The Effects of Intellectual Property on Innovation:
Implications for R&D in Biotechnology

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Submitted to the Engineering Systems Division in Partial Fulfillment of the
Requirements for the Degree of
Master of Science in Technology and Policy
at the
Massachusetts Institute of Technology
June 2010

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ABSTRACT

The effects of Intellectual Property Rights (IPRs) on innovation in the field of biotechnology are considered through assessment of their effects on upstream innovation and downstream development. Two case studies involving research tools representing forms of upstream innovation are analyzed to identify factors enabling or hindering downstream innovation. The proprietary technologies of recombinant DNA (rDNA) and Polymerase Chain Reaction (PCR) are assessed in relation to both their development and their diffusion strategies. Factors considered are: the type of IPRs, legal circumstances, the strategy regarding disclosure, whether a basic research exemption exists, enforcement of IPRs, the invention's characteristics, the economic resources available (private vs. public), and the development setting.

Assessment of these cases requires consideration of the current intellectual property regime and its associated problems. These principally include the importance of the context (including the legal framework), the strategy adopted by the owners of the IPRs regarding diffusion, the type of development setting, and the invention's characteristics. Ways of dealing with these issues within the traditional IPR systems are assessed, such as patents and trade secrets, for which corresponding types of licenses can provide solutions. Additionally, new approaches are assessed, such as patent pools, clearinghouses, open source models, liability regimes, experimental use exemption, and compulsory licensing. These alternatives are considered both in the United States and under different international regimes. Finally, the potential policy implications of IPRs, both in the United States and internationally, are evaluated with regard to their effects on innovation in biotechnology.

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Table of Contents

List of Tables

List of Figures

Chapter 1

INTRODUCTION

1.1.Topic: Effects of Intellectual Property on Innovation in Biotechnology

This thesis addresses the effects that intellectual property rights have on innovation in biotechnology and, in particular, on the development of research tools and hence products. The current intellectual property regime has been traditionally seen as providing a good structure of incentives for R&D, by creating conditions that promote private investment. On the one hand, according to mainstream economic models, rational economic actors may invest in uncertain, expensive and long term projects only if they can capture the value they create. On the other hand, for current technologies based on information such as biotechnology, strong intellectual property rights tend to diminish or even prevent the sharing of information (e.g., research tools), clearly affecting second generation innovation (e.g., products) or research in areas that are not very profitable (e.g., orphan drugs). Also in question is what the current IPRs rules establish regarding the existence or not of a basic research exemption for academic institutions. It has been suggested that there is a negative effect on diffusion of these technologies and knowledge, which in turn are affected by investment and by the lack of sharing among the parties. Finally, there is a problem of enforcement regarding these technologies.

The exchange of research tools within biomedical research usually involves negotiations over terms and value. Owners and users of research tools usually manage to negotiate successfully when the transactions are important to both sides, but difficult negotiations often cause delays in research and can, sometimes, lead the parties to abandon research plans altogether. Transaction costs have remained high as the heterogeneous institutions involved in the exchange have been unable to agree upon standardized ways of addressing the negotiations.

This could be seen as a market failure or simply as a market, characterized by the existence of transactions costs that make some low value transactions prohibitively expensive. However, something else characterizes this particular market. Even if the value of any particular transfer of

a research tool seems small in advance, many of these transfers may eventually make the bargaining process difficult due to the terms of exchange that increase the total value. Hence, the transaction costs associated with the transfer of IPRs are not negligible in the case of cumulative innovation, meaning innovation that requires the use of prior inventions.

Even if the institutions involved have, on some occasions, informally tried to diminish these transaction costs, they remain important. Their relevance is the reason that makes it so important to assess these costs when considering the adoption and management of IPRs, because the negotiations between the parties (namely, owners and users) may not necessarily lead to an allocation of resources that would not compromise innovation. Nonetheless, the current IPRs regime has been successfully used in the past as the two case studies that are considered in this study prove. However, it has to be acknowledged that it may not be possible in many cases to replicate these examples since they present particular characteristics, and given that the context has since changed.

The emphasis here is to assess the degree to which IPRs on research tools can negatively affect the diffusion of innovations. In other words, this work stresses how the dissemination of these technologies, which may be required for subsequent innovation, may be affected by a series of factors. These factors may be either economic, as is the case with transaction costs; or they may be of a different nature, as is the case with the legal framework and/or the characteristics of these research tools, among other potentially relevant factors. All these different variables may either facilitate or even inhibit the negotiations over the transfer of research tools, which in turn may affect the dissemination of innovation.

1.2.Methodological Considerations

A case-study approach is adopted, since it is more fitting at this stage of the research in order to explain the causal relationships between IPRs and innovation in biotechnology. Furthermore, a comparative approach is used, in dealing with the case studies, so as to try to determine these causal relations. The case studies involving the traditional intellectual property rights approach

(namely, PCR and recombinant DNA techniques) allow the exploration of the implications of the current regime based on what happened at the different stages in these historical cases.

This approach presents several advantages. Case studies, more so than other methodological approaches, allow for a detailed consideration of contextual factors. This better enables one to consider concepts such as path dependency and historical idiosyncrasies, which are difficult to measure. Moreover, case studies are also better at helping one identify new, causally relevant variables. However, the case study methodology has its limitations such as case selection bias and potential lack of representativeness.

Finally, some case study approaches are more suited to particular research goals than others. Furthermore, a cross-case approach (as opposed to the within-case approach) is better when: 1) external validity is a major concern (as opposed to internal validity), 2) studying causal effects (as opposed to causal mechanisms), and 3) the scope of the proposition is broad (as opposed to deep).[1]

Given the characteristics of the approaches mentioned in the previous paragraphs, it can be stated that this thesis has two main parts, which fall under different categories according to Van Evera's classification.[2] The first part falls under a "historical evaluative" style. It concentrates on analyzing a series of variables in relation to both case studies. These variables are: diffusion (meaning the potential for dissemination), access to information (disclosure), basic research exemptions (whether they are present or not), characteristics (e.g., profitability and applicability, where applicability means the potential different uses, among others), firms/institutions (developing setting), enforcement of IPRs, and economic resources available for R&D (public vs. private). The second part falls under the "predictive" style category that involves drawing conclusions regarding what happened in the historical cases and analyzing their implications for future policy making. It analyzes how and if the context has changed and what are the implications for R&D in this field. It tries to propose which would be the best practices for managing intellectual property of research tools, in order to avoid hindering second generation

[1] John Gerring, *Case Study Research: Principles and Practices* (New York: Cambridge University Press, 2007), 38.
[2] Sthephen Van Evera, *Guide to Methods for Students of Political Science* (New York: Cornell University Press, 1997), 87-95.

innovation instead of promoting it. The latter includes the consideration of alternative approaches to deal with the issue of intellectual property in order to foster innovation.

1.3.Case Studies

Both case studies involve technologies that can be characterized as research tools, that is, first generation innovation which may be required to develop second generation applications. The term "research tools" has many meanings depending on the perspective taken by the different actors in the biotechnology field. For instance, research tools constitute 'tools' for the researchers who use them while they are considered 'end-products' by the companies that produce and sell them.[3] In the last three decades or so, the exchange of research tools in the field of biotechnology has become more diverse, both regarding the participants and the objects of exchange. This is mainly due to regulatory, market and institutional changes that have been taking place.[4] These cases allow for an assessment of the effects of first generation innovation on second generation.

A research tool is used for research purposes and it is not considered an application (e.g., end-use product). In other words, "research tools are part of a sequential process of innovation, being situated upstream from the development of applications such as new drugs." Innovations that follow are based on the previous invention, and the diffusion and usage of research tools serve as a starting point for these downstream innovations. What characterizes research tools is that they feed subsequent research and development, which is why they are considered 'enabling technologies' or 'platform technologies'. Researchers are hence the 'consumers' of research tools.[5]

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[3] Irina Haracoglou, *Competition Law and Patents: A Follow-on Innovation Perspective in the Biopharmaceutical Industry* (Northampton, MA, USA: Edward Elgar Publishing Inc., 2008), 7.

[4] Rebecca S. Eisenberg, *"Bargaining Over The Transfer of Proprietary Research Tools: Is This Market Failing Or Emerging?,"* in *Expanding the Boundaries of Intellectual Property: Innovation Policy for the Knowledge Society*, eds. Rochelle Dreyfuss, Diane L. Zimmerman, and Harry First (New York: Oxford University Press Inc., 2004), 223-249.

[5] Julien Penin and Jean Pierre Wack, "Research Tool Patents and Free-Libre Biotechnology: A Suggested Unified Framework," *DIME Working Papers on Intellectual Property Rights,* No 36 (April 2008): 3-4. http://www.dime-eu.org/working-papers/wp14/36.

Thus, research tools are the typical example of an upstream innovation required to develop a downstream innovation (e.g., PCR is used to replicate samples that are used in further research). A high percentage of the basic research tools used in biotechnology is subject to proprietary restraints (such as patents) or material transfer agreements. Frequently, patents provide the means to secure the rights over these tools in order to allow the developing organization to recover the investment it made in R&D. Besides, research in the field of biotechnology involves the need to have access to many different research tools, and this reality makes the process of acquisition more difficult.[6]

In this context, intellectual property regarding research tools used in biotechnology demonstrates the importance of transactions between prior and subsequent innovators. This is especially true with regard to prior patent claims, since these IPRs grant the owner absolute power to exclude others from using the proprietary technology in question. In an article that focuses on biomedical research, Heller and Eisenberg argue that too many patent rights on 'upstream' inventions can negatively affect 'downstream' research and development by increasing transaction costs, and, hence, by increasing the likelihood of bargaining failures taking place.[7]

Current issues associated with the exchange of biomedical research tools have several institutional changes at their base. The passage of the Bayh-Dole Act was a relevant policy shift that took place in 1980 along with other regulatory changes that encouraged those who received federal research funds to patent their results. This has resulted in an increase in the number of patents filed by institutions that used to make their discoveries more readily available to either the public or other institutions.[8] As Eisenberg states:

> *"Two dimensions of this change are particularly relevant to current problems surrounding the exchange of research tools".* First, the effect of these laws is to have *"expanded and diversified the types of 'institutions' claiming proprietary rights in their discoveries, as academic and nonprofit institutions have established technology transfer offices to patent faculty inventions and*

[6] Haracoglou, *Competition Law and Patents*, 7-8.
[7] Michael Heller and Rebecca Eisenberg, "Can Patents Deter Innovation? The Anticommons in Biomedical Research," *Science* 280 (1998): 698.
[8] Eisenberg, *"Bargaining Over The Transfer of Proprietary Research Tools,"* 226.

to market them to commercial firms. Secondly, is a corresponding expansion and diversification in the types of 'discoveries' that are the subject of proprietary claims to include the early-stage discoveries, considerably removed from product development, which typically emerge from government-sponsored biomedical research. The domain of proprietary exchange has thus become more diverse in terms of both participants and the objects of exchange."[9]

Another relevant change has been the emergence of biotechnology firms whose founders are academic scientists. In addition, these firms are based on public funding, and have links with academic institutions. Their work does not involve end-products but selling research tools and research services, which explain their necessity to protect the value of their research tools.[10]

In an environment such as the one described in the previous paragraphs, many institutions that develop these research tools consider them as valuable intellectual property. Hence, they try to capture this value by inhibiting potential access to research tools that could be sold or licensed to others. There are cases where the owners decide to keep these research tools from their competitors with the objective of preventing their use in research that may provide an advantage for others.[11]

This is opposite to the traditional posture of many scientists and institutions that advocate for the widespread sharing of these research tools in order to promote scientific progress. In this context, there is a high probability that in some cases IPRs concerning research tools in particular can seriously deter innovation or delay scientific progress. This is even more of a concern in fields that are not so lucrative, such as research on orphan drugs.

In addition, "when one institution's research tool is another firm's end product, it becomes difficult to agree upon the materials that should be exchanged on standardized terms", given that the value that it may have for a party may not necessarily coincide with that of the other interested party. The firm for which it represents an end-product will want to capture what it considers its full value. This, however, may turn out to be an overestimation of the value that the

[9] Eisenberg, *"Bargaining Over The Transfer of Proprietary Research Tools,"* 226-227.
[10] Ibid, 227.
[11] Ibid, 228.

product has for the firm that requires it as a research tool since it would make its process too expensive.[12]

In this context, characterized by sequential innovation, "where the value of an invention may be in boosting further innovation, the question of the adequate patent dimension is vital." A research tool, as a first generation innovation, can be essential for developing a second generation application. However, given the fact that in many cases more value is associated with products that are the result of further research, and considering that in many instances that value is not linked with the research tool itself, the invention of a research tool "can only be rewarded through partial returns from the sale of the end-use application." Nonetheless, exceptions to this can be found as in the cases of rDNA and PCR. A key point, then, is to ensure that "the earlier innovators are compensated for their contribution, while ensuring that later innovators also have an incentive to innovate."[13]

In order to structure and organize the division of profits among sequential innovators, intellectual property rights can play a major role. In the case of patents, this type of IPR on research tools makes it possible to establish a 'reach-through' licenses approach. The latter makes the scope of these patents on research tools relevant since it determines how the value of second generation innovation is distributed. On the one hand, if the patent is too broad, then most of the value will end with the research tool's IPR owner while the second generation developer will receive insufficient reward for the invention. On the other hand, if the patent is too narrow, it may occur that the second generation developer may avoid having to reward the research tool's IPR owner. This is what makes the design of patents so critical so as to try to provide the right incentives in order to foster first and second generation innovation.[14]

Another issue regarding patents on research tools and the necessity of extensive licensing is that it raises the costs for others (namely, second generation participants). In addition, this is not restricted to just one patent on a research tool, but to the many that may be necessary for certain research objectives, and this further increases the transactions costs. This problem particularly

[12] Eisenberg, *"Bargaining Over The Transfer of Proprietary Research Tools*, 229.
[13] Penin and Wack, "Research Tool Patents and Free-Libre Biotechnology," 4.
[14] Ibid.

arises when the transactions involve 'reach-through' licensing that comprises "potential future inventions made by the user of the research tool." However, this approach "creates a problem for users of multiple research tools faced with similar reach-through demands from multiple owners."[15]

Regarding research tools, patents present contrasting results. On the one hand, they increase incentives to produce first generation innovation. On the other hand, they clearly may increase the cost of access to research tools, which may hinder second generation innovation if the transaction costs are too high.

There have been cases that involved the diffusion of proprietary research tools through licenses that made it possible for the owner of the IPRs to obtain returns out of the patent while allowing subsequent research to take place. Two examples that present a different degree of success in the realm of biomedical research are the recently expired patents on recombinant DNA technologies, and on the polymerase chain reaction (PCR).[16] The former took place in a different time, when the culture regarding research involved more information sharing, which translated in a faster and higher level of diffusion of the rDNA technology. The context had changed when the discovery of PCR took place, and this, along with other variables (such as the type of development setting among others), might have contributed to slow the dissemination of the technology and in certain cases inhibit, even if for a while, its diffusion due to the approach adopted for its dissemination. However, as Eisenberg finds this trend did not continue, and "exchanges between universities and private firms are usually problematic", especially due to the terms proposed by the research tools' providers from the early stages of negotiations.[17]

This situation only becomes worse when there is more than one research tool being negotiated with different owners, which translates into problems for users of multiple research tools who may eventually face similar demands from multiple owners over their future discoveries. In addition, these numerous aggregated agreements create significant administrative delays that slow the pace of research. This issue has been referred to as a potential "tragedy of the

[15] Eisenberg, *"Bargaining Over The Transfer of Proprietary Research Tools,"* 230.
[16] Ibid, 229.
[17] Ibid, 230.

anticommons". Heller and Eisenberg argue that biomedical research is one of the several areas where competing patents could prevent useful products from reaching the market, which can potentially imply less innovation. Hence, if the creation of a certain product involves the use of many patented techniques, whose rights belong to different people or companies, then the negotiations can be difficult and the result may involve the payment of so many licenses fees that the product becomes too expensive to develop. In this scenario, all the stakeholders lose which makes it a form of market failure.[18]

The objective of assessing the previously mentioned case studies is to consider the following question: Do IPRs on first generation innovation (e.g., research tools) in biotechnology deter innovation? Most of the issues previously mentioned that characterize this topic are present in these case studies. This allows for the assessment of the variables that explain the characteristics that made these two cases successful examples of the diffusion of innovation although to a different degree. For once, the diffusion of rDNA was more widespread than that of PCR as it will be discussed later on. Furthermore, this assessment allows for a detailed analysis of what these inferences imply for R&D in biotechnology, considering that not all cases share the same characteristics.

The cases mentioned in the previous paragraph, are the rDNA (recombinant DNA) and the PCR (Polymerase Chain Reaction) cases; both considered successful examples of the current IPRs regime, even if they involve a different degree of diffusion. The reason to do a case study of these examples is based on the fact that in both instances, the patents have expired so that the whole life cycle of the IPR can be fully assessed in order to draw conclusions. Additionally, these cases present a series of different characteristics and took place under different circumstances, which allows one to determine what variables affect the diffusion of innovation the most.

Both cases involve patents as the preferred form of intellectual property rights.[19] A patent grants its owner "the right to exclude others from making, using, offering for sale, or selling" the

[18] Heller and Eisenberg, "Can Patents Deter Innovation?," 698 -701.
[19] See Annex I

patented invention.[20] In order to obtain a patent the invention has to be a 'new, useful, and non-obvious' "process, machine, manufacture, or composition of matter, or any new and useful improvement thereof."[21] According to the USPTO:

> *"The word "*process*" is defined by law as a process, act or method, and primarily includes industrial or technical processes. The term "*machine*" used in the statute needs no explanation. The term "*manufacture*" refers to articles that are made, and includes all manufactured articles. The term "*composition of matter*" relates to chemical compositions and may include mixtures of ingredients as well as new chemical compounds. These classes of subject matter taken together include practically everything that is made by man and the processes for making the products."*[22]

Recombinant DNA (rDNA) is a form of DNA that does not exist naturally, which is created by combining DNA sequences that would not normally occur together. This DNA technology was developed in universities and was the result of publicly funded research. Cohen and Boyer applied for a patent in 1974. The patent was granted in 1980. The original claim ended up splitting into three patents, a process patent for making molecular chimeras and two product patents. Over the lifespan of the patents (they expired in December of 1997) the technology was widely licensed and contributed to the emergence of the biotechnology industry.[23]

Polymerase chain reaction (PCR) is a technology that was "discovered, developed, and patented in an industry setting." The technology allows segments of DNA to be distinguished and large number of copies of a certain segment to be replicated very fast. These samples are then ready for further analysis. Since the first of its core patents expired in March of 2005, it has become possible to view the entire lifespan of the patent, making it feasible to assess how the intellectual property rights have impacted its use. Due to the importance that PCR has played in the field of

[20] See Annex II
[21] United States Patent and Trademark Office: An Agency of the Department of Commerce. http://www.uspto.gov/.
[22] United States Patent and Trademark Office. http://www.uspto.gov/.
[23] Maryann P. Feldman, Alessandra Colaianni and Connie Kang Liu, "*Lessons from the Commercialization of the Cohen-Boyer Patents: The Stanford University Licensing Program,"* in Intellectual *Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*, Vol 2, eds. Anatole Krattiger, Richard T. Mahoney, Lita Nelsen, et al. (Oxford, U.K.: MIHR, and Davis, USA: PIPRA, 2007), 1797.

molecular biology and also to its commercial success, the technology serves as a case study for evaluating the effects on research of granting IPRs over research tools.[24]

1.4.Objectives

Considering the topic and the methodology used, the following questions are addressed: What can be inferred about the effects of IPRs (particularly patents) on innovation in biotechnology from the case studies of rDNA and PCR? What similarities as well as differences were present to turn them into successful cases that present nonetheless a different level of diffusion? In more general terms: Has there been a change in the context? What characterizes IPRs on research tools that can potentially affect innovation? What are the issues to overcome? What are the mechanisms available both within the traditional system and the new approaches? Finally: What is the legal framework regarding these issues both in the United States and internationally? What could be the potential role of policy regarding the issue of IPRs and innovation?

The outline presented in this thesis involves the introduction of the topic, methodology and the issue of the case studies in chapter 1. Chapters 2 and 3 cover the case studies of recombinant DNA and PCR, respectively. Chapter 4 presents the assessment of the case studies and also addresses the topic in more general terms. Furthermore, this chapter considers the broader implications regarding intellectual property and innovation, and takes into account possible implications, both in the United States and internationally. Finally, the chapter presents the potential role of policy in dealing with these issues. Chapter 5 presents the conclusions and recommendation.

[24] Joe Fore Jr, Ilse R. Wiechers and Robert Cook-Deegan, "The Effects of Business Practices, Licensing, and Intellectual Property on Development and Dissemination of the Polymerase Chain Reaction: Case Study," *Journal of Biomedical Discovery and Collaboration* 1:7 (2006). http://www.j-biomed-discovery.com/content/1/1/7.

Chapter 2

Case Study I: RECOMBINANT DNA (rDNA)[25]

The Cohen-Boyer technology for recombinant DNA is frequently referred to as the most successful patent in the history of university licensing. It involves three patents: one is a process patent for making molecular chimeras and two are product patents. Many argue that recombinant DNA defines modern molecular biology, and is the foundation of the biotechnology industry. The first firm to form based on this technology was Genentech, in 1976.[26]

The success of this technology was mainly due to its usefulness as well as to the way in which its dissemination was handled. Two main factors contributed to the wide diffusion of the technology. The first was the 'research culture' of the time that promoted ample sharing of information, something that can be observed in the fact that the IP was disclosed before any patent claim had been filed. The second factor was the approach adopted regarding its licensing once the IPRs were granted, which was characterized by constant adaptation and flexibility. These issues are further discussed in the following sections.

2.1.What is rDNA?

Recombinant DNA is a form of DNA that does not exist in nature. It is created by combining DNA sequences in a way that would not normally occur in nature. In the case of genetic modifications, rDNA is introduced through the addition of relevant DNA into an existing organismal DNA for a specific purpose. Thus, it is different from genetic recombination because it is engineered. Vento and Gillum provide possible definitions of recombinant DNA (rDNA):

1. A DNA molecule containing DNA from two or more sources.
2. Artificial DNA from two or more sources combined into a single recombinant molecule.

[25] *The National Research Council provides most of the content of the different sections. The details described in the licensing section are provided by Feldman, Colaianni and Liu. See each section for specific references.*

[26] National Research Council, *Intellectual Property Rights and Research Tools in Molecular Biology: Summary of the Workshop Held at the National Academy of Sciences, February 15-16, 1996* (Washington, DC: The National Academies Press, 1997), 40-41, http://www.nap.edu/openbook.php?record_id=5758&page=40.

3. According to the NIH guidelines, *"recombinant DNA are molecules constructed outside of living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell, or molecules that result from their replication."*[27]

2.2. History

Recombinant DNA technology was first realized during the period between 1972 and 1974. Herbert Boyer and Stanley Cohen met during a conference in 1972.[28] The first publications took place during that time frame. All these publications described techniques to isolate and amplify genes or DNA segments and insert them into another cell with precision.[29]

The first patent application (U.S. Patent 4,237,224) was filed by Stanford University in November of 1974 (*Process for producing biological functional molecular chimeras*).[30] Stanley Cohen (Stanford University) and Herbert Boyer (University of California San Francisco (UCSF)) developed the technique together. By 1978, the NIH had decided in favor of patenting recombinant DNA inventions by universities. Hence, in December of 1980, the process patent was issued and the product patents were issued in 1984 and 1988. These were jointly granted to Stanford and UCSF and were also shared with Cohen and Boyer. The first license agreement took place in December of 1981. By early 1995, the licensing agreements were showing an exponential increase in value over time.[31]

This case has three important and defining elements: the technology was economically and technically accessible, there were no alternatives available, and the technology was essential and relevant for research in molecular biology.[32]

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[27] Amy B. Vento and David R. Gillum, *Fact Sheet Describing Recombinant DNA and Elements Utilizing Recombinant DNA Such as Plasmids and Viral Vectors, and the Application of Recombinant DNA Techniques in Molecular Biology* (Durham, University of New Hampshire, Office of Environmental Health and Safety, 2002), 2.
[28] David P. Clark and Nanette J. Pazdernik, *Biotechnology: Applying the Genetic Revolution* (Burlington, MA: Elsevier Academic Press, 2009), 73.
[29] Donald S. Fredrickson, *The Recombinant DNA Controversy: A Memoir – Science, Politics, and the Public Interest: 1974 – 1981* (Washington, DC: ASM Press, 2001)
[30] Ibid, 92.
[31] National Research Council, *Intellectual Property Rights and Research Tools in Molecular Biology*, 41.
[32] Ibid.

This DNA technology was developed in universities and it was the result of publicly funded research. The strategy in relation to intellectual property was to make licenses economically accessible to all, in order to attract small interested parties. In other words, the interested parties did not have to be big firms or institutions in order to be able to afford obtaining a license. The number of licenses granted made the patent very profitable, but it has to be acknowledged that the technology had certain characteristics not necessarily shared with all inventions. First, not all inventions are as relevant as rDNA proved to be in the field of molecular biology, and second, not always there is an absence of alternative technologies. Without the characteristics mentioned above, the licensing program would have been less successful. For the licensees, this technique constituted a research tool to be used to generate second generation innovations. This means that, had an alternative been available or had it not been such an important element for research, the number of licenses granted would have been lower, making the strategy not so profitable and successful for the owners of the patent of rDNA (recombinant DNA).[33]

In spite of this patent being considered as an example of the purpose sought by the Bayh-Dole Act, it, nonetheless, did not exactly comply with what had been envisioned by advocates of the Act. The diffusion of these techniques transformed how intellectual property was managed. It also, as the NRC states, "changed the financial environment and culture of biological research." It became common practice to patent the results of publicly funded research so that, over time, the number of patents filed increased while the sharing of information became less frequent.[34]

2.3. The Licensing Process

The adoption of an approach that involved non-exclusive (instead of exclusive) licenses was essential for the industry and its development, since this practice prevented the industry's being controlled by one company and/or having major firms challenging the patent. Thus, this approach allowed for the development of the industry instead of either generating the conditions for a monopoly of a necessary tool for research or, creating the conditions that could have

[33] National Research Council, *Intellectual Property Rights and Research Tools in Molecular Biology*, 41.
[34] Ibid, 41-42.

inhibited all kind of development until the dispute among firms could be settled.[35] The latter would have been the worst scenario for all the parties involved and for society, in terms of overall development.

2.3.1. Early times of the Cohen-Boyer Patents

Profit was not the main objective, even if the licensing program proved to be very successful. Four different goals were considered by Stanford University for the design of the licensing program: fulfilling a public-service purpose, giving incentives for the diffusion of genetic engineering, reducing the eventuality of biohazard by adequate management, and securing income destined for education and research.[36]

These commitments were demonstrated when Stanford made the decision not to seek to extend the life of the patent. Since the original patent application (1974) was broad (considering that it comprised the products created by the method), it was divided into the process patent (for making rDNA) and two product patents. The university announced that all applications resulting from the use of recombinant DNA would expire in 1997, which was the expiration date for the 1980 process patent.[37] Stanford also allowed other nonprofit research institutions access to the technology without a license. By doing so the "licensing practice established a *research exemption*, or research-use exemption which is consistent with the norms of open science, and stands in contrast to recent developments in research-use exemptions policies."[38]

The university established legal funds to deter the potential use of the technology without a license. However, when cases of non-compliance arose Stanford could settle without going to trial, which clearly differs from the current tendency.[39]

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[35] National Research Council, *Intellectual Property Rights and Research Tools in Molecular Biology*, 42.
[36] Maryann P. Feldman, Alessandra Colaianni and Connie Kang Liu, "*Lessons from the Commercialization of the Cohen-Boyer Patents: The Stanford University Licensing Program,*" in *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*, Vol 2, eds. Anatole Krattiger, Richard T. Mahoney, Lita Nelsen, et al. (Oxford, U.K.: MIHR, and Davis, USA: PIPRA, 2007), 1798.
[37] Ibid, 1798-1799.
[38] Ibid, 1799.
[39] Ibid.

In spite of intellectual property usually being associated with restricted disclosure, the university began consulting with several stakeholders in order to gather support for its goals. A compromise consensus emerged that "Stanford should be able to patent recombinant DNA research but with non-exclusive licensing." Even if this type of licensing could be less profitable, it went against what the Bayh-Dole Act advocated, and did not comply with the interests of Genentech and Cetus regarding exclusivity; the approach was consistent with the objectives of the university. Since rDNA was considered a 'platform technology', the selected licensing approach created the conditions for the full development of the technology and, consequently, the industry.[40]

Successful university technology transfers are usually characterized by relationships that develop over time. In other words, "signing a licensing agreement represents a transaction that is a first step in a relationship that requires maintenance and oversight." When it came to designing the licensing program, Stanford adhered to its policy of consulting with potential stakeholders. The OTL (Office of Technology Transfer) categorized the rDNA products into the following categories: basic genetic products, bulk products, end-products, and process improvement products. Then, royalty rates were established for each category, so as to foster adherence.[41]

To summarize, Stanford made pragmatic decisions regarding the value of its IP, by developing annual fees and royalty rates that did not attempt to exploit the university's position. Furthermore, in 1989 the university designed special provisions for lower licensing fees and royalty rates for small companies. By then, 209 biotechnology firms had acquired licenses.[42]

2.3.2. The Cohen – Boyer Patents Licensing Agreements over time

The whole licensing process, as it evolved over the lifespan of the patent, can be observed in Table 1, which describes the Cohen-Boyer Standard Licensing Agreements History.

[40] Feldman, Colaianni and Liu, "*Lessons from the Commercialization of the Cohen-Boyer Patents,*" 1799.
[41] Ibid, 1799-1800.
[42] Ibid, 1800.

TABLE 1 - Cohen-Boyer Standard Licensing Agreements History (in U.S. dollars)

VERSION	EFFECTIVE DATE	SING-UP FEE & MINIMUM ANNUAL ADVANCE (MAA)	EARNED-ROYALTY RATES			NUMBER OF COMPANIES SIGNED	REVENUE (SHARE)
			END PRODUCTS	BULK PRODUCTS	BASIC GENETIC PRODUCTS AND PROCESS IMPROVEMENTS		
1	12/2/1980	Each $10,000; with special five times credit	Graduated rate: 1% (first $5M); 0.75% (next $5M); 0.5% (over $10M)	Graduated rate: 3% (first $5M); 2% (next $5M); 1% (over $10M)	10% for basic products sales; 10% of cost savings and economic benefits	73	$215,663,697 (84.66%)
2	1/1/1982	Each $10,000	Graduated rate: 1% (first $5M); 0.75% (next $5M); 0.5% (over $10M)	Graduated rate: 3% (first $5M); 2% (next $5M); 1% (over $10M)		15	$14,229,566 (5.59%)
3	8/1/1985	Each $10,000	Same as above, but started write-in	Same as above, but started write-in		10	$3,338,347 (1.31%)
4	11/1/1986	Each $10,000	1%	3%		21	$5,355,889 (2.1%)
5	9/1/1989	Each $10,000 if <125 employees; Each $ 50,000 if > 125 employees	2%	6%		209	$12,120,719 (4.76%)
Alternative license	Mid-1991	No MAA	4%	6%	N/A	12	$2,630,195 (1.03%)
R & D Agreement	End of 1994	Sign-up payment waived; All future MAA as one-time payment	N/A	N/A	N/A	36	$553,083 (0.22%)
Final year	1996	No sign-up fee of $10,000; MAA is prorated and payable upon execution	N/A	N/A	N/A	6	$39,680 (0.02%)

Source: Maryann P. Feldman, Alessandra Colaianni and Connie Kang Liu, "*Lessons from the Commercialization of the Cohen-Boyer Patents: The Stanford University Licensing Program,*" in *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*, Vol 2, eds. Anatole Krattiger, Richard T. Mahoney, Lita Nelsen, et al. (Oxford, U.K.: MIHR, and Davis, USA: PIPRA, 2007), 1801-1802.

Over the 17 years of the licensing program, Stanford subsequently presented five versions of the standard licensing agreement and it came up with three special licensing agreements. By the time the patent expired, 468 companies had licensed the technology.[43] Licensing the patents required flexibility and adaptation, in order to attract as many interested parties as possible over time.

By the beginning of the licensing program, the technology had already been made public (through publication and the open patent files) and many companies were already using rDNA. Companies were encouraged to get a license, by the terms offered by the first version of the license. First, the companies received up to a total of US$ 300,000 toward the first five years future royalties. The second incentive was that firms considered the possibility of the terms of licensing changing in the near future. The first license's terms involved an up-front fee with a MAA (*minimum annual advance*). The royalty rates were a graduated percentage on sales based on the type of products involved in the license (namely, bulk products or end-products) and, were fixed based, when they were based on production cost savings for process improvements on existing products. So, under the licensing agreements, known as *reach-through* licensing, Stanford earned royalties on downstream products (as a percentage of sales). The IPRs comprised all the products that resulted from applying the technology.[44]

In January of 1982, the second standard licensing agreement abandoned the incentive of the royalty-credit and 15 more companies were granted a license.[45] The rest of the license program remained the same with the graduated royalty rates (for bulk products and end-products) and a fixed percentage for the process improvement on products.

In August of 1985, the third standard version of the license agreement allowed for negotiation by providing the possibility of 'write in agreed-upon rates'. However, it turned out that the royalty rates were frequently the same as the ones provided by the second version. In other words, the licensing program still had the same format although with a greater degree of flexibility, given by the possibility of negotiating the graduated rates.[46] The percentage for the process

[43] Feldman, Colaianni and Liu, "*Lessons from the Commercialization of the Cohen-Boyer Patents,*" 1800.
[44] Ibid.
[45] Ibid, 1803.
[46] Ibid.

improvement on products remained the same on the agreements. This time, ten additional firms signed up under this agreement.

In November of 1986, the fourth standard licensing agreement was issued, which replaced the graduated-royalty rates by a flat rate of 1% on end products and a rate of 3% on bulk products. This proved the fact that the patents could earn high rates, since those rates were the highest under the previous version of graduated rates (1% for end-products and 3% for bulk products respectively, in the graduated rates scheme). After this change in the licensing program took place, 21 more companies signed.[47]

The fifth version was introduced in September of 1989 and it sought to increase the number of small start-up companies that were granted a license. To accomplish this objective, the size of the company seeking a license began to be taken into account. The number of employees that established the difference was 125, so that, for companies with more than 125 employees the amount to pay was increased in relation to the previous version of the license. The strategy resulted in more firms acquiring a license.[48]

There were three 'non-standard licensing agreements' that allowed Stanford to capture more revenues while taking into account firms that had 'special circumstances'. The first was aimed at small distributors of rDNA applications. By the end of 1994, the university came up with a R&D license agreement that consisted of a one-time payment covering all future MAA, in order to attract small firms whose sales on products were not going to take place during the lifetime of the patent. In 1996, the final year of the patent (since it expired in 1997), there was a third agreement that aimed at covering any potential licensees that had been left out previously.[49]

During 17-year period of the Cohen-Boyer licenses, they generated US$ 254 million in revenue for the owner of the IPRs. About 10% of the total income came from the initial sign-up and annual fees. Finally, 90% of the total revenue came from royalties over product sales, which reflects "the commercial success of rDNA products." The success of the licensing program was

[47] Feldman, Colaianni and Liu, "*Lessons from the Commercialization of the Cohen-Boyer Patents,*" 1803.
[48] Ibid.
[49] Ibid.

definitely due to its successive adaptations.[50] This success, which refers to the level of diffusion of the technology of rDNA, was definitely not just due to the importance of rDNA for the field of molecular biology, but to the flexibility adopted by a licensing program that was constantly being adapted over the years (Table 1). The latter had the objective of attracting as many interested parties as possible, by making the technology accessible.

[50] Feldman, Colaianni and Liu, "*Lessons from the Commercialization of the Cohen-Boyer Patents,*" 1803.

Chapter 3

Case Study II: PCR (POLYMERASE CHAIN REACTION)[51]

Polymerase chain reaction (PCR) technology presents a contrast to the Cohen-Boyer technology. Both are innovations broadly used and frequently considered essential for research in molecular biology. However, the licensing strategies have been different as were the contexts under which both processes took place.[52]

The two technologies achieved a difference in the degree of success, as far as dissemination is concerned, mainly because of the strategies adopted by the IP holders regarding diffusion. In the case of PCR, disclosure and diffusion of the technology were slower than in the case of rDNA. Nonetheless, PCR technology was disseminated mainly due to its usefulness as well as to the way in which its dissemination was handled once the IPRs were secured. The main factors that contributed to the diffusion of the technology were the importance that it had and still has as a research tool, and the fact that, after the IPRs were secured through patents, the owners had every interest in promoting the dissemination of the technology so as to profit from it. This interest is reflected by the successive changes to the licensing program made by the different owners of the IPRs in order to facilitate access to the technology to different interested parties over the years. These issues are further discussed in the following sections.

3.1. What is PCR?

PCR technology allows segments of DNA to be distinguished and millions of copies of a certain segment to be replicated very fast. At the end of many cycles, the amplified sample of genetic material is ready for further analysis. A *polymerase* is an enzyme that exists in nature which catalyzes the formation and repair of DNA (and RNA). This process involves using '*Taq*

[51] *The National Research Council along with Fore Jr, Wiechers and Cook-Deegan provide most of the details and content of the different sections. Rabinow provides some of the material on the first two sections. See each section for specific references.*

[52] National Research Council, *Intellectual Property Rights and Research Tools in Molecular Biology: Summary of the Workshop Held at the National Academy of Sciences, February 15-16, 1996* (Washington, DC: The National Academies Press, 1997), 43, http://www.nap.edu/openbook.php?record_id=5758&page=43.

polymerase' (which is thermo-stable). It also involves a *chain reaction* since it allows the target DNA to be exponentially amplified.[53]

Basic research has been greatly influenced by the development and availability of PCR technology, since it made possible to perform experiments that were not feasible prior to its diffusion. For example, the genetic analysis of small biological samples, such as the analysis of small blood samples performed for forensic purposes.[54]

3.2. History

PCR rapidly became a "standard technique in almost every molecular biology laboratory, and its versatility as a research tool continues to expand." Kary Mullis came up with the notion behind PCR in 1983 and he developed it while working at Cetus Corporation. Unlike recombinant DNA (rDNA) technology, which was developed in collaboration by university researchers, PCR was developed in an industry setting with the objective of applying it for diagnostics in human genetics. As a consequence of this specific original objective, its success as a research tool was not foreseen from the beginning.[55]

In the decade preceding the development of PCR technology, the field of molecular biology had changed. This change involved: the emergence of the biotechnology industry, different intellectual property laws, the increment of agreements in the biotechnology realm (among universities, the industry and government), and universities filing for patents in the life sciences. The controversy that had taken place a decade before, over the patenting of rDNA, was something of the past. A versatile research tool as PCR should be granted a patent and, at the same time, the notion of licensing the technology and charging fees was already accepted.[56]

The case study of PCR incorporates many elements that are not traditionally found in the realm of university research, given its discovery and development within an industry setting. The

[53] Paul Rabinow, *Making PCR: A Story of Biotechnology* (Chicago: The University of Chicago Press, 1996), 1-5.
[54] National Research Council, *Intellectual Property Rights and Research Tools in Molecular Biology*, 43.
[55] Ibid.
[56] Ibid, 43-44.

norms of "proprietary research" called for a strategy that involved fully developing the method, securing the intellectual property rights and, only after, contemplating some form of disclosure (which included publication). As a result of this commercially oriented approach, it may be stated that, PCR did not initially disseminate as fast as it could have if its discovery had taken place in a different type of institution. However, after the technology entered the public domain, the firm had a clear incentive to find uses for the technique in order to generate revenue.[57]

Mullis was working with oligonucleotides and experimenting with the denaturation and renaturation of DNA. He was trying, with the aid of computer programs, to estimate the influence of time and temperature. Mullis' work made extensive use of iterative loops, which showed the capacity of exponential growth as a mean of producing big numbers fast. With these two notions, which involved "understanding the complex denaturation/renaturation properties of DNA and the concept of iterative loops", the moment for a breakthrough was near.[58]

According to Mullis, he first came up with the notion behind PCR in April of 1983. Mullis returned to Cetus and, after some searching, he was unable to find any prior attempt of a 'polymerase chain reaction'. So, after thinking the relatively simple process, he began working on it. Mullis claims that he first saw what he believed to be evidence of amplification in December of 1983. After the first successful results, he communicated the news to Al Halluin, Cetus' Chief Patent Counsel, who began to work on the claims for a patent application.[59] This early interaction reflects a key difference between innovation taking place in an industry setting, as opposed to academia. The industry emphasis is on commercialization of new technologies.[60]

Due to the promising results, Mullis decided to move to a more complicated system. In June of 1984, he presented the PCR replication of the beta-globin gene at the Cetus' annual scientific meeting, but he was generally ignored. The summer of 1984 presented a time of uncertainty

[57]Joe Fore Jr, Ilse R. Wiechers and Robert Cook-Deegan, "The Effects of Business Practices, Licensing, and Intellectual Property on Development and Dissemination of the Polymerase Chain Reaction: Case Study," *Journal of Biomedical Discovery and Collaboration* 1:7 (2006). http://www.j-biomed-discovery.com/content/1/1/7.
[58] Ibid.
[59] Rabinow, *Making PCR*, 93-104.
[60] Fore Jr, Wiechers and Cook-Deegan, "Polymerase Chain Reaction: Case Study," http://www.j-biomed-discovery.com/content/1/1/7.

given that Cetus was a start-up company in the biotechnology industry forced to invest in projects it deemed most likely of achieving short-term commercial success and profitability. Moreover, at that time, the company was centered on diagnostics, cancer therapeutics, and agriculture. In spite of these obstacles, Mullis was offered to work for one year on only PCR. [61,62]

The development of PCR focused on improving the technique, in order to make it feasible to apply it to diagnostics, which could have some immediate commercial value. In order to achieve this objective, a group was assembled during the summer of 1984. Until that time, only Mullis and his lab technician, Fred Faloona, had been working on PCR. The task of the group involved furthering the development of the technology.[63]

Early in 1985, it was clear that disclosure was at the verge of happening, and hence, the company needed to secure its rights on the invention, in order to recover its investment and make a profit out of it. The chosen strategy involved patenting before publishing. This approach was also out of concern, due to the fact that in some countries previous publications are considered prior art (where priority is given on a basis of *first-to-file*), something that could risk the international patents filings. The company filed for a patent in March of 1985.[64]

After taking the necessary measures to protect the rights to PCR, Cetus began to focus on disseminating the technology in the research community. However, there was some disagreement over how to do it this. Even keeping PCR as a 'trade secret' was suggested, but this strategy was easily discarded because of the likelihood of reverse engineering and, the fact that the patents had already been filed.[65] Additionally, some managers within Cetus thought that disclosure of PCR would render the technology less appealing to Kodak, with whom there was the opportunity of a partnership based on PCR. In the end, it was decided to present PCR

[61] Rabinow, *Making PCR*, 101-110.
[62] Fore Jr, Wiechers and Cook-Deegan, "Polymerase Chain Reaction: Case Study," http://www.j-biomed-discovery.com/content/1/1/7.
[63] Ibid.
[64] Ibid.
[65] See Annex III.

diagnostics' results at the annual meeting of the American Society for Human Genetics that was to take place in October of 1985.[66]

Regarding publication, the chosen strategy involved two papers: a "fundamentals" or theory paper, written by Mullis, and an "applications" paper. However, the applications paper was ready for publication before the other one, appearing in the 1985 December issue of *Science*. This reflected the fact that Cetus was focused on applications and not on potential basic research tools. Publishing the other paper afterwards turned out to be difficult. Mullis submitted it to *Nature* but it was rejected. It would be then accepted by *Methods of Enzymology*, but its publication was delayed until 1987.[67]

The strategy of publishing after patenting differs from cases of technologies discovered in an academic setting. In the particular case of the Stanford's Cohen-Boyer patent on recombinant DNA (rDNA), the patenting took place "after publication and a front-page New York Times story heralding the technique."[68]

After taking care of the intellectual property issues with the patent applications as well as the publication issues with the two papers, commercialization was the next step. Cetus went for strategic partnerships with other corporations that could add their expertise. Due to the increased attention, Cetus came to the conclusion that it had to develop adaptable licensing schemes, in accordance with the demands of the scientific community, in order to make the technology accessible. This occurred at a time when "researchers around the world continued to find still newer applications for the technology."[69]

However, in order for PCR to be completely automated and, hence, ready for market, it was necessary to find a better polymerase enzyme. Since the PCR technique involves heating the sample to 95 degrees Celsius, a thermostable enzyme was necessary. The group settled on the

[66] Fore Jr, Wiechers and Cook-Deegan, "Polymerase Chain Reaction: Case Study," http://www.j-biomed-discovery.com/content/1/1/7.
[67] Rabinow, *Making PCR,* 119-128.
[68] Fore Jr, Wiechers and Cook-Deegan, "Polymerase Chain Reaction: Case Study," http://www.j-biomed-discovery.com/content/1/1/7.
[69] Ibid.

Thermus aquaticus YT1 DNA polymerase, or *Taq.*[70] The work was so relevant that it ended up leading to a patent (US patent 4,889,818). The change to *Taq* polymerase incremented the efficacy of PCR and, created the conditions for making possible the automation of the technique through thermal cyclers (devices designed to heat and cool the reaction mixtures during the cycles involved in the PCR process). At this point, everything was ready for the technique to become a standard in almost every lab.[71]

In spite of the success of PCR, the internal environment at Cetus was not the best. While Mullis was increasingly turning into the public face of PCR, Cetus increased the fears of some of the other group members regarding loss of recognition. This happened when, in the spring of 1986, Mullis was given a US$ 10,000 bonus, while everyone else in the team received the usual sum of one dollar. This situation eventually led to Mullis leaving the company in September of 1986.[72]

In response to the increasing demand for PCR, Cetus adopted three business strategies for the three major fields in which PCR could be marketed: human diagnostics, research applications, and forensics. The strategy for the fields of diagnostics and research applications involved granting licenses for the use of PCR to other firms. Besides, in order to capitalize on possible applications Cetus decided to manufacture the devices and reagents through joint ventures. The first reagents and thermal cyclers were on the market in November of 1987. This cooperative approach resulted from necessity, since at that time the focus of Cetus was still on pharmaceuticals (mainly drugs and therapeutics), and cooperation was the only way of funding other projects. The only field whose applications were considered to be feasible to manage, without having to resort to any cooperative enterprise, was forensics.[73]

Soon, numerous organizations approached Cetus regarding licensing PCR for its use in diagnostics. In November of 1988, Cetus announced the creation of a division dedicated to PCR which would focus on business partnerships and licensing programs. Since the Cetus-Kodak

[70] Rabinow, *Making PCR*, 128-133
[71] Fore Jr, Wiechers and Cook-Deegan, "Polymerase Chain Reaction: Case Study," http://www.j-biomed-discovery.com/content/1/1/7.
[72] Rabinow, *Making PCR*, 132-133
[73] Fore Jr, Wiechers and Cook-Deegan, "Polymerase Chain Reaction: Case Study," http://www.j-biomed-discovery.com/content/1/1/7.

partnership was about to expire in December of 1988, Cetus began to leverage on PRC popularity when looking for co-sponsors, including Hoffmann-La Roche, among others. Roche was an interesting partner for Cetus since it was the owner of the patent rights to IL-2 (a recombinant form of interleukin 2) whose production was one of Cetus' major sources of revenue. They reached an agreement in January of 1989. Roche would fund diagnostic research, pay royalties on the sale of products or services that came out of the partnership and buy shares of Cetus' stock, while it would allow Cetus to use IL-2 without risking a lawsuit.[74]

The following table (Table 2) shows a timeline of key events in the early development of PCR.

Table 2 – Timeline of key events in the early development of PCR

Date	Event Description
May 1983	Mullis first conceives PCR concept
August 1983	Mullis presents PCR idea at Cetus in-house seminar, the reaction is unenthusiastic
8 September 1983	Mullis performs first PCR experiment
16 December 1983	According to Mullis, first successful amplification achieved
June 1984	Mullis presents poster at annual Cetus scientific retreat
Summer 1984	"PCR group" is formed and charged with the task of developing PCR as a diagnostic tool
15 November 1984	First "knock out" experimental data
Spring 1985	PCR group achieves "reliable and quantifiable data". Presentation of diagnostic potential of PCR to possible partners
28 March 1985	First PCR process patents filed with USPTO
September 1985	PCR "applications" paper is submitted to *Science*
October 1985	Presentation of PCR's applications in diagnostics at the meeting of the American Society for Human Genetics
December 1985	Cetus enters joint venture with Perking – Elmer to develop diagnostics instruments for use with PCR Mullis "theory" paper is rejected by *Nature*
20 December 1985	PCR "applications" paper appears in *Science*
4 February 1986	Cetus enters into agreement with Kodak to develop *in vitro* PCR diagnostics
May 1986	Mullis presents PCR at Cold Spring Harbor Symposium; receives ovation for his talk
28 July 1987	Patent #4 683 202 "Process for Amplifying Nucleic Acid Sequences" and #4 683 195 "Process for Amplifying, Detecting, and/or Cloning Nucleic Acid Sequences" issued to Cetus

Source: Adapted from Joe Fore Jr, Ilse R. Wiechers and Robert Cook-Deegan, "The Effects of Business Practices, Licensing, and Intellectual Property on Development and Dissemination of the Polymerase Chain Reaction: Case Study," *Journal of Biomedical Discovery and Collaboration* 1:7 (2006). http://www.j-biomed-discovery.com/content/1/1/7.

[74] Fore Jr, Wiechers and Cook-Deegan, "Polymerase Chain Reaction: Case Study," http://www.j-biomed-discovery.com/content/1/1/7.

In August of 1989, DuPont filed suit against Cetus alleging that the PCR patents did not comply with the requirement of being novel, due to the fact that the process had been described in the 1970s. DuPont claimed that the work named "repair replication", performed at the Massachusetts Institute of Technology by scientists working with Dr. Gobind Khorana, made PCR not novel.[75,76] As a consequence, the United States Patent and Trademark Office (USPTO) decided to reexamine the PCR patents claims. Cetus request, that the trial was delayed until the USPTO completed their assessment, was granted by the court. In August of 1990, the USPTO uphold the validity of both patents, rejecting that any of the papers had fully anticipated PCR and, that none of the papers mentioned 'exponential replication' (something stated in the patent claims). The court could consider issues such as "commercial success of the patent and failure of others to perform the invention as signs that the patent was non-obvious." These considerations, along with the sales' profits of the reagent and the thermal cyclers, and the time gap of practically fifteen years between Khorana's work and the development of PCR by Cetus, worked in favor of Cetus. On February 28, 1991, the validity of the patents was confirmed by a verdict in Cetus' favor.[77]

In the meantime, PCR was becoming an essential research tool in molecular biology. Along with this, came the profits earned through the sales of the PCR reagent kits and thermal cyclers. In spite of this, Cetus was facing financial problems. This situation only got worse when, in July of 1990, the FDA did not approved IL-2 for treatment in the United States, a program that had great significance to the company. Cetus turned towards Hoffman-La Roche as a potential purchaser of the PCR patents. The two parties eventually reached an agreement and the rights were acquired by Hoffmann-La Roche, a company with the resources to further develop the technology and increase its access for researchers.[78]

[75] Fore Jr, Wiechers and Cook-Deegan, "Polymerase Chain Reaction: Case Study," http://www.j-biomed-discovery.com/content/1/1/7.
[76] Rabinow, *Making PCR*, 8-9.
[77] Fore Jr, Wiechers and Cook-Deegan, "Polymerase Chain Reaction: Case Study," http://www.j-biomed-discovery.com/content/1/1/7.
[78] Ibid.

In July of 1991, Chiron Corporation announced that it would merge with Cetus. However, before either the Roche deal or the merger could take place, Cetus faced another lawsuit filed by Kodak in November of 1991. Kodak wanted to stop the transfer of the PCR rights to Roche by claiming that it would be seriously affected by it. The court considered that the damage to Kodak, due to the agreement between Cetus and Roche, was the result of the 1989 Cetus-Roche partnership and that that the transfer of the PCR rights did not increase it. Hence, the court denied the injunction sought by Kodak.[79]

In December of 1991, Hoffmann-La Roche acquired the rights to PCR for the price of US$300 millions and, hence, it assumed control of all access to the PCR technology. Nonetheless, Cetus (now merged with Chiron) would retain the right to use PCR in the development of therapeutics.[80]

Now, the situation was different. When it came to designing the licensing program for the use of PCR for research purposes, Roche clearly had a business objective of selling products for use. This allowed the company to grant rights to use the technology through the acquisition of products instead of offering direct license agreements, like Stanford had done before. It was a licensing approach developed by Cetus. However, an initial approach, presented by the president of Cetus to the scientific community, involving reach-through royalties on products generated by the use of PCR was heavily criticized.[81]

3.3.The Licensing Process

Roche created a series of license categories based on the applications and the users of PCR. They included: research applications, diagnostic applications, production of large quantities of DNA, and human diagnostic testing services. Licenses in the last category are very broad and, they are the most extensive of the PCR licensing program.[82]

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[79] Fore Jr, Wiechers and Cook-Deegan, "Polymerase Chain Reaction: Case Study," http://www.j-biomed-discovery.com/content/1/1/7.
[80] Ibid.
[81] National Research Council, *Intellectual Property Rights and Research Tools in Molecular Biology*, 44.
[82] Ibid.

In order to expand and commercialize all possible applications of PCR, Roche formed a new subsidiary, Roche Molecular Systems, to manage the manufacturing of reagents and the licensing of PCR rights to other companies. The original licensing scheme, conceived by Cetus, was facing increasing opposition from researchers. At the beginning, Cetus contemplated an approach that involved 'reach-through' licensing agreements (RTLAs) that would have required users to pay royalties on any invention or product created using PCR. This generated a lot of criticism from the scientific community, and researchers also complained about the high costs of buying the licensed reagents (e.g., *Taq* polymerase). In January of 1992, Roche came up with a new licensing strategy and it stated that the objectives were to: "1) expand and encourage the use of the technology; 2) derive financial return from the use of the technology by others; and 3) preserve the value of the intellectual property and the patents that were issued on it." The company came up with new categories for the use of PCR and, it also developed royalties and fees schemes for each category. Roche also decided to remove the up-front fee of US$ 15,000 for non-profit and academic labs that had been established by Cetus. The company also announced a reduction of the royalties on sales of products developed using PCR and on tests performed using the technology (to lower values such as 9%).[83]

Seeking to encourage authorized use of the technology, Roche made it easier to obtain a license. From that moment on, licenses would have two parts: "an up-front fee component, which could be satisfied simply by purchasing a thermal cycler from an authorized dealer, and a 'running royalty' component, which required using licensed reagents to perform PCR."[84]

Finally, in order to expand the potential uses of the technology, Roche began "granting licenses for applications in paternity testing and infectious disease diagnostics" (areas for which PCR rights had been previously denied). This move hastened the diffusion of PCR into previously unreached markets, which set the "conditions for PCR to become the standard technology for genetic testing."[85]

[83] Fore Jr, Wiechers and Cook-Deegan, "Polymerase Chain Reaction: Case Study," http://www.j-biomed-discovery.com/content/1/1/7.
[84] Ibid.
[85] Ibid.

Chapter 4

R&D OF RESEARCH TOOLS AND PRODUCTS IN BIOTECHNOLOGY

4.1. Lessons from the Past: *Their Implications for Future R&D*

The following table (Table 3) shows the main characteristics of the previously described Case Studies (namely, rDNA and PCR) so as to observe the similarities as well as the differences between them. Both cases were successful up to a different degree regarding IPRs in terms of diffusion of knowledge and innovation, but the levels of dissemination differed, especially during their early stages.

TABLE 3 – Characteristics of the Case Studies

Characteristics of the Case Studies		Case Study	
		Recombinant DNA (rDNA)	PCR (Polymerase Chain Reaction)
Legal Framework	Type IPR	Patent	Patent
	Legal Circumstances	Granted two months before the Bayh-Dole Act	After the Bayh-Dole Act
	Access to Information	Public before patenting	Public after patenting
	Dissemination	Licensing Non-exclusive Direct License Agreements *Royalties based on categories* - basic genetic products - bulk products - end-products - process improvement products	Licensing Non-exclusive Licensing of products *Depending on the application and the users* - Research applications - Diagnostic applications - Production of large quantities of DNA - Human diagnostic testing services (most extensive type of licensing)
	Basic Research Exemptions	No (since the *beginning* just for non-profit institutions)	No (some provision was introduced *later*)
	Enforcement	Until the expiration of the patent (1997)	Until the expiration of the first patent (2005)
Characteristics of the Research Tool	Diffusion	Wider (*since the beginning*)	Wide (*slow at the beginning*)
	Potential Applicability	High *Critical for research in molecular biology*	High *Versatility as a research tool turned it into a standard technique*
	Profitability	High	High
	Alternatives	No	No

Economic resources available for R&D	Public	✓	
	Private		✓
Developing Settings (Institutions/Firms)	Industry		Industry Setting *(Increment in university-industry-government alliances and university patenting in the life sciences)*
	University/Research Institutions	Collaboration between university researchers	

The data presented in Table 3 show that, despite the differences in the two case studies, the diffusion of both technologies was possible. However, the level of diffusion was not the same, especially during the early stages.

In both cases, patents were the *type of IPR* selected. On the one hand, the Cohen-Boyer patent on recombinant DNA was granted in 1980, two months prior to the passage of the Bayh-Dole Act. Even if the discovery protected by this patent was the result of publicly funded research, the approach regarding its licensing and dissemination did not exactly followed what is advocated by the Act. The university decided to disseminate the technology under non-exclusive direct license agreements, and by doing so, fostered innovation since it made the technology available to all those who might have required access and could comply with the licensing program requirements. The owners of the patent also contributed to the diffusion of the technology by adopting a flexible approach that was translated into a licensing program that was adapted over time in order to attract all possible interested parties. On the other hand, in the case of PCR, the first patent application was filed in 1985, and the discovery took place in an industrial setting (Cetus) and its development was funded by private resources. The company decided to protect its intellectual property by filing a patent application before any kind of disclosure took place. The latter may have caused a delay regarding dissemination of the technology but once it entered the public domain the company had every interest in making profit out of it. The approach adopted by the original owner of the PCR rights involved a licensing program that granted non-exclusive licenses on products that differed depending on the applications and the users (rather than negotiating direct licensing agreements as Stanford had done). This approach contributed to the dissemination of the technology, especially due to the adoption of non-exclusive licenses, so that any interested party that could comply with the licensing terms could access the technology.

Regarding the latter, most of the critiques over time involved the costs of the reagents, as well as the rates established by the reach-through licensing agreement. When the PCR rights were transferred to Hoffman-La Roche in 1991 the licensing program continued and was subsequently adapted, in order to maximize the dissemination of the technology and attract all possible interested parties. Following this trend, the company decided to develop royalties and fees schemes for the different categories. Another strategy involved the reduction of the royalties on sales of products developed using PCR and on tests performed using the technology in order to make it more accessible. The company developed a way that made it easier to obtain a license by establishing that the up-front fee could be satisfied by acquiring the device needed to perform the PCR technique, and that the royalties should be satisfied by acquiring the licensed reagents. Finally, it was decided to grant licenses to other users that had not been previously given a license. All the strategies mentioned above contributed to making PCR a standard technique and, contributed to its diffusion. This promoted innovation in spite of the early approaches that may have delayed the dissemination of the technology.

Regarding the *legal circumstances* the context under which both technologies were developed was different. When the Cohen-Boyer patent application was filed in 1974 there was some controversy over granting a patent on a discovery such as recombinant DNA. Back then, the field was new and there were no precedents on the matter. The patent was finally granted in 1980. Even if it is considered as an example of the original purpose of the Bayh-Dole Act, the approach followed by the owners did not exactly comply with what was advocated by the Act regarding licensing and dissemination. However, by the time the PCR patent application was filed in 1985 there was no controversy over whether such a discovery should be granted a patent or regarding the charging of royalties for the usage of the technology. Nonetheless, even if the legal environment can have a major impact on the dissemination of any technology, in these cases, the technologies in question were diffused and innovation was not hindered.

The issue of the level of *access to information* (*disclosure*) was handled differently. In the case of the recombinant DNA technology, public disclosure and consultation took place before any kind of action was taken to protect the intellectual property rights. The interested parties had access to information regarding the technology and, as a result of the public consultation, it was

agreed that rights should be granted over the technology but under non-exclusive licenses in order to facilitate the access to the technology and foster innovation. The approach followed by the university was to disclose first while filing for a patent, in order to secure its intellectual property rights. The patent was granted in 1980. By the time the rights were conferred the information regarding the technology was already in the public domain so that the owners had to come up with a licensing program that would nonetheless attract all interested parties and avoid potential unlicensed use of the technology. This approach clearly fostered innovation since information entered the public domain from the very early stages of the discovery and, then, the trend continued through the design of a licensing program that was subsequently adapted. This allowed interested parties to access the technology, which contributed to promote innovation. In the case of the PCR technology, the strategy followed by the company (Cetus) was to secure the intellectual property rights first and, then, to assess how to best approach the issue of disclosure, including publication. The early discoveries took place between 1983 and 1984 while the first application for a patent occurred in early 1985 followed by a couple of papers, authored by members of the group working on PCR, and submitted for publication towards the end of that year. The public presentation of PCR also took place in 1985 after the patent application had been filed. It can be said that this approach of 'patenting first and publishing later' could have potentially delayed the dissemination of the technology at the beginning, but, once it was in the public domain, the owners had every interest in sharing information in order to disseminate the technology as much as possible with the objective of attracting interested parties. Hence, can be observed that an important the difference exists when a discovery takes place in an industrial setting whose main objective is to profit and to recover the investment. The strategy that is followed may not necessary contribute to the maximum possible dissemination of the technology, since adopting 'trade-secrecy' is always a possibility that at a point was considered in the case of PCR, even if for a brief period of time.[86] Nonetheless, even if the technology may have disseminated more slowly during its early stages, it eventually got diffused to the point of becoming a standard technique so that innovation was allowed to take place.

Regarding the topic of *basic research exemptions* there was a clear difference between both cases that has had an important impact on innovation. From the beginning, the recombinant DNA

[86] See Chapter 3, Section 3.2.

technology was made available to non-profit institutions which constituted a form of basic research exemption even if just for a certain subgroup of the interested parties. Regarding the issue, Roche also decided to remove the up-front fee for non-profit and academic labs established by Cetus, the first owner of the rights on PCR. The company also decided to reduce the royalties on sales of products created using PCR and on tests conducted using the technology. This initial policy in the case of the recombinant DNA technology and the adaptation in the case of PCR, clearly constituted an attempt to make the technologies available for basic research, which would otherwise not have taken place, given that this type of research may render something profitable or not, making licenses inaccessible. This certainly contributed to foster innovation by allowing some interested parties that could not potentially obtain a license to perform research that had the potential of rendering, at least in some cases, important results.

As for the *enforcement of IPRs*, the way adopted by the patent holders was similar in both cases. To begin with, both technologies were protected by patents and, after they were granted, the rights clearly belonged to the owners until they expired. In the case of the Cohen-Boyer patent, even if a fund was created to deter unlicensed use of the technology, all cases could be settled without going to court, and the validity of the patents was not contested. However, in the case of PCR the validity of the patents was contested based on the claim that the technology was not novel since it had being mentioned in the 1970's. Nonetheless, the USPTO and the court found the patent valid. Another issue regarding enforcement could be the company's (Roche) attempts to redesign the licensing program so as to make the acquisition of a license more accessible and, hence, fomenting compliance. An important issue to be observed regarding enforcement is that promoting compliance from the beginning and coming up with strategies that make the technology accessible is a relevant issue. This is mainly due to the fact that having to rely on the legal system can be very expensive and does not work in the best interest of any of the involved parties. The approaches adopted in both cases allowed for the technology to disseminate, although at a slower pace in the case of PCR, while encouraging compliance and avoiding unlicensed use of the technologies; all of which contributed to the diffusion of the technologies and to innovation taking place.

An important issue that can be inferred from these two cases is that the *characteristics* (e.g., profitability, applicability, alternatives, and potential for diffusion) of the research tools (or any other first generation innovation) have a major impact in their subsequent diffusion and, hence, on how much innovation is promoted or discouraged. First, the greater the potential regarding applicability (namely, the number of potential different uses of the technology), the greater the demand for the technology will be, making it more feasible for the owner of the intellectual property rights to come up with more demanding conditions for use of the technology. In other words, more potential applications also mean more potential interested parties which also calls for a more sophisticated and flexible strategy when it comes to disseminating the technology. Also, a high level of potential applicability means that there is more potential for a technology to serve as a platform for second generation innovation. All the issues mentioned above regarding applicability imply that it is an important factor in relation to innovation and, it is something that both case studies have in common. This, clearly, contributed to their success in every level, including the diffusion of the technology and subsequent fostering of innovation. Second, another characteristic that both cases share is the fact that there were no alternatives to the technology in question. If in any of the cases a potential substitute technology had existed, it would have meant that the bargaining position of the respective owners would not have been so strong. In other words, had a more accessible alternative existed both technologies would not have been such a success regarding diffusion. Nonetheless, in both cases and in spite of the absence of alternatives, diffusion took place and innovation was not hindered, even if in the case of PCR, more than with rDNA, access to the technology might have been more expensive than under a more competitive environment given by the presence of alternatives. Third, there is the issue regarding the research tool (or first generation innovation) potential for diffusion. This refers to the characteristic of being a technology with wide and necessary applications or not. Not all technologies are as essential to further development in a field as the ones mentioned in these case studies were, something that can be observed by their turning into standard techniques that are still currently used in laboratories all over the world. They both contributed to foster innovation as first generation inventions that served as platforms for further innovation. Finally, there is the issue of profitability, meaning how profitable these first generation inventions proved to be and whether they allowed to recover the investment required to develop them, and, even to profit from them or not. This is a major issue, especially for inventions that take place in an

industrial setting, since companies do development as part of their business plan. The more likely that a potential innovation may render profits the greater the possibilities that those who work on it receive the resources that are necessary to develop the new invention. At the same time, a profitable innovation, meaning that its diffusion may render important revenues for the developer, is more likely to get diffused and, hence, foster further innovation that uses this first generation innovation as a platform. What is mentioned above regarding profitability is the main reason why most basic research whose potential is unknown takes place outside of industry (with some exceptions). For example, in the case of PCR those working on it did not receive much support until it was clear that the technology had a great potential in spite of not being in line with the company's priorities at the time. Nonetheless, in the cases previously mentioned the technologies in question proved to be highly profitable and their level of diffusion was and still is wide. So, to conclude, the technologies considered here share a series of characteristics that made their diffusion easier and more likely to occur, which in turn fostered innovation as a consequence. However, it has to be acknowledged that not all inventions share these characteristics and their diffusion may prove to be less likely, which would instead hinder innovation.

Regarding the *economic resources available for R&D* (*public vs. private*) these two cases present different scenarios. In the case of the Cohen-Boyer patent, the discovery of recombinant DNA was the result of publicly funded research. Besides, the approach was different since the information was made public from the beginning and, after some controversy, the patent was jointly granted to the discoverers and the universities. Moreover, even if it is associated with the purpose of the Bayh-Dole Act, the patent was granted two months prior to the passage of the Act and the diffusion strategy did not exactly comply with what the Act advocates in this regard. In the case of the PCR patent the situation was very different since it was developed in an industry setting using private resources. The company (Cetus) had other priorities at the time and those who were working on PCR had to demonstrate the relevance (especially its commercial potential) in order to receive the full support of the company. When R&D takes place in industrial settings, using private funds, it means that there could potentially be more resources available, but there is also the issue of whether or not the development is among the priorities of the company at that time. The latter may end up inhibiting some potential new discoveries unless

they proved to be potentially highly profitable, as was the case with PCR. So, to conclude, the origin of the sources may play a role in fostering or hindering innovation (both first and second generation innovation).

Finally, the type of *firms or institutions* where these developments took place and that ended up being the ones holding the IPRs over their discoveries present a series of differences that also affected innovation. The interests and, even more clearly, the strategies that are followed can differ considerably depending on the type of institution where the discovery takes place. This is particularly true in cases where discovery and development takes place in an industrial setting. On the one hand, when developments occur in institutions such as universities the sharing of information is more likely to take place, especially if it is the result of public funding. The latter does not mean that such institutions would not seek to secure the intellectual property rights associated with the new discovery, but that at the same time information would more likely enter the public domain, even if after the rights have been conferred to the institution in question. The level of information sharing was higher in the past as can be observed in the case of recombinant DNA where the information was made public before the rights to the technology were secured. However, this trend did not continue as such, and it has become less and less common to disseminate information as it was done in the past, and it has also become more common for these institutions to file for patents. There may be differences depending on the source of the funds but the trend is to secure the intellectual property rights. On the other hand, when development occurs in an industrial setting the business priorities of the firm in question are more likely to dictate how the process is handled, as was the case with PCR. During its early stages, securing the company's rights and potential future profits was the main concern and the reason why disclosure followed patenting. Another important issue regarding development in an industrial setting is that the type of intellectual property that is selected may not necessarily be a patent or, other form of intellectual property that guaranties the information reaching the public domain. Companies may decide to protect their IP as a trade-secret which means that it may never be public. This has become more common, although in the field of biotechnology is more difficult to adopt this type of IPR since reverse engineering is always a possibility. However, it is still possible to keep a new discovery as an in-house trade secret and just sell the services of performing whatever it is that the new innovation allows. This clearly hinders innovation at all

levels and is the worst case scenario for society as a whole, in terms of development. Nonetheless, in the cases considered, both technologies got diffused, although more slowly during its early stages in the case of PCR, and innovation was not hindered, in spite of having taken place in different environments and under different circumstances and contexts.

4.2.Do IPRs deter innovation?

4.2.1. Processes (Research Tools) and Products Framework

Three events contributed to define the turning point regarding the advantages and disadvantages of granting intellectual property rights over research tools:

1. The *emergence of the field of molecular biology* that made possible certain areas of research whose products are 'platform technologies' and not end-products.
2. The *Chakrabarty case* (Diamond vs. Chakrabarty) where the U.S. Supreme Court ruled that genetic inventions (such as the one considered in this case which was a genetically engineering bacterium that could break down crude oil) could be patented under the law of the United States. This opened the possibility of earning revenues through the licensing of such inventions for which the owners were granted a patent (on research tools or any type of upstream innovation).
3. The *Bayh-Dole Act,* passed in 1980, granted the universities permission to patent inventions that were the result of publicly funded research. Most of these inventions turned out to be research tools that were later commercialized. This approach was later pursued by the majority of the developed world.[87]

4.2.2. What characterizes research tools that influences IPRs and innovation

The implications of different intellectual property rights approaches regarding research tools in biotechnology and biomedical research involve participants in this market facing a series of

[87] Charles Clift, "*Patenting and Licensing Research Tools,*" in *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*, Vol. 1, eds. Anatole Krattiger, Richard T. Mahoney, Lita Nelsen, et al. (Oxford, U.K.: MIHR, and Davis, USA: PIPRA, 2007), 80.

issues regarding access to these tools and, therefore innovation may be hindered if access to these technologies is not properly managed.

Among the main issues are *transactions costs*, which constitute a more serious problem in the case of 'low value exchanges' (e.g., either small firms or the case of research on orphan drugs) as opposed to cases that involve 'high value exchanges'. In other words, there is a higher probability that transactions costs associated with the exchange of research tools end up making unfeasible those experiments with a low likelihood of generating considerable revenues. It can be stated that when high transaction costs are involved only high value transactions are worthy. In the particular case of 'collaborative research agreements', they involved conditions over future value that are more demanding for all those involved than the ones associated with mere MTAs (Material Transfer Agreement). The terms and conditions that present the greater challenges usually "involve the allocation of speculative future value and risks."[88]

One potential way of dealing with the aggregated transaction costs would be to minimize them by deferring the bargaining over the terms up until the associated value is more evident and does not involve, as many times, unsubstantiated speculation. There are companies that attempt to apply this approach by assuming that they can come to an agreement if they discover anything important and, in the meantime, they use patented research tools without first obtaining a license. There is also yet another approach that involves agreements that do not cover the more challenging issues up-front (e.g., the division of future IP), but what they do is to preserve the parties' interests and force them to bargain later if something valuable is discovered.[89]

As it was mentioned in previous sections, there is also a problem associated with research that involves the use of several research tools associated with different patents (or some form of IPR).

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[88] Rebecca S. Eisenberg, *"Bargaining Over The Transfer of Proprietary Research Tools: Is This Market Failing Or Emerging?,"* in *Expanding the Boundaries of Intellectual Property: Innovation Policy for the Knowledge Society*, eds. Rochelle Dreyfuss, Diane L. Zimmerman, and Harry First (New York: Oxford University Press Inc., 2004), 231-233.
MTA *"is a standard abbreviation for "material transfer agreement" that establishes the terms of access to a (typically unpatented) biological material. Thus, exchanges for which a MTA is used are usually of low value to the provider of the material or it would otherwise propose a more substantial relationship (e.g. collaboration, etc.)".*
(Eisenberg, *"Barganing Over The Transfer of Proprietary Research Tools,"* 232).
[89] Ibid, 233-234.

This situation not only increases the transaction costs, but it also makes negotiations more difficult and can deter innovation altogether. This is a case of what has come to be known as the *"tragedy of the anticommons"*, where the "lack of coordination due to the existence of numerous rights holders" impedes achieving a desirable outcome for society mainly due to a series of "coordination failures" that can be difficult to overcome.[90]

Another issue is that the *heterogeneity* that exists among the different institutions that constitute the biomedical research community tends to make more complicated the search for mutually acceptable terms of exchange, regarding handling IPRs for research. For instance, universities, pharmaceutical firms, and biotechnology firms find it easy to deal with their peers but not with different kinds of institutions. As Eisenberg states, it is usually "the would-be user who is frustrated by the provider's terms of exchange" regardless of where the research tool was developed.[91] In other words, the heterogeneity of the institutions involved, that have not only different priorities but also different 'cultures', can make the negotiations more difficult. This is mainly due to the fact that in the absence of standardized terms of exchange, not even the objectives of the parties coincide; making the bargaining process more complicated and, this may even lead to unsuccessful negotiations.

There is also the issue of *conflicting interest* among the agents involved, even within the same institution. For example, the interest of those who create and use this research tools (namely, scientists) and those who bargain over the terms (namely, lawyers and business people) differ, which explains why they do not always appear united when negotiating.[92] This clearly makes the bargaining process even more complicated. The situation arises mainly due to the fact that, for example, scientists in academia have the pressure to come up with results and publish them, which explains their priority over the acquisition of research tools as something they need in order to comply with their main task. However, those who work in university's technology transfer offices have as their main task to license 'university-owned inventions' to the industry in

[90] Michael Heller and Rebecca Eisenberg, "Can Patents Deter Innovation? The Anticommons in Biomedical Research," *Science* 280 (1998): 698 -701.
[91] Eisenberg, *"Bargaining Over The Transfer of Proprietary Research Tools,"* 235.
[92] Ibid, 231.

order to bring resources to the institution.[93] These 'conflicts of interests' also contribute to making the bargaining process more difficult given that the priorities, even within the same party, are not necessarily the same, a situation that tends to complicate the negotiations.

Finally, another issue regarding research tools is the *evaluation or valuation* of the tools themselves. In other words, this refers to "estimation of the contribution that they might make to potential future discoveries" and the impact that this has on the negotiations, something that is highly "speculative and subjective."[94] On many occasions if the valuations are too high, this could lead to a lower dissemination of a certain research tool that could contribute to research in not so profitable areas. Or, even more, the uncertainties associated may inhibit innovation altogether for all sorts of applications.[95]

4.2.3. Issues with IPRs that affect Innovation

It can be stated that some type of intellectual property right is associated with all developments in the fields of biotechnology and chemistry. As a consequence, if these inventions are licensed (which would not be the case if the selected IPR is a trade-secret), the licensees may either have to pay rates on sales of the products they develop or, for the use of these products protected by IPRs. Besides, most biotechnology developments require the use of more than one patented research tool, some or all of which may establish reach-though royalty duties. This creates a situation where there is an obligation to pay a percentage on sales of the product developed using these research tools. This situation is further complicated when development requires using several technologies whose patents belong to a series of different owners. In other words, when developing a product involves potential royalty obligations that taken together are too high, this may not allow the development to take place.[96]

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[93] Eisenberg, *"Bargaining Over The Transfer of Proprietary Research Tools,"* 240.
[94] Ibid, 232.
[95] Ibid, 243-248.
[96] Keith J. Jones, Michael E. Whitham, and Philana S. Handler, *"Problems with Royalty Rates, Royalty Stacking, and Royalty Packing Issues,"* in *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*, Vol. 2, eds. Anatole Krattiger, Richard T. Mahoney, Lita Nelsen, et al. (Oxford, U.K.: MIHR, and Davis, USA: PIPRA, 2007), 1121-1122.

There are a series of problems that arise regarding this issue some of which are described in the following paragraphs.

Royalty stacking takes place when several patents are associated with a single product, which means multiple licenses. This requires that the several royalty demands have to be 'stacked' together in order for the company that develops the product to estimate the total amount of royalties involved in developing the product. Since 'royalty stacking' involves several IPRs owners, the development of the product in question may be delayed or even impeded due to the problem referred to as 'royalty stacking'.[97]

Royalty packing takes place when a requirement to bundle exists regarding one technology with others (e.g., a vaccine administered simultaneously with others where the royalties on each of the products are 'packed' together). This requirement can be demanded by the licensor or could be the result of a practice imposed within an industry or by a ministry of health, for example. Under these circumstances, royalty packing may turn out to generate an aggregation of costs of the packed products that end up being too high.[98]

The majority of the definitions of *patent tickets* involve a large number of patents. Nonetheless, it is also possible that a small number of scattered patents, with their corresponding transaction costs and royalties, may lead potential interested parties to decide not to engage in certain areas of research. Van Overwalle considers that "a 'patent ticket' refers to a multitude of essential, 'blocking' patents which are held by a multitude of patent owners." In other words, a 'patent ticket' is most "likely to emerge when the patent ownership of a number of essential patents is highly fragmented."[99]

[97] Jones, Whitham, and Handler, *"Problems with Royalty Rates, Royalty Stacking, and Royalty Packing Issues,"* 1121-1124.
[98] Ibid, 1124.
[99] Geertrui Van Overwalle, *"Of tickets, blocks and gaps: Designing tools to resolve obstacle in the gene patents landscape,"* in Gene *Patents and Collaborative Licensing Models. Patent Pools, Clearringhouses, Open Source Models and Liability Regimes*, ed. Geertrui Van Overwalle (New York: Cambridge University Press, 2009), 383-389.

Another 'anticommons' effect may arise from the existence of what has come to be known as *'blocking patents'*. From a broad point of view any patent has the potential of becoming a 'blocking patent' since this type of IPR confers, according to the USPTO, "the right to exclude others from making, using, offering for sale, or selling" the patented invention. More specifically, a 'blocking patent' is a patent "covering essential features of the invention which cannot be invented around." Finally, it can be stated that a 'blocking patent' is "a patent covering essential features which are licensed in a very restrictive manner" (e.g., an essential technology under an exclusive license which precludes others from being able to have access to it).[100]

4.3.Current Intellectual Property (IP) Alternatives

The current IP alternatives that are more common regarding biotechnology are patents and/or trade-secrets. In this section, they are both described with their advantages and disadvantages and then a comparison of the two types of IP is presented. Finally, potential different types of licensing that can be used are described.

4.3.1. IP options currently available

4.3.1.1.Patents

There are both benefits and disadvantages associated with the patent system for the parties holding the IPR. Among the former, there is the fact that the patent holder for the duration of the patent has the 'monopoly' over the product or process protected, along with the issue that the "administration of patent maintenance" (once obtained) is relatively easy. However, the disadvantages include the fact: that the knowledge associated with the patent is in the public domain and after the expiration of the patent it can be used by competitors, that litigation can be

[100] Van Overwalle, *"Of tickets, blocks and gaps,"* 389- 391.

expensive, and also problems regarding the "lack of harmonization of patent laws and other trading" issues that may lead to misuse.[101]

4.3.1.2.Trade Secrets

In contrast with patents, trade secrets present a different set of benefits and disadvantages to the parties holding the IPR. Among the benefits are that the knowledge is not public and, hence, is not available to competitors, and the fact that there is "no time limit on the available protection" as long as it remains secret. However, among the disadvantages are: the issue that someone can come up with the "same idea and exploit it", the fact that some "countries may not recognize the protection of confidential information", that the necessity for *secrecy* requires that "in-house procedures" have to be elaborated which are time and resources consuming, and finally, the issue that the "enforcement of the confidentiality procedures can be problematic."[102]

4.3.2. Types of Licensing

There are *commercial evaluation licenses* (also known as 'options'), which allow a company to evaluate a new technology during a certain period of time without having to commit resources that would be required by a typical patent license. If, after that short period of time, the licensee decides that the technology is what it needs, then a negotiation takes place in order to agree over a new either excusive or non-exclusive patent license.[103]

The 'options' to license patents or a "mix of know-how and patents" are in several occasions a "necessary precursor to a license of a technology or product." Companies may need some more confirmatory evidence regarding a new patent. The "option is very much a time-dependent

[101] John E. Smith, *Biotechnology,* 4th Ed., Studies in Biology (New York: Cambridge University Press, 2004), 232-233.
[102] Ibid.
[103] Hans H Feindt, *"Administration of Technology Licenses,"* in *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*, Vol. 2, eds. Anatole Krattiger, Richard T. Mahoney, Lita Nelsen, et al. (Oxford, U.K.: MIHR, and Davis, USA: PIPRA, 2007), 1395-1398.

agreement" and such limited grant ends abruptly at the end of the period established by the option.[104]

There are *patent commercialization licenses* that grant the licensees the right to use a technology that has been patented. On the one hand, an *exclusive patent commercialization license* gives to a single licensee the right to use the technology in question and to exclude others from using it until the expiration of the patent. Since this type of licenses provide a considerable competitive advantage the financial obligations are usually important. On the other hand, *non-exclusive patent commercialization licenses* provide to several potential licensees the right to use the patented technology. These licenses may last for a certain period of time or until the expiration of the patent. Besides, this type of licenses creates the conditions for the technology to disseminate faster into the market. With this type of non-exclusive licenses the issue of royalties and other obligations vary considerably depending mostly on the technology.[105]

Exclusive licenses may create the conditions for the market to be controlled by one company and/or having major firms challenging the patent. In other words, they may create the conditions for a monopoly of a necessary tool for research or, generate the conditions that would inhibit all kind of development until the dispute among firms could be settled. The latter would be the worst scenario for all the involved parties and for society in terms of innovation and development. As opposed to that, non-exclusive licenses constitute a better alternative to foster the diffusion of a given research tool and, by doing so, maximize the opportunities for R&D to take place and facilitate second generation innovation.

A *non-exclusive patent license for internal use* gives to a licensee access to a technology that has been patented which may only be used as a tool or process. The license does not allow turning the technology into a product to take to the market, the right is granted for internal purposes only.[106]

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[104] Florent Gros, *"Technology Transfer Issues in Biotechnology: The Industry Point of* View," in *Technology Transfer in Biotechnology. A Global Perspective*, eds. Prabuddha Ganguli, Rita Khanna, and Ben Prickril (Weinheim: WILEY-VCH Verlag GmbH & Co. KGaA, 2009), 151-154.
[105] Feindt, *"Administration of Technology Licenses,"* 1395-1398.
[106] Ibid.

There are also *biological material licenses*, which in the biotechnology field give licensees "access to non-patented material or biological constructs that were prepared at great effort and expense and that may be available only from the laboratory that made them." On the one hand, a *non-exclusive biological materials license for internal use* allows using unpatented technology that is not easily replicable, saving the licensee resources in its own development. On the other hand, *biological material licenses for commercial sale* aim at the ample use of 'unique materials or biological constructs' in both research and commercial developments.[107]

TABLE 4 – Typical License obligations

	Types of Technology Licenses					
Financial Terms and Other Obligations Found in Technology licenses	**Evaluation**	**Exclusive patent for Commercial Use**	**Non-exclusive patent for Commercial Use**	**Non-exclusive patent for Internal Use**	**Biological Materials for Commercial Sale**	**Biological Materials for Internal Use**
License execution fees	+	+	+	+	+	+
Annual (minimum annual) royalties	+/-	+	+	+/-	+	+/-
Past patent-prosecution fees	-	+	+/-	-	-	-
Ongoing patent-prosecution and patent-maintenance fees	-	+	+/-	-	-	-
Annual, periodic, or final reports on commercial development or research progress	+	+	+	+/-	+/-	+/-
Report of performance benchmark achievement	-	+	+	-	+	-
Performance benchmark royalties	-	+	+	-	-	-
Report of first commercial sale	-	+	+	-	+	-
Annual, periodic, or final reports on sales and earned royalties due	-	+	+	-	+	-
Earned royalties on product sales (*reach-through*)	-	+	+	-	+	-
Report of sublicensing activity	-	+	-	-	-	-
Report of sublicensing considerations and royalties due	-	+	-	-	-	-
Sublicensing royalties	-	+	-	-	-	-
License renewal or term extension fees	-	-	+/-	+	+	+
References: + = generally in license , +/- = may or may not be in license , - = generally not in license						

Source: Adapted from Hans H. Feindt, "*Administration of Technology Licenses,*" in *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*, Vol. 2, eds. Anatole Krattiger, Richard T. Mahoney, Lita Nelsen, et al. (Oxford, U.K.: MIHR, and Davis, USA: PIPRA, 2007), 1397.

[107] Feindt, "*Administration of Technology Licenses,*" 1395-1398.

When it comes to trade-secrets, since 'secrecy' is the key component of this type of intellectual property, the alternative in terms of licensing is to sign a *'secrecy agreement'* (sometimes called a 'confidential disclosure agreement' or a 'prenegotiation agreement'). With this, the owner of the trade-secret would be securing its intellectual property, since unrestricted disclosure would mean losing the right, and the party seeking the agreement would be in a position of making an informed decision regarding what could potentially be licensed but is protected as a trade-secret.[108]

4.3.3. Patents and licensing vs. Trade Secrets

From the point of view of the diffusion of knowledge and, consequently the possibility of hindering or fostering innovation, trade-secrets represent a worse scenario than that presented by patents. In contrast to trade secrets, patents imply that the knowledge enters the public domain and the duration of the IPRs is limited in time. After the expiration of a patent anyone can have access to the knowledge previously protected by it and, nonetheless, during the lifespan of the patent diffusion is possible if adequate agreements are reached between the interested parties. All of the above does not occur when it comes to protecting intellectual property through trade-secrets since the protection remains for as long as what is being protected is not transmitted or discovered by others, 'secrecy' ensures the protection of the IPR in question. The latter involves only the dissemination of end-products given that in the field of biotechnology reverse-engineering is always a possibility. Because of this, research tools protected by trade-secrets should remain outside the public domain in order for the owners to protect their intellectual property and hence being able to profit from it. This scenario has clearly the potential to hinder innovation since it would make potential R&D impossible due to the incapacity to have access to these research tools.

[108] Karl F. Jorda, *"Trade Secrets and Trade-Secret Licensing,"* in *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*, Vol. 2, eds. by Anatole Krattiger, Richard T. Mahoney, Lita Nelsen, et al. (Oxford, U.K.: MIHR, and Davis, USA: PIPRA, 2007), 1054.

4.4.Potential Approaches

The following table (Table 5) summarizes some of the potential approaches that can be used in order to cope with the issue of the potential effects that intellectual property can have on innovation if not well managed. Most of them are referred to as 'clearing mechanisms' given their purpose of attempting to 'clear' patent tickets.

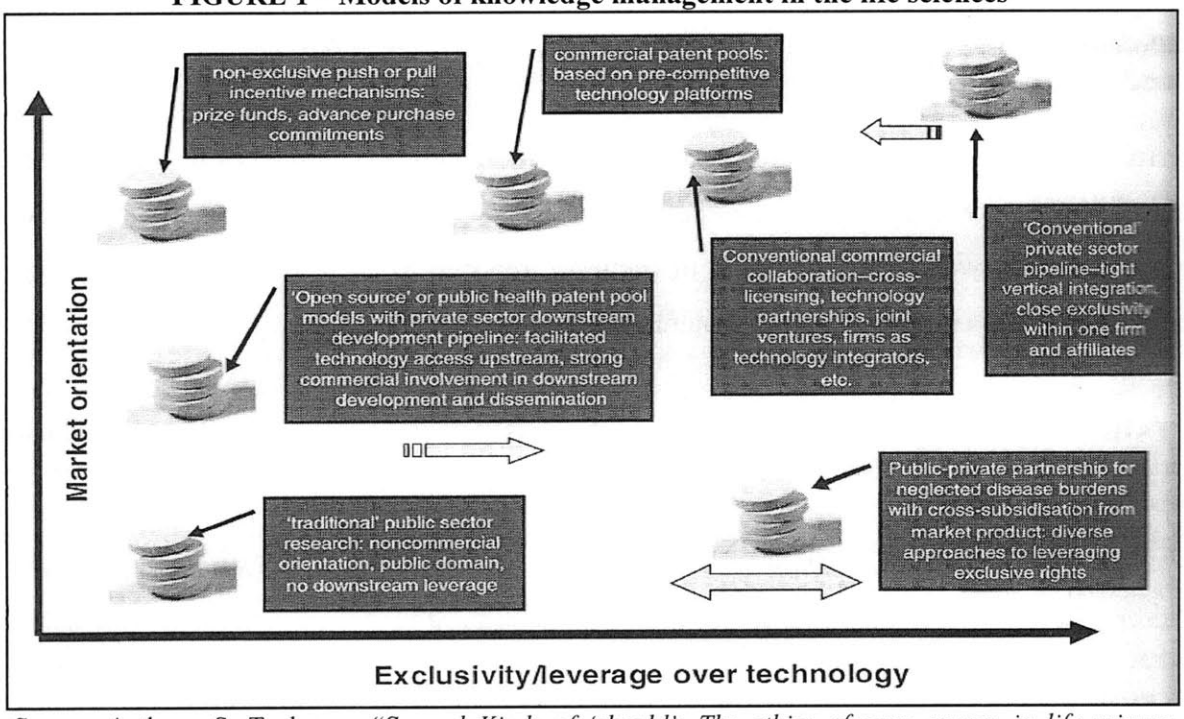
TABLE 5 – Models facilitating access, use and translation of proprietary (genetic) inventions

Clearing mechanisms (*Any mechanism aiming to clear patent tickets*)	*Working solutions*		*Ignoring the patent* *Inventing around*
	Non-collaborative models		*Research exemption*
	Collaborative models	*Conventional*	*Bilateral licensing* *Cross licensing* *Multiparty licensing*
		New	Patent pool Clearinghouse Open source Liability regime

Source: Adapted from Geertrui Van Overwalle, "*Of tickets, blocks and gaps: Designing tools to resolve obstacle in the gene patents landscape,*" in *Gene Patents and Collaborative Licensing Models. Patent Pools, Clearinghouses, Open Source Models and Liability Regimes*, ed. Geertrui Van Overwalle (New York: Cambridge University Press, 2009), 404.

The following figure (Figure 1) presents the different models of knowledge management in the life sciences, from the most conventional ones to the less traditional alternatives, some of which are still under development in terms of their applicability. They are classified based on their level of market orientation and their exclusivity (and how this can provide leverage over technology).

FIGURE 1 – Models of knowledge management in the life sciences



Source: Anthony S. Taubman, *"Several Kinds of 'should': The ethics of open source in life science innovation,"* in *Gene Patents and Collaborative Licensing Models. Patent Pools, Clearinghouses, Open Source Models and Liability Regimes*, ed. by Geertrui Van Overwalle (New York: Cambridge University Press, 2009), 228.

4.4.1. Design of Agreements: managing 'royalty stacking', 'royalty packing' and 'trade-secrets'

One of the objectives of an intellectual property license is that the owner of the IP can be compensated for the use of the proprietary technology, or receive a percentage on sales of products developed using the technology. The license should establish that reports have to be filed regarding sales so as to estimate the corresponding royalties. This task can become difficult when there has been a bundle of different licensed products. These issues can be dealt with by designing the licenses so that the agreements contemplate: (1) stipulations that differentiate royalties from the technologies involved (assuming there is more than one and also providing for a difference between royalties for the use of patented technologies and the use of trade-secrets); (2) stipulations that establish the elimination of royalties over expired or invalidated patents; (3) stipulations that contemplate the situation when a trade-secret becomes known or is patented;

and (4) stipulations that establish that a license concerning a trade-secret or know-how is not terminated by the expiration of a patent but it continues.[109]

In order to deal with the issues of 'royalty stacking' and 'royalty packing', a license may include some provisions in order to prevent or minimize these situations which can hinder innovation. On the one hand, the licensee may want to include a *ceiling* for royalties in the agreements (e.g., a certain percentage as a ceiling for combined royalties on sales). With this provision, if the 'stacked royalties' exceed the stipulated percentage it would mean that the licensors would be paid royalties "reduced on a pro rata basis" so that the total amount would not exceed the agreed ceiling. These types of agreements require that the involved parties have a clear notion of how and when a reduction may apply. It is also important that the parties be informed when new technologies are included in the product since this could potentially affect the future royalties that correspond to each licensor. Another issue that arises is that it may be necessary to differentiate among the various types of royalties (e.g., proprietary technologies used vs. reach-through licenses associated with the use of research tools). The objective is to avoid compromising the 'economic break-even', a situation that is not in the best interest of any of the involved parties. On the other hand, the licensor may want to include a *floor* that establishes a minimum level for the royalties that it receives. There may be cases where the licensor could agree to lower the floor if a new license from an important patent is required to be able to use the licensor's technology. Another possibility involves both sides agreeing upon having *variable royalties* depending on the relevance of the technology in question for the development of the product. Finally, 'royalty packing' issues can be dealt with by demanding that the royalty has to be estimated on the base of the price of the product if sold alone.[110]

When a trade secret is involved, a written agreement "is the safest way of preserving secrecy and the best way to arrange an agreement." These types of agreements should: contemplate a precise definition of the area of technology, establish a "confidential legal relationship between the parties", provide proprietary information for a specific objective, compel the recipient to keep the information confidential and stipulate exceptions to "secrecy obligations", along with the

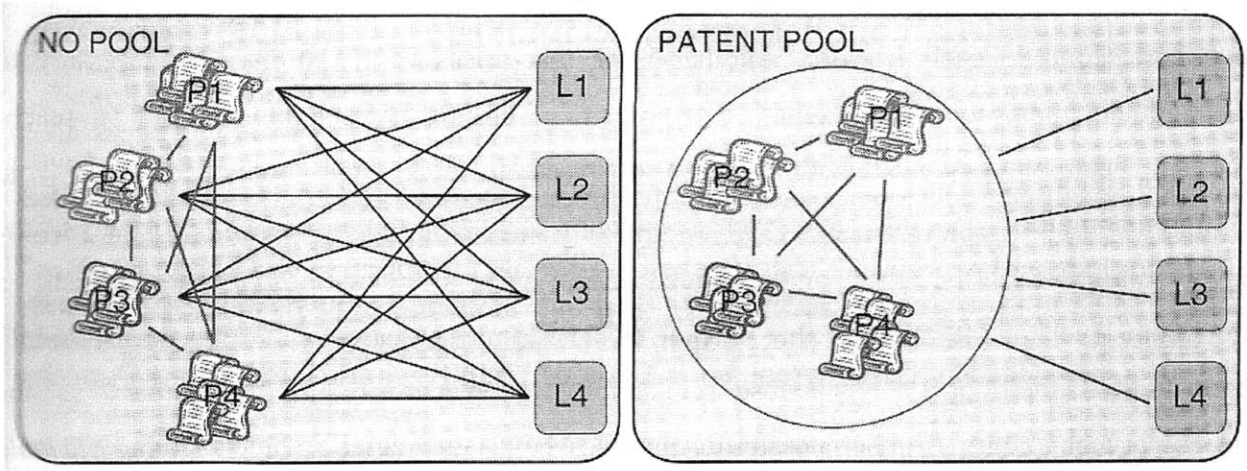
[109] Jones, Whitham, and Handler, *"Problems with Royalty Rates, Royalty Stacking, and Royalty Packing Issues,"* 1122-1124.
[110] Ibid, 1125.

typical clauses regarding license grants, royalty payments, indemnities, warranties, termination issues and any other necessary terms.[111]

4.4.2. Patent Pools

A patent pool provides another way of overcoming an 'anticommons' effect. It is an agreement among two or more patent holders with the objective of licensing one or more of their patents either between them (lines within the circle in Figure 2) or together as a package to a third party usually through an out-license-agreement (lines outside the circle in Figure 2).[112]

FIGURE 2 – Comparative illustration of the different licenses needed in the absence or presence of a patent pool



Source: Birgit Verbeure, *"Patent pooling for gene-based diagnostic testing: Conceptual framework,"* in *Gene Patents and Collaborative Licensing Models. Patent Pools, Clearinghouses, Open Source Models and Liability Regimes*, ed. by Geertrui Van Overwalle (New York: Cambridge University Press, 2009), 5.

There are various types of patent pools based on their characteristics. *Joint licensing schemes* are established by a group (generally big) of licensors of a certain technology (or standard) where one of them may play the role of the agent of the joint licensing contract. Eventually these types of pools accept other owners of critical IPRs to the standard. *Patent pools with a licensing administrator* begin with an open call by an independent entity for critical patents for a given

[111] Jorda, *"Trade Secrets and Trade-Secret Licensing,"* 1054-1055.

[112] Birgit Verbeure, *"Patent pooling for gene-based diagnostic testing: Conceptual framework,"* in *Gene Patents and Collaborative Licensing Models. Patent Pools, Clearinghouses, Open Source Models and Liability Regimes*, ed. Geertrui Van Overwalle (New York: Cambridge University Press, 2009), 5.

standard. Then the independent licensing administrator conducts an evaluation of the patents in order to establish whether they are critical to the standard or not. It is also the licensing administrator the one who sets (in consultation with the licensors) the royalty rates for the pool and it is also the one in charge of collecting them and giving them to whom they belong. *Patent platforms* constitute an organizational approach that covers multiple technologies (standards) and numerous product groups (involving patents that are critical to a given standard). Besides, being more adaptable regarding the agreements between licensees and licensors is another objective. This approach involves one supra-organization and several entities that develop licensing programs for certain standards so that the objective is to provide "a standard offer (bundle) available."[113]

There are four types of patents that are relevant when considering establishing a patent pool. First, c*omplementary* patents are "for different aspects of the same technology that can be used together", in other words, they are the opposite of substitutes. Second, c*ompeting* patents represent substitute technologies. Third, *blocking* patents are required to develop the technology. Finally, e*ssential* patents "claim technologies that have 'no technical alternative' and are critical for the end product." A pool should contain complementary, blocking and/or essential patents in order to allow development and foster innovation. Another matter that relates to patent pools is the 'holdout problem' where a holdout is the owner of a patent that is either essential, blocking, or complementary, who thinks that it can manage on its own by negotiating with the pool's licensees in an attempt to obtain potential higher royalties.[114]

So, even if the main goal of patent pools is to prevent that access to critical inputs is not denied, the predominantly situation involves complementary and numerous patents that are independent and can be 'inter-blocking' without some form of coordination (the patent pool). Patent pools are especially useful in cases that involve complementary (not substitute) patents by reducing transaction costs (that would arise from the negotiation of many licenses) and hold-out problems. In the field of biotechnology they can help by integrating technologies, minimizing transaction

[113] Verbeure, *"Patent pooling for gene-based diagnostic testing: Conceptual framework,"* 7-9.
[114] Jorge A. Goldstein, *"Biotechnology patent pools and standards setting,"* in *Patent Law and Theory: A Handbook of Contemporary Research*, ed. Toshiko Takenaka (Northampton, MA, USA: Edward Elgar Publishing Inc., 2008), 714-721.

costs, avoiding blocking situations, preventing expensive litigations, and fostering the diffusion of technology and hence promoting innovation. However, patent pools are useful to address the issue of patent tickets (that involve access to several technologies protected by IPRs), but if what is necessary is to have access to only one critical upstream technology, as could be the case sometimes with a research tool, then a direct agreement could be the best approach.[115] Regarding the latter, if a certain research project requires the use of one research tool a direct agreement is more adequate, but if the project requires a research tool as an essential requirement among other proprietary technologies (whether they constitute research tools or not) then a patent for a research tool or even several such patents can be part of the group of patents involved in a 'patent pool'. This patent pool would most likely not involve just proprietary research tools but also applications that are deemed necessary for a certain purpose.

TABLE 6 – Summary and the Pros and Cons of Patent Pools

Pros	Cons
Integrates complementary technologies	Difficult to agree on the value of individual patents contributed to a pool
Reduces transaction costs	Complex to set up and avoid antitrust problems (collusion and price fixing)
Clears blocking positions	May inflate licensing costs through non-blocking or unnecessary patents
Promotes the dissemination of technology	Complex when many patents are under litigation, as is the case with biotechnology
Levels the playing field	May shield invalid patents and thus prevent much technology from entering the public domain

Source: Anatole Krattiger and Stanley P. Kowalski, *"Facilitating Assembly of and Access to Intellectual Property: Focus on Patent Pools and a Review of Other Mechanism,"* in *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*, Vol. 1, eds. Anatole Krattiger, Richard T. Mahoney, Lita Nelsen, et al. (Oxford, U.K.: MIHR, and Davis, USA: PIPRA, 2007), 139.

4.4.3. Clearinghouses

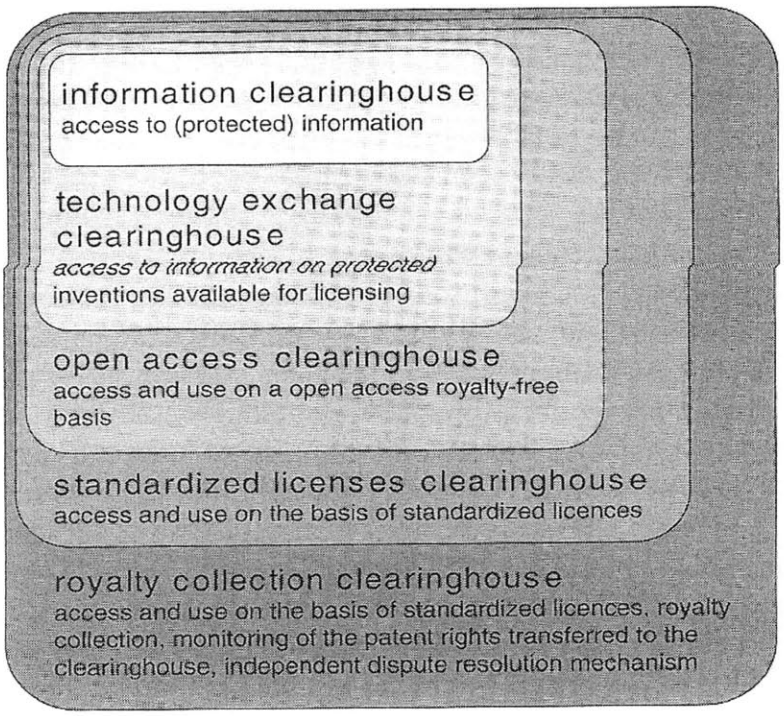
The term 'clearinghouse' derives "from the banking institutions and refers to the mechanism by which checks and bills are exchanged amongst member banks in order to transfer only the net

[115] Irina Haracoglou, *Competition Law and Patents: A Follow-on Innovation Perspective in the Biopharmaceutical Industry* (Northampton, MA, USA: Edward Elgar Publishing Inc., 2008), 51-53.

balances in cash". Currently, the term is also used to refer to any mechanism that involves the matching of providers and users of goods, services and information.[116]

According to Van Zimmeren there are five types of clearinghouses: the first two just give access to information that is protected, while the other three have the objective of providing both access to and use of inventions (in a standardized manner). Even if this typology is arbitrary it tries to be based on the type of services that the clearinghouse can provide in relation to patent licensing.[117]

FIGURE 3 – Types of clearinghouses



Source: Esther Van Zimmeren, *"Clearinghouse mechanisms in genetic diagnostics: Conceptual framework,"* in *Gene Patents and Collaborative Licensing Models. Patent Pools, Clearinghouses, Open Source Models and Liability Regimes*, ed. Geertrui Van Overwalle (New York: Cambridge University Press, 2009), 80.

These different kinds of clearinghouses do not have the same potential to deal with the impediments presented by the presence of patent tickets and 'unilateral restrictive licenses'. The

[116] Esther Van Zimmeren, *"Clearinghouse mechanisms in genetic diagnostics: Conceptual framework,"* in *Gene Patents and Collaborative Licensing Models. Patent Pools, Clearinghouses, Open Source Models and Liability Regimes*, ed. Geertrui Van Overwalle (New York: Cambridge University Press, 2009), 69.
[117] Ibid, 69-70.

first issue is the associated transaction costs that arise due to the numerous negotiations that are needed to obtain all the necessary licenses. The second issue is the potential accumulation of royalties that may give rise to a 'royalty stacking' situation. The third issue arises when there is a 'non-cooperative patent holder' who leads to a blocking situation by impeding the process of obtaining a license. Finally, a clearinghouse can be administered "either as a voluntary scheme or as a statutory framework on a compulsory basis."[118]

This approach is rather novel and may have the potential to deal with the problems mentioned above. If well established, it could be possible for this type of mechanism to approach these issues and facilitate the negotiations involving proprietary technologies. Whether they are applications or research tools, the idea, particularly regarding the last three, is to provide both access to and use of inventions (in a standardized manner), which would reduce the transaction costs and facilitate the negotiations.

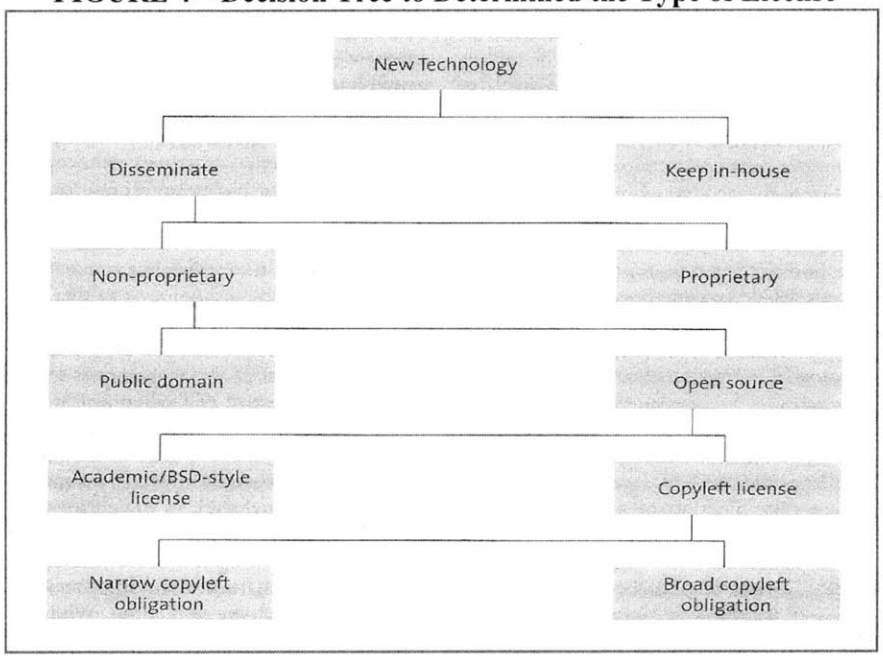
4.4.4. Open source models

Although most examples are associated with the software industry, 'open source' schemes can be applied to other fields. Open source models can be particularly useful in "niche markets that are too small to be profitable for companies that make off-the-shelf, proprietary technology." Such a model can also be useful for small "agricultural and pharmaceutical markets in developing countries (where *small* may refer either to the number of potential users or the amount that potential users can afford to pay)." Open source style of development can also play a role in fields characterized by "proprietary strategies" such as the life sciences. It may have started with bioinformatics software programs licensed under 'open source terms', but there are already some life-science initiatives that try to follow some open source principles in order to deal with the increasingly challenging intellectual property issues that keep arising.[119] Nonetheless, it has to be acknowledged that before an 'open source' model can become a potential alternative, further development is needed in order to assess how and under what circumstances this approach can

[118] Van Zimmeren, *"Clearinghouse mechanisms in genetic diagnostics: Conceptual framework,"* 70.
[119] Janet Hope, *"Open Source Licensing,"* in *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*, Vol. 1, eds. Anatole Krattiger, Richard T. Mahoney, Lita Nelsen, et al. (Oxford, U.K.: MIHR, and Davis, USA: PIPRA, 2007), 107-117.

be a potential effective solution for some situations involving IP in the field of biotechnology that has many characteristics unlike those of the software industry.

FIGURE 4 – Decision Tree to Determined the Type of License



Source: Janet Hope, *"Open Source Licensing,"* in *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*, Vol. 1, eds. Anatole Krattiger, Richard T. Mahoney, Lita Nelsen, et al. (Oxford, U.K.: MIHR, and Davis, USA: PIPRA, 2007), 109.

Regarding the previous figure (Figure 4) a *copyleft* or *reciprocal* license allows "the user to modify and redistribute a software program at will." The obligation of the licensee is to make available to everybody (including the licensor) all relevant downstream innovation under the same terms as where established in the original license. Nobody obtains any special privilege, since the objective is to promote downstream innovation that remains available (free to all those interested) which in turn preserves this tendency so as to generate as much innovation as possible.[120]

4.4.5. Liability regimes

In relation to the problem of patent tickets, the 'liability regime' has been considered an possible alternative to deal with it. The concept of 'liability rules' has its origin in the 'entitlement

[120] Hope, *"Open Source Licensing,"* 113.

theory'. This theory distinguishes between "entitlements protected by property, liability or inalienability rules." An entitlement (right) is "protected by a property rule if someone must buy it from its holder in a voluntary transaction in which the value of the entitlement is agreed upon by the seller." So, property rules involve a decision regarding who can receive an entitlement but not regarding the value of it. An entitlement is "protected by a liability rule, if someone may use or destroy the initial entitlement if he is willing to pay an objective determined value of it." Liability rules "thus involve state intervention: the state does not only decide whom to entitle, but determines the value of the transfer or destruction." In other words, liability rules can be said to be "'take now, pay later' rules: others can use the entitlement without permission of the owner, so long as they adequately compensate the owner later." A great difference between liability rules and IPRs is that the rule "does not allow to control follow-on applications", they make possible for companies to "borrow one another's innovation" for a period of time as long as "they contribute to the costs of development." Nonetheless, "translating the liability regime in a biological sphere is rather unseen exercise."[121] Hence, although this approach may present a feasible alternative, it remains to be seen if it can be adequately applied in the biology and biotechnology fields.

4.4.6. Experimental use exemption

The experimental use exemption, when applicable and if contemplated by law, is a narrow exception that "excuses the infringement of a patent." This exemption exists in Europe and it is governed by national laws. The basic notion behind is that it does not constitute infringement to incur in an experimental use of an invention that has been patented with the objective of verifying the patent specification or, to conduct non-commercial experiments. Most importantly, the existence of an experimental use exemption has the main objective of preventing a situation where technical and scientific progress could be delayed or even stopped. In other words, the existence of an experimental use exemption is related to the issue of the high transaction costs that may hinder innovation by preventing experiments from taking place.[122]

[121] Van Overwalle, *"Of tickets, blocks and gaps,"* 431-437.
[122] Haracoglou. *Competition Law and Patents*, 39-42.

A distinction has been established between 'experimenting on' and 'experimenting with' an invention that has been patented. While 'experimenting on' involves using to study the technology and inventing around the patent that is considered exempted, 'experimenting with' involves using to study something else that the exemption does not cover. In the USA, the 'experimental use doctrine', even though it exists, its scope is unclear regarding applicability and policy. This is mainly due the fact that it relies on how "curiosity, amusement and philosophical experiment" are defined, which are the purposes that a potential infringer should have in order to be granted an exemption.[123]

Nonetheless, the experimental use exemption ultimate purpose is to prevent technical and scientific innovation from taking place, in other words, to make sure that progress is not hindered. The latter can easily happen when the transaction costs involved are too high so that they may impede new developments and therefore stop further research that could potentially benefit society. For these reasons, this type of exemption, when is contemplated by law, usually applies to either academic or other non-profit institutions; and not to anyone who may have a commercial purpose in using the technology in question. The idea is to ensure that research takes place in settings that may work in projects whose results are highly uncertain. Moreover, they may not render considerable profits making the acquisition of these proprietary technologies inaccessible, which may hinder research in areas that can produce important results.

4.4.7. Compulsory licensing

A *compulsory license* constitutes an authorization granted by a 'national authority' to a third party to use an invention protected by a patent without the consent of the owner of the patent. Compulsory licenses are particularly "important when there are no close substitutes for a product or process and a research exemption is not available or is too narrow." These licenses can be required when patents compromise the 'freedom to operate' regarding R&D in a certain field. Nonetheless, compulsory licenses are subject to a series of conditions such as compensating the patent holder with a reasonable remuneration. Regarding the latter, the criterion used to

[123] Haracoglou. *Competition Law and Patents*, 42-47.

determine the royalty rates for a product is different from the one used for a research tool. This is especially true given the fact that there is no product in the market which tends to lower the royalties in the case of research tools. In all cases the licenses are non-exclusive.[124]

Compulsory licensing has had both support and opposition. On the one hand, this type of licensing is usually supported when the demand for a product cannot be supplied, when it can make certain inventions possible by allowing further research (including improvements on prior patents), and when it is needed in order to develop products that are necessary for reasons of public health and welfare among others. It is also advocated for when associated to potential deadweight loss concerns such as the case of consumers not being able to afford prices under monopoly conditions. On the other hand, this type of licensing is opposed mainly due to the fact that it may reduce the incentives to innovate by reducing the level of investment because of lack of incentives and due to the potential lost in revenues that would have been used in further research. Nonetheless, there is no certain empirical evidence regarding the above mentioned issues.[125]

In order to be granted a compulsory license, the European and International IP laws show that three priority reasons exist: blocking by a dependent patent, a patent not being used, or public interest reasons such as health or antitrust issues among others. In accordance with the TRIPS (Trade-Related Aspects of Property Rights) Agreements there three cases for compulsory licensing to be granted including: "the non-use of a patent for three years from its grant or four years from its application"; "when necessary to use a second otherwise infringing patent that constitutes an important technical advance of considerable economic significance"; and "in cases of extreme urgency, crisis, or to remedy anti-competitive behavior." Another situation, contemplated by the TRIPS, is the main objective of supplying the domestic market. These agreements nonetheless stipulate some criteria that should be followed when deciding whether to grant a compulsory license. These criteria involve that governments have to assess each case individually, that before granting the authorization there has to be an attempt to negotiate

[124] Carlos Maria Correa, *"Compulsory Licensing: How to Gain Access to Patented Technology,"* in *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*, Vol. 1, eds. Anatole Krattiger, Richard T. Mahoney, Lita Nelsen, et al. (Oxford, U.K.: MIHR, and Davis, USA: PIPRA, 2007), 274-277.
[125] Haracoglou, *Competition Law and Patents*, 54-56.

voluntary a license on reasonable terms and, that the authority makes sure that remuneration is provided in accordance with the value.[126]

4.5.IPRs and Different International Regimes

International patent law has been developing since the *Paris Convention* in 1883. However, international norms are facing new challenges nowadays mainly due to the increasing role of the patent system in the current knowledge-based economy. Even if all the member States were to adopt the treaties that are administered by WIPO (*World Intellectual Property Organization*), it is up to each State to decide whether or not to enter into an international agreement. In the particular area of patents a series of multilateral treaties have aimed at dealing with areas that present severe difficulties if left only to the national patent legislation. One fundamental principle involves ensuring 'equitable legal protection at the international level'. Another important role of international instruments regarding patents involves the adoption of common rules so as to "increase legal certainty at the international level and enhance accessibility to the international patent system." The Strasbourg Agreement states the *International Patent Classification* (IPC) that classifies all field of technology. The *Patent Cooperation Treaty* (PCT) is an international cooperation agreement in relation to the "filing, searching and preliminary examination of patent applications and dissemination of technical information" that appears in the applications which was adopted in 1970 but it only became operational in 1978. The treaty involves two phases: the international phase and the national phase. In 1991 the *Draft Harmonization Treaty* included issues such as the filing date and the claim of priority among other formalities. The *Patent Law Treaty* (PLT) was concluded in the year 2000 although its development started in 1995, and it mostly refers to a "simplification of the formality requirements set by national and regional offices and the streaming of the procedures for obtaining and maintaining a national and regional patent." The TRIPS Agreement was "contained in the Annex to the WTO (World Trade Organization) that entered into force in 1995." The TRIPS Agreements bind all WTO members and is the "first international instrument to focus on trade-related aspects of IPRs", which regarding patents establishes standards in relation to "availability, scope, and use of patent rights." In the year 2000 and due to the increase

[126] Haracoglou, *Competition Law and Patents*, 57-58.

interest of WIPO members to address issues of harmonization regarding requirements of patent law it was decided to discuss the topic which turned into the *Draft Substantive Patent Law Treaty* (SPLT). Currently, two issues are present in the international patent discussions that are mutually opposing, a situation that makes the task of finding common principles at the international level more difficult. On the one hand, there is a tendency in the direction of harmonization and integration aiming at the development of an 'international patent system', which would be accessible and would promote legal certainty, patent quality and international cooperation. On the other hand, there is a tendency in the direction of diversity and flexibility mainly due to the acknowledgement of the "importance of IPRs for technological, cultural and social development" and, considering that countries differ in their policy priorities, which translate into a request for differential treatment based on the level of development.[127]

The following table (Table 7) describes the main differences and similarities among three major patent offices: the European Office, the Japanese Office, and the United States Office. The most important difference is over *priority* since in the United States the priority is given on a *first-to-invent* basis where in other countries the basis is given by a *first-to-file* approach, which in many cases leads to litigations.[128]

TABLE 7 – Significant Differences between the Three Main Patent Offices

Issue	EPO (*European Patent Office*)	JPO (*Japan Patent Office*)	U.S.PTO
Status of successful patent applicant	First to file	First to file	First to invent
Patent duration	20 years	20 years	20 years
Application language	English, French, or German	Japanese	English
Area in which the patent is valid	Designated EPC (*European Patent Convention*) member and extension countries	Japan	United States

[127] Tomoko Miyamoto, *"International treaties and patent law harmonization: today and beyond,"* in *Patent Law and Theory: A Handbook of Contemporary Research*, ed. Toshiko Takenaka (Northampton, MA, USA: Edward Elgar Publishing Inc., 2008), 154-187.

[128] John Dodds, *"Patenting Strategies: Building an IP Fortress,"* in *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*, Vol. 1, eds. Anatole Krattiger, Richard T. Mahoney, Lita Nelsen, et al. (Oxford, U.K.: MIHR, and Davis, USA: PIPRA, 2007), 911-912.

Request for re-examination of the patent	Yes, within 6 month	Yes, within 3 years	No provision
Time of publication of application	18 months from priority date	18 months from priority date	18 months from priority date (*the application for an invention that has not and will not be patented in foreign countries will not be published if the applicant so requests*)

Source: Adapted from Ronald Yin and Sean Cunninghan, *"Filing and Defending Patents in Different Jurisdictions,"* in *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*, Vol. 1, eds. Anatole Krattiger, Richard T. Mahoney, Lita Nelsen, et al. (Oxford, U.K.: MIHR, and Davis, USA: PIPRA, 2007), 954.

Regarding *compulsory licensing* (CL) there are a series of issues to consider. It may present a problem due to the costs of litigation. In the particular case of research tools, the dependency issue may not be sufficient since it would apply to secondary patents and not to research itself, and, besides, the research that requires the research tool may be in a stage where it would prove to be successful or not, which in turn diminishes the effectiveness of CL. Some empirical evidence from some European countries shows that even if some form of CL exists it is very rarely exercise due to its implications, among which it is the fact that governments have to face the uncertainty regarding potential compensation. The cases where this approach could be more helpful involve either 'extreme urgency' or 'anti-competitive behavior'. Among the European countries that have some provision regarding compulsory licensing the following are included: Austria, Denmark, Finland, France, Germany, Greece, Italy, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom, and the European Communities.[129] In the United States, compulsory licenses have been "widely used for government use and in settlements for antitrust cases." Compulsory licenses are used to obtain public policy objectives such as dealing with emergencies, counteracting anticompetitive behavior, or allowing the use of patents that are not being use and, hence, impede development. There are some different situations in other countries (such as Brazil and South Africa, among others) that have stated the possible use of

[129] Haracoglou, *Competition Law and Patents*, 63-69.

compulsory licensing so as to obtain cheaper medicines (something that has been done in the past by other countries).[130]

In general, the patent system in the majority of the developed countries has a provision regarding *research exemption* that in some cases even covers some forms of commercial R&D. The United States constitutes an exception to this tendency, given that the scope of the U.S. research use exemption is very narrow and practically inconsequential when it comes to protect and allow meaningful research to take place.[131] The research use exemption in most developed countries is broader. Among the European countries that have some provision regarding experimental use exemption the following can be mentioned: Denmark, Finland, France, Germany, Greece, Italy, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom, and the European Communities.[132]

The other alternative approaches such as patent pools, clearinghouses and open source models among others, are present in different countries although they are clearly more common in the developed ones given that most inventions take place in these countries. Moreover, in these countries the IP regime provides more legal certainty when considering new approaches for which the legal framework has not yet been established. This is very important given the fact that adopting or participating in these approaches is accompanied by a level of uncertainty about what are generally considered valuable IPRs. Some of these approaches have already been tried, such as 'patent pools', while others are in their early stages and may or may not end up being applicable in fields such as biotechnology.

Finally, it can be stated that at the policy level, the revolution in biotechnology has generated the necessity for a new approach regarding the interface between science and policy-making. One of the most important issues is the controversy regarding the setting of standards for the use of biotechnology. Regarding the latter and from a legal point of view the difficulty is mirrored in

[130] Correa, *Compulsory Licensing*, 274-275.
[131] Sean. O'Connor, "*Enabling research or unfair competition? 'De jure' and 'de facto' research use exceptions in major technology countries,*" in *Patent Law and Theory: A Handbook of Contemporary Research*, ed. Toshiko Takenaka (Northampton, MA, USA: Edward Elgar Publishing Inc., 2008), 525-541.
[132] Haracoglou, *Competition Law and Patents*, 66-69.

both the national and international attempts to address the issue of biotechnology applications, including issues related to ownership and control, use and marketing, among others. Regarding trade, under general international law "every State is free to restrict the import or export of biotech products on grounds of safety, environmental protection or other public policy considerations." All the above mentioned issues have promoted international efforts aiming at generating new legislation that allows an "acceptable and sustainable" use of biotechnology.[133]

4.6.Policy and IPRs on Biotechnology Innovations

As has been stated above, both in the United States and in the International Community there have been several attempts regarding the issue of IPRs management in biotechnology, mainly due to its impact on development.

Although the patent system tends to create the conditions to incentivize investment and, consequently, R&D that may render developments that are then protected by some form of IPR which allows for the recovery of the investment, the very same system can create problems for innovation. In other words, it is also true that this proprietary knowledge has given rise to sometimes difficult transactions in a very competitive environment. Also, in relation to the issue of patents, a very important topic is the scope of the patents, since too narrow patents may inhibit development given that they could most likely be worked around and; too broad patents can create the conditions that may hinder innovation since they may inhibit research, especially when research projects require the use of many proprietary technologies. This situation becomes especially relevant when it relates to patented research tools that are usually necessary for research. Another important issue that should be addressed is the one related to 'reach-through' licenses since there are mechanisms as the ones described in the previous sections (such as 'anti-stacking clauses) that could help to deal with this issue. There is also the possibility of holding the payments until it is clear whether the research in question will render revenues or not. All the alternatives mentioned before are relevant, not only in order to foster development and not

[133] Francesco Francioni, *"International Law for Biotechnology: Basic Principles,"* in *Biotechnology and International Law,* eds. Francesco Francioni and Tullio Scovazzi (Portland, OR, USA: Hart Publishing, 2006), 3-27.

hinder innovation that may prove profitable, but also to allow research on not profitable causes (such as the case of orphan drugs) to take place.[134]

Another policy concern relates to the creation of adequate incentives for the commercialization of the results of basic research as a way of generating adequate returns to the taxpayer (especially in the case of proprietary technologies or products that are the result of publicly funded research). Then, there is also the issue of technology transfer where IPRs play a major role. An adequate policy approach, would foment the adoption of strategies regarding IP that would not compromise innovation and, hence, development. Regarding the latter, issues such as the existence of research exemptions, and the way the patent system handles the design of the patents (particularly in term of scope), are examples of what could contribute to foster innovation. Besides, the government can play a role (as it has played in the past both in the U.S. and in other countries) by ensuring that cases that involve some kind of 'knowledge sequestration' do not occur as a consequence of IPRs owners that do not share their proprietary technologies or products. All of the above aims at ensuring that technology gets diffused and further innovation can occur.[135]

Finally, in the international field, there is the issue of technology transfer among the countries, especially between developed and developing countries, where these technologies may render important benefits. However, the latter would be facilitated by a stronger international IP regime, not to mention the harmonization of the existing systems up to the point that it may be desirable. This would certainly contribute to foster development and growth. There is a need for institutionalized models for "collective networking involving technology development" that involve adequate IP protection as well as "equitable benefit sharing", for which both traditional mechanisms of the IP systems and other new 'clearing mechanisms' could be useful in order to create the conditions for the development of necessary technologies for the benefit of society in a "cost-effective and affordable manner" that fosters innovation.[136]

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[134] Prabuddha Ganguli, Rita Khanna, and Ben Prickril, "*Defining the Future: Emergency Issues in Biotechnology, Intellectual Property Rights and Technology Transfer,*" in *Technology Transfer in Biotechnology. A Global Perspective*, eds. Prabuddha Ganguli, Rita Khanna, and Ben Prickril (Weinheim: WILEY-VCH Verlag GmbH & Co. KGaA, 2009), 1-8.
[135] Ganguli, Khanna, and Prickril, "*Defining the Future,*" 1-11.
[136] Ibid, 8-11.

Chapter 5

CONCLUSIONS AND RECOMMENDATIONS

The issue of intellectual property rights and their impact on innovation in the field of biotechnology may be addressed from different perspectives. It is clear that strong IPRs on upstream innovation (as is the case of research tools) can seriously deter or even inhibit downstream innovation.

The traditional intellectual property system can help to deal with the issue if used adequately. The most common form of IPR that protects these inventions is patents, which still serve the original purpose of fostering these first generation inventions by providing the incentives to invest resources in R&D. Besides, protection under patents means that the information enters the public domain through the application file and, eventually, it becomes accessible to all interested parties when the patent expires. This is the opposite of what happens when the chosen form of securing IPRs is through trade-secrets, since under such circumstances the knowledge may never reach the public domain if the owner so decides because of a strategic decision usually related to keeping a competitive advantage.

Nonetheless, both types of IPR, but most commonly patents, have to be accompanied by an adequate licensing program that is accessible to the interested parties while respecting the interests of the developer of the technology. There are several types of licenses as well as specific adaptations to these licenses (such as anti-stacking clauses) that can help to deal with the issues that arise when a certain development requires the use of several upstream proprietary technologies. This is why an important issue regarding patents is their scope, which can have a major impact in subsequent research (especially if it creates the conditions to have reach-trough licenses). In order to avoid a potential 'anticommons' effect these licensing schemes have to be designed so as to allow second generation innovation to take place.

Policies should try to encourage patenting over trade-secrets since it is best for development in general. However, regardless of the IPR involved, the governmental authorities should play a role in ensuring that situations such as holdouts (owners of an essential patent that refuse to

allow access to it) among others do not take place. In the event of these situations occurring, the governmental authorities should adopt some kind of clearing mechanism that allows for research to proceed whether the potential results are known or not. The governmental authorities also have a role to play when it comes to proprietary technology that is required under extreme situations, or when access is denied under anticompetitive behavior.

Another important issue is the establishment of some kind of research exemption not only for academic and non-profit institutions, that could not afford the costs of accessing these technologies, but also to make possible research in areas that are not going to be profitable (as is the case with orphan drugs). This would benefit society as a whole and, it would not mean that the owners of proprietary research could not profit from their discoveries with other interested parties so as to have the incentive to keep investing in R&D. Some form of this exemption exists in most developed countries, but in the U.S. is very narrow.

Regarding these new kinds of clearing mechanisms that are emerging (such as patent pools, clearinghouses, open source models, among others) they should be assessed in order to ascertain whether they can constitute a serious alternative to complement the traditional system so as to facilitate access to proprietary technologies that are necessary for second generation innovation. In some instances, they may present more efficient ways of dealing with the problems that arise regarding intellectual property that have the potential to hinder innovation depending on how they are managed. However, even if some of these approaches have been used, such as 'patent pools', others are in their early stages and it is not yet clear whether they will be applicable.

Finally, it is also important that the international community works with the objective of harmonizing the intellectual property systems so as to foster innovation as well as development. A strong international IP system would create better conditions for cases of technology transfer among the countries as well as provide more legal certainty regarding proprietary technologies. However, there are proponents of differentiating in some cases between countries when designing the transfer conditions, especially when the transfer involves some essential technology or product. In conclusion, a more harmonized and strong international IP regime would provide the conditions that would foster innovation and development, which would benefit all the interested parties as well as society as a whole.

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Appendix I

INTELLECTUAL PROPERTY

According to the United States Patent and Trademark Office, there are four ways to protect different types of intellectual property. The contents of the table included in this appendix come from the verbatim of the United States Patent and Trademark Office (USPTO).

PATENTS	Provide rights for up to 20 years for inventions in three broad categories:
Utility patents	Protect useful processes, machines, articles of manufacture, and compositions of matter. Some examples: fiber optics, computer hardware, medications.
Design patents	Guard the unauthorized use of new, original, and ornamental designs for articles of manufacture. Some examples: the look of an athletic shoe, a bicycle helmet.
Plant patents	Protect invented or discovered asexually-reproduced plant varieties. Some examples: Hybrid tea roses, Silver Queen corn, Better Boy tomatoes.
TRADEMARKS ®	Protect words, names, symbols, sounds, or colors that distinguish goods and services. Trademarks, unlike patents, can be renewed forever as long as they are being used in business. Some examples: the shape of a *Coca-Cola* bottle.
COPYRIGHTS ©	Protect works of authorship, such as writings, music, and works of art that have been tangibly expressed. The Library of Congress registers copyrights which last the life of the author plus 50 years. Some examples: recordings, video games.
TRADE SECRETS	Are information that companies keep secret to give them an advantage over their competitors. The formula for *Coca-Cola* is the most famous trade secret.

Source: Adapted from United States Patent and Trademark Office: An Agency of the Department of Commerce. http://www.uspto.gov/web/offices/ac/ahrpa/opa/museum/1intell.htm.

Appendix II

PATENTS

The contents of this appendix come from the verbatim of the United States Patent and Trademark Office (USPTO).[137]

What Is a Patent?

A patent for an invention is the grant of a property right to the inventor, issued by the United States Patent and Trademark Office. Generally, the term of a new patent is 20 years from the date on which the application for the patent was filed in the United States or, in special cases, from the date an earlier related application was filed, subject to the payment of maintenance fees. U.S. patent grants are effective only within the United States, U.S. territories, and U.S. possessions. Under certain circumstances, patent term extensions or adjustments may be available.

The right conferred by the patent grant is, in the language of the statute and of the grant itself, "the right to exclude others from making, using, offering for sale, or selling" the invention in the United States or "importing" the invention into the United States. What is granted is not the right to make, use, offer for sale, sell or import, but the right to exclude others from making, using, offering for sale, selling or importing the invention. Once a patent is issued, the patentee must enforce the patent without aid of the USPTO.

There are three types of patents:

1) **Utility** patents may be granted to anyone who invents or discovers any new and useful process, machine, article of manufacture, or composition of matter, or any new and useful improvement thereof;

2) **Design** patents may be granted to anyone who invents a new, original, and ornamental design for an article of manufacture; and

3) **Plant** patents may be granted to anyone who invents or discovers and asexually reproduces any distinct and new variety of plant.

What Can Be Patented

The patent law specifies the general field of subject matter that can be patented and the conditions under which a patent may be obtained.

In the language of the statute, any person who "invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent," subject to the conditions and requirements of the law. The word "process" is defined by law as a process, act or method, and primarily includes industrial or technical processes. The term "machine" used in the statute needs no explanation. The term "manufacture" refers to articles that are made, and includes all manufactured articles. The term "composition of matter" relates to chemical compositions and may include mixtures of ingredients as well as new chemical compounds. These classes of subject matter taken together include practically everything that is made by man and the processes for making the products.

[137] United States Patent and Trademark Office: An Agency of the Department of Commerce. http://www.uspto.gov/web/offices/pac/doc/general/index.html#functions.

The Atomic Energy Act of 1954 excludes the patenting of inventions useful solely in the utilization of special nuclear material or atomic energy in an atomic weapon 42 U.S.C. 2181 (a).

The patent law specifies that the subject matter must be "useful." The term "useful" in this connection refers to the condition that the subject matter has a useful purpose and also includes operativeness, that is, a machine which will not operate to perform the intended purpose would not be called useful, and therefore would not be granted a patent.

Interpretations of the statute by the courts have defined the limits of the field of subject matter that can be patented, thus it has been held that the laws of nature, physical phenomena, and abstract ideas are not patentable subject matter.

A patent cannot be obtained upon a mere idea or suggestion. The patent is granted upon the new machine, manufacture, etc., as has been said, and not upon the idea or suggestion of the new machine. A complete description of the actual machine or other subject matter for which a patent is sought is required.

Appendix III

TRADE SECRETS

The contents of this appendix come from the verbatim of the United States Patent and Trademark Office (USPTO).[138]

A fourth type of intellectual property, in addition to patents, trademarks, and copyrights, is **trade secrets**. Trade secrets consist of information and can include a formula, pattern, compilation, program, device, method, technique or process. To meet the most common definition of a trade secret, it must be used in business, and give an opportunity to obtain an economic advantage over competitors who do not know or use it.

As a member of the World Trade Organization (WTO) and a party to the Agreement on Trade Related Aspects of Intellectual-Property Rights (TRIPS), the United States is obligated to provide trade secret protection. Article 39 paragraph 2 requires member nations to provide a means for protecting information that is secret, commercially valuable because it is secret, and subject to reasonable steps to keep it secret. The U.S. fulfills its obligation by offering trade secret protection under state laws. While state laws differ, there is similarity among the laws because almost all states have adopted some form of the Uniform Trade Secrets Act. The language of the Uniform Trade Secret Act is very similar to the language in TRIPS.

Courts can protect trade secrets by enjoining misappropriation, ordering parties that have misappropriated a trade secret to take steps to maintain its secrecy, as well as ordering payment of a royalty to the owner. Courts can also award damages, court costs, and reasonable attorneys' fees. This protection is very limited because a trade secret holder is only protected from unauthorized disclosure and use which is referred to as misappropriation. If a trade secret holder fails to maintain secrecy or if the information is independently discovered, becomes released or otherwise becomes generally known, protection as a trade secret is lost. Trade secrets do not expire so protection continues until discovery or loss.

Trade secret protection is an alternative to patent protection. Patents require the inventor to provide a detailed and enabling disclosure about the invention in exchange for the right to exclude others from practicing the invention for a limited period of time. Patents do expire, and when that happens the information contained within is no longer protected. However, unlike trade secrets, patents protect against independent discovery. Patent protection also eliminates the need to maintain secrecy. While most anything can be kept secret, there are limitations on what can be protected by a patent. If a given invention is eligible for either patent or trade secret protection, then the decision on how to protect that invention depends on business considerations and weighing of the relative benefits of each type of intellectual property.

[138] United States Patent and Trademark Office: An Agency of the Department of Commerce. http://www.uspto.gov/ip/global/patents/ir_pat_tradesecret.jsp.