present thesis not only creates new subjects, fields, and technologies for ethnography, it also proves that

ethnography is still a useful tool for capturing the changing world of science and technology. As for new subjects, my study shows that the state is an appropriate subject of ethnographic inquiry. Like other artifacts created by modernity, the state is a regulatory body, an intermediate matrix between individuals and the world. Although it cannot be felt by most of its people, who do not visit other states, the state is not transparent: it does not faithfully deliver to the local at the behest of the world. If it is to interact with others while maintaining its ruling legitimacy, the state has to create ways to survive, develop visions, and accomplish goals. In addition, in order to make ethnography feasible at an international level, I have treated conferences as international fields.

I have also developed several technologies seldom applied together in anthropology. First of all, in investigating a modern institution such as the scientific conference, the ethnographer most employ a rather free definition of fieldwork, including interviews, archival research, and analysis of legal documents and e-mail communications. Second, to study modern societies, I have relied on documents in local languages to grasp how the state conceives of itself and the world. Third, to deal with a universal culture such as science, I have approached it from outside, using social factors to disassemble the logic of science from within. In other words, a careful reading of scientific materials is necessary.

I have one more note for cultural anthropologists on how to treat old concepts like the state and race in their future works. One of the elements crucial to the construction of nation-states and nationalism, race was perhaps the first to be challenged by and buried under the waves of globalization. This has been particularly true of East Asian states, where the "imagined communities" are shored up by many factors other than race. But when anthropologists hastily shift their subjects from biological race to socially driven factors such as ethnicity, class, or gender, it is time to remind them that the epistemic configuration of race, though fictitious, has not been completely usurped by talk of populations and the genome (Haraway 1997: Chapter 6). These up-to-date subjects are part of the discussion of Japanese national character, a discussion in which visions of race thrive. As a social concept, race is fluid and always questionable. It can be an essential part of Japan's insistence on equal representation in clinical trials; nonetheless, it is easily dropped when it is time to construct the CDE's policy on bridging studies. And like other social factors in anthropology, race works as a probe or a lens to excite the observer's attention.

My second group of readers, specialists in regional studies, may find in my study some new ideas about what the local means in a global context. This is particularly true

for Japan and Taiwan, which have been viewed as racist and willful. I want to show that both dichotomies between the East and the West and between culture and science are no longer appropriate in the technoscientific world, where science and culture penetrate each other, as do the global and the local.

Consider, for instance, the Japanese race under globalization. In a famous article by James Fallows entitled "Containing Japan" (1989), the influence of exposure to freer societies was pondered:

> The millions of Japanese who travel overseas each year, and the hundreds of thousands posted to foreign countries on long assignments, presumably come home with a more open, internationalized point of view. Eventually they will demand a fairer political system and a more consumer-minded economy, and will open their society in the way it is now most closed: the visceral reaction against non-Japanese intruders among the "pure race" Japanese. At that point, according to the optimists, Japanese and Americans (and other foreigners) will work alongside one another as individuals, aware of their national identities but not separated by them.

But this argument is a straw man, says Fallows, who insists that Japan is much more stubborn than people think. I do not know who is right, but the familiar contrast of Japan and the world deserves careful examinations. Of course, as I described in Chapter 8, *kokusaika* has complicated the landscape of the Japanese *minzoku* over the past two decades. But this does not mean that Japan cannot build its global nationhood by shifting to a "consumer-minded economy." The nation-state of Japan should be conceived in its establishment of locality, yet this locality should always be related to its attempts to participate in globalization. While Chapter 4 records Japan's participation in the ICH as a step toward globalization, Chapter 6 sees Japan's move toward a genomic definition of race as an attempt to impose a new global standard. Cultural resistance is a term for a bilateral world: we need a new framework, a topology that maps the complicated twists and folds of the spaces where we live and think.

Similarly, Taiwan's diplomatic problems should be seen in a global context instead of an international one. The problem here is not whether Taiwan should be a country or not; at stake is Taiwan's "nationalist reality," something Horng-leun Wang defined as "the reality that is defined, reified, and reproduced by institutions of nation-states or their agents" (2002: 141). Again, this locality has to be understood together with the global. In another paper, Wang (2000) has suggested that Taiwan's nationalistic politics, which are *par excellence* of an international nature, are intertwined with its involvement with such effects of globalization as transnational mobility and cultural experience overseas. The

distinction between the international and the domestic does not match the phenomenon examined in the present study. The reality is that with the advent of globalization, Taiwanese no longer need to go abroad to feel their country as a whole in the world; this embarrassing, weird identity can be seen and felt even in domestic scenes. The CDE's performance at the 2003 APEC welcoming banquet is just one example.

The controversy at the 2001 Asian Women's Football Championship, which was hosted in Taipei, is an example of what Michael Billig (1995: 6) calls "banal nationalism," namely, "the ideological habits which enable the established nations in the world to be reproduced." Organized by the Asian Football Confederation, this biannual championship has been held for over a quarter of a century. The myth that political differences do not exist in sports permits North Korea, South Korea, the PRC, and Taiwan to attend. However, in compliance with International Olympic Committee rules, Taiwan's national colors are replaced by its Olympic flag (fig. 5.3, upper left). While this rule is always applied in international sporting events, it was galling for Taiwanese athletes and spectators to be confronted with the flag of the PRC flying on Taiwanese soil and not a proper Taiwanese flag in sight. It cannot have come as a great surprise when a number of Taiwanese soccer fans brought Taiwanese flags to the soccer stadium. When police officers tried to stop the fans from waving the national flag, fights broke out. Later criticism of Taipei's mayor was met with the official statement that the city government had only followed international conventions.[13] A globalized Taiwan has prepared for its people a stage on which the drama of national identity is played out. The sense of injustice, of being an "international orphan," can be found in every field. As Wang Horng-leun reminded us (2001: 255), "Inasmuch as the nation-state's institutions imply a complete social entity, no place can be ruled out as a battlefield when it comes to nationalist politics."

My analysis of the ICH can show medical policymakers, the third group of readers, how traditional international organizations, such as the WHO, remain oblivious to trends in healthcare that involve heavy investments of industry and capitalist logic. To identify the pressing issues confronting organizations charged with international health, I have proposed moving away from institutional hierarchies and toward the dynamic relations among regulators and drug makers. Though communication among anthropologists and policymakers faltered for a long time, there are excellent works on the vertical structure

[13] In fact, as the National Council on Physical Fitness and Sports explained, no rules prohibit spectators from waving flags at international sporting events. Presumably the police actions were dictated by political concerns and pressure from Beijing.

of health policy practice, such as Judith Justice's analysis (1986) of the aid administered in Nepal by the WHO. By tracing this institutional structure from the global level to rural villages, and by investigating the cultural concerns that exist at each level, Justice showed how anthropologists can help fill in the communication gaps between the levels. The present thesis is a similar attempt to lay out the structure of health policy in the era of globalization. I have tried (Kuo 2003, 2005) to heed Justice's suggestion that anthropologists need to present the information they collect in a form that planners can use (Justice 1986: 154).

The explosion of online pharmacies and medical tourism (for example, cosmetic surgery trips to Thailand and Venezuela, organ sales in the PRC and India) represent major challenges to the state's commitment to protecting its people's health. In this sense, my study may appeal to those who are interested in learning about race and state in East Asia. Japan and Taiwan bring their own concerns to ICH meetings, and these are often unrelated to health per se. But rather than think of these concerns as political, we should think of them as a hybrid of political and health concerns. Relatively homogenous nonwhite populations need to be protected against the rampant imposition of medical standards based on Western ideas. This resistance is cultural, and it has to be done through the state.

This reminds me of the rather odd conclusion to the ICH-GCG meeting I attended in July 2003. Rather abruptly, the committee invited Francis P. Grawley, the representative of Strategic Initiative for Developing Capacity in Ethical Review, to explain how ethical codes in clinical trials could be standardized. Although his presentation was interesting, nobody paid any attention — they had other concerns. The representatives of the pharmaceutical industry, as always, did not really care about ethical issues: they only really care about lowering the cost of these trials. The developing countries, which cannot afford good clinical trials, saw such matters as utterly irrelevant to themselves. Some countries that do conduct fine trials remained silent: the struggles they have undergone because of racial difference have haunted them for over ten years, and should such a standard come into being they have no idea how population differences will be handled. After a long and embarrassing silence, the meeting was concluded.

After reviewing how the present thesis can evoke different sets of questions and issues in different readers, I want to conclude by citing Michael Fischer's portrait of culture:

> Culture is not a variable; culture is relational, it is elsewhere, it is in passage, it is where meaning is woven and renewed, often through gaps and silences, and

> forces beyond the conscious control of individuals, and yet the space where individual and institutional social responsibility and ethical struggle take place. (2003: 7)

I wonder whether this portrait applies to states at the global level, if we swap the words *state* for *individual* and *global* for *society.* Globalization does not sweep all things away, as many have claimed; in the genomic/global world the state and races take on new lives. I have tried to depict the culture of globalization and how it changes and is changed by struggles and discussions over the state and race. Nation-states may eventually decline, but they are thriving today and will thrive tomorrow. Like it or not, people still need a nationality and the state is an indispensable category in the institutionalized grid of the world. Gellner was right: in the age of globalization, the state still matters.

As I take my leave, let me borrow Tonio's last line in *Pagliacci* to announce the end of this social (melo)drama: *La comedia e finita* (the story is over).

Appendix 1: Basic Information on the ICH Conferences

ICH conferences	Dates	Places	Numbers of participants
ICH1	November 6-8, 1991	Brussels, Belgium	about 1,200
ICH2	October 27-29, 1993	Orlando, Florida	about 1,600
ICH3	November 29-December 1, 1995	Yokohama, Japan	about 2,400
ICH4	July 16-18, 1997	Brussels, Belgium	about 1,600
ICH5	November 9-11, 2000	San Diego, California	1,309
ICH6	November 12-15, 2003	Osaka, Japan	over 1,800

Appendix 2: ICH guidelines, 1991-2003

Note:

The ICH set a highly technically process for making guidelines; even so, as seen in this appendix, it has achieved the finalization of fifty-six guidelines, including twenty-three in the category of quality, fifteen in that of safety, and fourteen in that of efficacy, along with four multidisciplinary guidelines. Every ICH member has different processes for the implementation of these guidelines, which, adopted from the ICH website (http://www.ich.org) in alphabetical order, will be introduced in the following:

EU. The ICH guidelines were submitted to the Committee for Proprietary Medicinal Products (CPMP) for endorsement once they have reached Step 2 or Step 4 of the ICH Process. The CPMP decided on the duration for consultation with interested parties (usually six months). The European Agency for the Evaluation of Medicinal Products (EMEA) publishes and distributes the Step 2 drafts of guidelines for comments. At Step 4 the drafts are endorsed by the CPMP and a timeframe for implementation is established (usually six months). The guidelines are subsequently published by the European Commission in Volume III of the *Rules Governing Medicinal Products in the European Union.*

FDA. When Step 2 or Step 4 drafts have been reached, FDA publishes a notice with the full text of the guidance in the *Federal Register*. Notices for the Step 2 drafts of guidelines include a date for receipt of written comment; the Step 4 drafts of guidelines are available for use on the date they are published in the *Federal Register*.

MHLW. When Step 2 or Step 4 drafts have been reached, the ICH texts are translated into Japanese. Subsequently Pharmaceutical and Medical Safety Bureau (PMSB) Notification for the promulgation or consultation of guidelines is written in Japanese issued with a deadline for comments in the case of consultation drafts, or an implementation date for finalized guidelines. The notifications on guidelines in Japanese and also English attachments (ICH Texts) are available from PMSB or on the website of the National Institute of Health and Science.

ICH Guidelines

Quality

Topic number	Guidelines	Date of implementation (Step Five)	
Q1A	Stability testing of new drug substances and products	All regions	1994
Q1A (R1)	Stability testing of new drug substances and products (first revision)	All regions	2001
Q1A (R2)	Stability testing of new drug substances and products (second revision)	CPMP	March 2003
		MHLW	June 2003
		FDA	November 2003
Q1B	Photostability Testing of New Drug Substances and Products	CPMP	December 1996
		MHLW	May 1997
		FDA	May 1997
Q1C	Stability Testing for New Dosage Forms	CPMP	December 1996
		MHLW	May 1997
		FDA	May 1997
Q1D	Bracketing and Matrixing Designs for Stability Testing of Drug Substances and Drug Products	CPMP	February 2002
		MHLW	July 2002
		FDA	January 2003
Q1E	Evaluation of Stability Data	CPMP	March 2003
		MHLW	June 2003
		FDA	June 2004
Q1F	Stability Data Package for Registration Applications in Climatic Zones III and IV	CPMP	March 2003
		MHLW	June 2003
		FDA	November 2003
Q2A	Text on Validation of Analytical Procedures	CPMP	November 1994
		MHLW	July 1995
		FDA	March 1995
Q2B	Validation of Analytical Procedures :	CPMP	December 1996

	Methodology	MHLW	October 1997
		FDA	May 1997
Q3A	Impurities in New Drug Substances	All regions	1995
Q3A (R)	Impurities in New Drug Substances (Revised)	CPMP	February 2002
		MHLW	December 2002
		FDA	February 2003
Q3B	Impurities in New Drug Products	All regions	1997
Q3B (R)	Impurities in New Drug Products (revised)	CPMP	March 2003
		MHLW	June 2003
		FDA	November 2003
Q3C	Impurities: Guideline for Residual Solvents	CPMP	September 1997
		MHLW	March 1998
		FDA	December 1997
Q3C (M)	Impurities: Guideline for Residual Solvents (Maintenance)	CPMP	September 2002
		MHLW	December 2002
		FDA	November 2003
Q5A	Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin	CPMP	April 1997
		MHLW	February 2000
		FDA	September 1998
Q5B	Quality of Biotechnological Products : Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products	CPMP	December 19995
		MHLW	January 1998
		FDA	February 1996
Q5C	Quality of Biotechnological Products : Stability Testing of Biotechnological/Biological Products	CPMP	December 1995
		MHLW	January 1998
		FDA	July 1996
Q5D	Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products	CPMP	September 1997
		MHLW	July 2000
		FDA	September 1998
Q5E	Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process	CPMP	November 2003
		MHLW	May 2004
		FDA	March 2004
Q6A	Specifications : Test Procedures and	CPMP	November 1999

	Acceptance Criteria for New Drug Substances and New Drug Products : Chemical Substances	MHLW	May 2001
		FDA	December 2000
Q6B	Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products	CPMP	March 1999
		MHLW	May 2001
		FDA	August 1999
Q7A	Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients	CPMP	November 2000
		MHLW	November 2001
		FDA	September 2001

Safety

Topic number	Guidelines	Date of implementation (Step Five)	
S1A	Guideline on the Need for Carcinogenicity Studies of Pharma- ceuticals	CPMP	December 1995
		MHLW	April 1997
		FDA	March 1996
S1B	Testing for Carcinogenicity of Pharmaceuticals	CPMP	September 1997
		MHLW	July 1998
		FDA	February 1998
S1C	Dose Selection for Carcinogenicity Studies of Pharmaceuticals	All regions	1994-1996
S1C (R)	Addendum : Addition of a Limit Dose and Related Notes	CPMP	September 1997
		MHLW	July 1998
		FDA	March 1997
S2A	Guidance on Specific Aspects of Regulatory Genotoxicity Tests for Pharmaceuticals	CPMP	September 1995
		MHLW	July 1996
		FDA	April 1996
S2B	Genotoxicity: A Standard Battery for Genotoxicity Testing for Pharma- ceuticals	CPMP	September 1997
		MHLW	July 1998
		FDA	November 1997
S3A	Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies	CPMP	November 1994
		MHLW	July 1996
		FDA	March 1995
S3B	Pharmacokinetics: Guidance for Repeated	CPMP	November 1994

	Dose Tissue Distribution Studies	MHLW	July 1996
		FDA	March 1995
S4	Text on Validation of Analytical Procedures	All regions	1993
S4A	Duration of Chronic Toxicity Testing in Animals (Rodent and Non-Rodent Toxicity Testing)	CPMP	November 1998
		MHLW	April 1999
		FDA	June 1999
S5A	Detection of Toxicity to Reproduction for Medicinal Products	CPMP	September 1993
		MHLW	July 1994
		FDA	September 1994
S5B (M)	Maintenance of the ICH Guideline on Toxicity to Male Fertility: An Addendum to the Guideline on Detection of Toxicity to Reproduction for Medicinal Products	CPMP	December 1995
		MHLW	April 1997
		FDA	April 1996
S6	Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals	CPMP	September 1997
		MHLW	February 2000
		FDA	November 1997
S7A	Safety Pharmacology Studies for Human Pharmaceuticals	CPMP	November 2000
		MHLW	June 2001
		FDA	July 2001

Efficacy

Topic number	Guidelines	Date of implementation (Step Five)	
E1	The Extent of Population Exposure to Assess Clinical Safety for Drugs Intended for Long-Term Treatment of Non-Life-Threatening Conditions	CPMP	November 1994
		MHLW	May 1995
		FDA	March 1995
E2A	Clinical Safety Data Management : Definitions and Standards for Expedited Reporting	CPMP	November 1994
		MHLW	March 1995
		FDA	March 1995
E2B (M)	Maintenance of the Clinical Safety Data Management including : Data Elements	CPMP	November 2000
		MHLW	March 2001

	for Transmission of Individual Case Safety Reports (Version 4.4.1)	FDA	April 2002
E2C	Clinical Safety Data Management : Periodic Safety Update Reports for Marketed Drugs	CPMP	December 1996
		MHLW	March 1997
		FDA	May 1997
E2C (A)	Periodic Safety Update Reports for Marketed Drugs	CPMP	March 2003
		MHLW	April 2003
		FDA	February 2004
E2D	Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting	CPMP	November 2003
		MHLW	
		FDA	
E3	Structure and Content of Clinical Study Reports	CPMP	December 1995
		MHLW	May 1996
		FDA	July 1996
E4	Dose-Response Information to Support Drug Registration	CPMP	May 1994
		MHLW	July 1994
		FDA	November 1994
E5	Ethnic Factors in the Acceptability of Foreign Clinical Data	CPMP	March 1998
		MHLW	August 1998
		FDA	June 1998
E5 (Q&A)	Ethnic Factors in the Acceptability of Foreign Clinical Data Questions & Answers	CPMP	November 2003
		MHLW	February 2004
		FDA	June 2004
E6	Good Clinical Practice : Consolidated Guideline	CPMP	July 1996
		MHLW	March 1997
		FDA	May 1997
E7	Studies in Support of Special Populations : Geriatrics	CPMP	September 1993
		MHLW	December 1993
		FDA	July 2001
E8	General Considerations for Clinical Trials	CPMP	September 1997
		MHLW	April 1998
		FDA	December 1997
E9	Statistical Principles for Clinical Trials	CPMP	March 1998
		MHLW	November 1997

		FDA	September 1998
E10	Choice of Control Group and Related Issues in Clinical Trials	CPMP	July 2000
		MHLW	February 2001
		FDA	May 2001
E11	Clinical Investigation of Medicinal Products in the Pediatric Population	CPMP	July 2000
		MHLW	December 2000
		FDA	April 2000

Multidisciplinary guidelines

Topic number	Guidelines	Date of implementation (Step Five)	
M1	Medical Terminology	All regions	1999
M2/ E2B (M)	Electronic Standards for Transmission of Regulatory Information (ESTRI)	All regions	February 2001
M2/ eCTD	Electronic Common Technical Document	CPMP	November 2003
		MHLW	May 2004
		FDA	
M3	Timing of Pre-clinical Studies in Relation to Clinical Trials	FDA	November 1997
		MHLW	November 1998
		FDA	November 1997
M4	The Common Technical Document	CPMP	November 2003
		MHLW	May 2004
		FDA	

(R): revision; (M): maintenance; (A): Addendum. (Q&A): questions and answers.

Terms and Names in East Asian Languages

Note:

It is always a problem when people deal with topics outside of the English-speaking world. Researchers who do not know East Asian languages may prefer translations rather than romanization of these terms. However, the necessity of accuracy must be stressed that translations would unacceptably change the meaning of these terms. More importantly, people who have mastered the languages will want to know precisely what the author has translated, particularly since the names and terms are often rendered in English or roman letters in several different ways. For these purposes, in this thesis some terms and names are retained in romanization to indicate their Asian origins, and tables are provided to correlate these terms with the local languages from which they are phonically transcribed.

Like other literature concerning this region, Japanese and Taiwanese personal names are given in the local manner, surname followed by given name unless quoted or appearing in the materials written in English. Some readers may also have difficulties in distinguishing among the numerous names of Asian people that occur in this thesis. Nakamura, Nagamura, Nakayama, Chang, Chung, Cheng are all distinctive names when articulated in their languages, but in English they tend to blur. On the other hand, some names that look distinctive, such as Chern and Cheng or Kuo and Quo, are in fact different spellings of the same character. It is particularly common in Taiwan where there exist no rigid regulations imposing a "standard" way of romanization for people's names. I do not apologize for this, since to tell these names is a starting point to achieve a mutual understanding on these people and their activities studied. In addition, everyone has the freedom to choose the way s/he prefers to be called. Thus, in the following correlation tables are provided for people who want to know their names in the original language.

Japanese terms

ainoko; konketsuji; hafu; daburu	合いの子; 混血児; ハーフ; ダブル
amae	甘え
bonkure	盆暮れ
buraku; tokushu Buraku	部落; 特殊部落
Bushido	武士道
dassaioka	脱西欧化
datunihonka	脱日本化
egao no uragawa	笑顔の裏側
esunikku gurupu	エスニック グループ
esunishitei	エスニシティ
fukoku kyohei	富国強兵
gaiatu	外圧
gendaiyogo no kisochishiki	現代用語の基礎知識
gizyutsu kei kanryo	技術系官僚
hanshuken kokka	半主権国家
hone	本音
iemoto	家元
Issho	一緒
Jieitai	自衛隊
jikohonyi	自己本位
jimukan	事務官
jin, jinjutsu,	仁、仁術
jinshu	人種
jitsu taizei; jitsu mondai	G2 体制; G2 問題
kanari nihonzin	かなり日本人
kazamidori	風見鶏
keiken	経験
keizaishakai kaihatu keikaku	経済社会開発計画
kenkyuhan	研究班
keizaishakai	経済社会
kenzen; tadashii	健全;正しい
kenzenna nashonarizumu	健全なナショナリズム
kohatu kigyo	後発企業
kokumin-shugi, kokusui, kokusui-shugi, junketsu-shugi	国民主義、国粋、国粋主義、純血主義
kokusaijin	国際人
kokusaika	国際化
kokusaika; naru no kokusaika; suru no kokusaika	国際化;なるの国際化;するの国際化
kokusaikyodochiken	国際共同治験
kokuseki	国籍
Kudoka; chiken no kudoka	空洞化;治験の空洞化
kunihiki	国引き
kusurizuke	薬漬け
kyojyu	居住
kyoka	許可
kyokai	境界
kyosaikumia	共済組合
manga	漫画
mattaku nihonzin	まったく日本人
meijinohito	明治の人
minzoku	民族
minzoku sabetu	民族差別
Minzoku gakko	民族学校
naiatu	内圧
naniwabushi	浪花節
Nihon bashingu;	日本バッシング;

Nihon tataki	日本叩き
nihonmaru	日本丸
okigusuri	置き薬
puropa	プロパー
sakoku jitai	鎖国時代
sashimi	刺身
seijyukuka	成熟化
senmonka	専門家
senpatsu kigyo	先発企業
shalei	謝礼
shamisen	三味線
shikatanasi kokusaika	仕方なし国際化
shinyo	信用
shonin	承認
shudan	集団
shujji	出自
shuzoku	種族
sogo shonin	相互承認
sukoshidake nihonzin	少しだけ日本人
Taikaku, taishitsu	体格,体質
Taiwan soutokufu	台湾総督府
tatemae	建前
wa	和
wakaru	解る
wareware	われわれ
yakka saeki	薬価差益
yakkeigikan, yakumugikan	薬系技官 薬務技官
yamato tamashi	大和魂
yidenshishudan	遺伝子集団
yiryohojin	医療法人
yisichusin shugi	医師中心主義
yiyakubungyo	医薬分業
yojo	養生
zorohin	ぞろ品

Terms in Chinese and Taiwanese

ao ke	奧客
bentuhua	本土化
chianxia	嗆聲
da Zhongguo zhuyi	大中國主義
dongezozu	當家作主
fasheng	發聲
fan zoguo bi liuxia henji	凡走過必留下痕跡
Fulao sawen zhuyi zhe	福佬沙文主義者
gezhi guojia zhuchuan	擱置國家主權
guoji kongjian	國際空間
haiwai xueren	海外學人
hanminzu	漢民族
hanze bu lianli	漢賊不兩立
huaren	華人
huaxia	華夏
Jibo ji kain	一步一腳印
jongzu	種族
kaiyeyi	開業醫
kinfun	Kinfun
kuojiajentong	國家認同
laobao,jianbao, chidaobao	勞保, 健保, 吃到飽
minzhu	民族
nakasi	那卡西
ni hao	你好
propa	Propa
shei li nimen	誰理你們
shenjichingje	省籍情結

shimin; guomin	市民;國民
sihai duyo zhongguoren	四海都有中國人
waishenren	外省人
xing hui	幸會
yaojia heidong	藥價黑洞
xin shidai Taiwanren	新時代臺灣人
xiaocheng gushi	小城故事
xin Taiwanren	新臺灣人
yibien yiguo	一邊一國
wo ye shi Taiwanren	我也是台灣人
yiliaofaren	醫療法人
yipan sansha	一盤散沙
Yueh	越
Zhongguo Taibei	中國台北
Zhunghua	中華
zhonghua Taibei	中華台北
zuchun	族群
zuchun zhenzhi	族群政治
zuchunsirie	族群撕裂
Zhongguoren bu da Zhongguore	中國人不打中國人

Japanese Personal Names

Asami Chiaki	浅見 千秋
Doi Osamu	土井 脩
Goto Simpei	後藤 新平
Hirayama Yoshinobu	平山 佳伸
Hiroi Yoshinori	広井 良典
Itakura Mizuo	板倉 光夫
Kitamura Kazuyuki	喜多村 和之
Kumagai Akira	熊谷 暉
Kurokawa Tatsuo	黒川 達夫
Matsushita Masatoshi	松下 正寿
Mizushima Yutaka	水島 裕
Naito Chikayuki	内藤 周幸
Nakamura Kazuo	中村 和男
Nakamura Yusuke	中村 祐輔
Narikawa Mamru	成川 衛
Nitobe Inazo	新渡戸 稲造
Shintani Tetsuro	新谷 鉄郎
Shiobara Matasaku	塩原 又策
Takeshita Akira	竹下 彰
Tanba Tokichiro	丹波 藤吉郎
Taniguchi Toshiichiro	谷口 俊一郎
Tominaga Toshiyoshi	富永 俊義
Tsutani Kiichiro	津谷 喜一郎
Uwoi Tohru	魚井 徹
Yasuhara Hajime	安原 一
Yoshimura Hitoshi	吉村 仁

Personal Names in Chinese

Chang Hong-Jen	張鴻仁
Chang Hsiu-Gang	章修綱
Chen Shi-Hsin	陳詩欣
Chen Shui-Bian	陳水扁
Cheng Kung-Pei	陳拱北
Chern Herng-Der	陳恆德

Chiang Ching-kuo	蔣經國
Chu Mong-Ling	朱夢麟
Deng Jou-fang	鄧昭芳
Ding Xuelang	丁學良
Hsiao Mei-Ling,	蕭美玲
Hsu Tse-chiu	許子秋
Hu Oliver Yoa-Pu	胡幼圃
Huang Weng-Foung	黃文鴻
Kuo Wen-Hua	郭文華
Lee Chen-yuan	李鎮源
Lee Jung-Jin	李勇進
Lee Pao-Jen	李寶珍
Lee Teng-Hui	李登輝
Lien Chan	連戰
Lin Yu-tang	林語堂
Ma Ying-Jiou	馬英九
Mao Pei-Ling	毛蓓領
Sha Zukang	沙祖康
Tien Weichen	田蔚城
Tsai Chen-Yuan	蔡正元
Tu Tsung-ming	杜聰明
Wu Chuo-Riu	吳濁流
Wu San-Lein	吳三連
Wu Shuh-min	吳樹民
Wu Yi	吳儀
Yang Shih-chien	楊世緘
Yeh Chin-Chuan	葉金川

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