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THERAPIES OUT OF REACH:
ANTICANCER DRUGS AND GLOBAL TRADE REGIMES

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Structured Abstract

Medical policy analysts and oncologists have cautioned against the high price of anticancer drugs. They argue that the current drug development model that relies on patents and short-term shareholder value is proving unsustainable, since the cost of the new generation of drugs puts many of them out of reach for the average consumer. The high price of cancer drugs is especially troubling in the context of middle and lower-income countries, where the burden of cancer carries disproportionately impact. To analyze the pricing of anticancer drugs, we examined legal controversies, regulatory treaties and documents, as well as the history of pricing data in India. We also conducted interviews with policy consultants, and surveyed financial data filings of major global and Indian pharmaceutical corporations. Our research revealed that global trade agreements have become key barriers to lowering anticancer drug prices. This article argues that in the shadow of the WTO and with TPP imminent, serious policy changes are necessary to ensure the survival of generic production in the market for anticancer drugs.

Introduction

Worldwide cancer diagnoses and deaths are increasing. 8 million people died from cancer in 2010, a 38% increase compared with 1990. Cancer diagnoses are estimated to double by 2030 (Lancet, 2013). Correspondingly, the oncology drug market is predicted to increase by a worth of US\$ 1.3 trillion by 2018, a 30% increase from 2013 (Burki, 2015). However, medical policy analysts and oncologists have cautioned against the high price of cancer drugs. They argue that the current drug development model that relies on patents and short-term shareholder value is proving unsustainable, since the cost of the new generation of drugs puts many of them out of reach for the average consumer (Cavalli, 2013). Researchers have also demonstrated that cancer drug pricing is based on what the market will bear, and not on more market-rational principles of novelty and efficacy (Mailankody & Prasad, 2015). The high price of cancer drugs is especially troubling in the context of middle and lower-income countries, where the burden of cancer carries disproportionately impact. Countries ranked low in the Human Development Index are projected to see a 93% increase in cancer incidence, compared to the global net increase of 60% (Bray, Jemal, Grey, Ferlay, & Forman, 2012). In the past, low-cost generic medicines have been vital to successful public health systems in the battle against common diseases. Yet, how will middle and lower-income countries find health systems based on drugs that have been difficult for high-income countries to fund?

There is a precedent for solving the pricing controversy over anticancer drugs—it involves declaring cancer a public health crisis. During the AIDS epidemic through the 1980s and 1990s, when the revolutionary antiretroviral therapy azidothymidine (AZT) was priced at \$10,000 a year in the United States, activist coalitions led a global struggle that forced dramatic price cuts. In 1997, South Africa began the process of importing generic AZT from India for

US\$295 per person per year. Euro-American pharmaceutical corporations – first supported then disavowed by the US government – strongly contested the legality of these exports and imports. They argued that such bilateral practices between India and South Africa would contravene the trade commitment of the two countries as signatories to the WTO agreement. This battle would lead to a historic trade negotiation at Doha that legalized the flow of essential drugs necessary to battle public health crises, within the global south (cf. George, 2011; Klug, 2012).

At the present however, the gains for global south access to drugs rights made during the HIV-AIDS crisis have now been comprised; the unaffordability of anticancer drugs indexes this trend. Responding to the significant rise in cancer incidence in recent years, the WHO added 16 new anticancer drugs to its Essential Medicines List in 2015. Over the last decade, pharmaceutical corporations set the price of anticancer drugs far higher than what they had for HIV-AIDS therapies. While the list is not an enforceable document, it aims to urge national governments to control the prices of essential medicines of their own accord.

Yet, essential cancer drugs such as Herceptin (one of the drugs on the WTO list) cost more than \$70,000 per person per year in the United States in 2016, many times higher than the controversial price for AZT of \$10,000. This is partly because since India's accession to the WTO, Indian companies have been prohibited from producing generic versions of on-patent drugs, even for sale within its national borders where such drugs are not readily available. The controversial Trans-Pacific Partnership Agreement (TPPA) introduces new strategies to further deter generic manufacturers in the global south. In January 2017, responding to public opinion against the treaty, the United States pulled out of the TPPA. While the decision was taken by the new Republican president Donald Trump, his opponents Hilary Clinton and Bernie Sanders had likewise announced their intention to withdraw from the deal during their campaigns for the

presidency. While concern about American jobs were certainly central to the public disapproval of the TPPA, the debate about affordable drugs also helped swing public opinion against the treaty, at least helping to delaying the passage of the bill until it was too late (Trimarco, 2016). Regardless, at the time of writing, the remaining signatory countries hope to not only salvage the deal, but to expand it to include new countries such as China and Indonesia (Karp, 2017). To better understand the relationship between trade treaties and the global poor's access to drugs, we examine here the main strategies deployed by Euro-American pharmaceutical corporations that leverage such global agreements to block generic drug manufacturing. Substantively, **we offer an account of how such treaties effect the global market for anti-cancer drugs, a class of medication that has already come under intense scrutiny for their exorbitant pricing.** In doing this, we build on scholarship that has critically examined the effects of the WTO agreement on pharmaceutical pricing, production and patenting in India (e.g., Chaudhuri, 2012; Chorev & Shadlen, 2015; Horner, 2013; Joseph, 2016; Sampat & Shadlen, 2015). Finally, we offer policy suggestions that could help curb the price increases in the anticancer drug market that make these drugs unaffordable to most cancer patients in the world. Our conclusion echoes Paul Farmer and the global oncology community's call to reject a distinction between 'drugs for the rich' and 'drugs for the poor' (Farmer et al., 2010; Moten, Schafer, Farmer, Kim, & Ferrari, 2014).

Undermining Indian Generics

Through the colonial and early postcolonial period, the Indian pharmaceutical market largely comprised of multinational drug companies whose products were prohibitively expensive for domestic consumers. After Indian independence in 1947, Indian policy makers began a discussion on the high cost of pharmaceuticals in India, and

the dominance of Euro-American pharmaceutical corporations in the region. These policy discussions culminated in the 1970 Indian Patents and Designs Act that allowed domestic drug manufactures to produce identical copies of drugs under patent elsewhere in the world, as long as they changed the process of manufacture. Accompanied by several other government interventions in pharmaceutical production – including the Drug Price Control Order that fixed a low ceiling on essential medicine, this

legislative change had a dramatic impact on Indian pharmaceutical production (Jha, 2007; Rangnekar, 2006; Selvaraj, 2007). By the 1990's, in large part due to the legislative shift in patents, Indian drug companies accounted for over 70% of domestic production. These companies also became a cheap source of generic medications for many other low-income countries across the world (Lanjouw, 1998). For example, in 2005, the global NGO Doctors Without Borders estimated that 80% of its 170,000 HIV patients received Indian generic therapies (MSF, 2005).

However, soon after India joined the World Trade Organization (WTO) in 1995, Euro-American pharmaceutical corporations began to challenge the legality of generic drugs produced in India. The first of these post-WTO efforts by Novartis – the Swiss pharma giant - drew international attention in 1997. At the time, ten Indian drug manufacturers sold generic copies of Novartis' revolutionary pill for chronic myeloid leukemia - Gleevec. Since its patent in 1993, Gleevec has become Novartis' most profitable drug. By 2004, Indian manufacturers were selling the drug at a fraction of the price within Indian borders: for about US \$4230 per patient per year, compared to Novartis' price of about US \$55,000. No concerns about patent infringement had been raised thus far, since Gleevec was discovered in 1993, and WTO laws were applicable only to drugs patented after 1995. However, Novartis initiated

legislation in the Indian courts in 2007 to test the impact of the new trade regulatory system upon generic production. The strategy that Novartis adopted goes by the name of ‘evergreening’ in intellectual property policy circles (Hemphill & Sampat, 2012). Specifically, Novartis argued that these Indian manufacturers were infringing a new 2001 Swiss patent on the drug, one that had significantly modified the original molecule. Novartis had thus previously ‘ever-greened’ its patent in 40 other countries.

In an unprecedented decision, the Indian Patent Office decision bucked this global trend of perpetual patent extensions. The Assistant Controller of Patents argued that there were no novel or inventive steps involved in the second patent filed after 1995. In other words, the Indian Patent Office called out Novartis’ petition as an attempt to ‘evergreen’ an old drug, not protected by WTO, as a new one that would be protected by the new trade regime. The corporation unsuccessfully challenged the decision in the Madras High Court in 2007 and the Indian Supreme Court in 2013. After the Supreme Court judgment, PhRMA (the primary US pharmaceutical lobby group) threatened to withdraw all investments in India (PhRMA, 2013). This strategy has made Gleevec widely available to cancer patients with CML in India; as prices for Gleevec continue to rise in the United States, generic Gleevec in India has fallen to even smaller fractions of Euro-American prices. Meanwhile, a group of over 100 CML experts have authored a letter expressing their frustration at the unaffordability of the drug elsewhere in the world (Abboud et al., 2013).

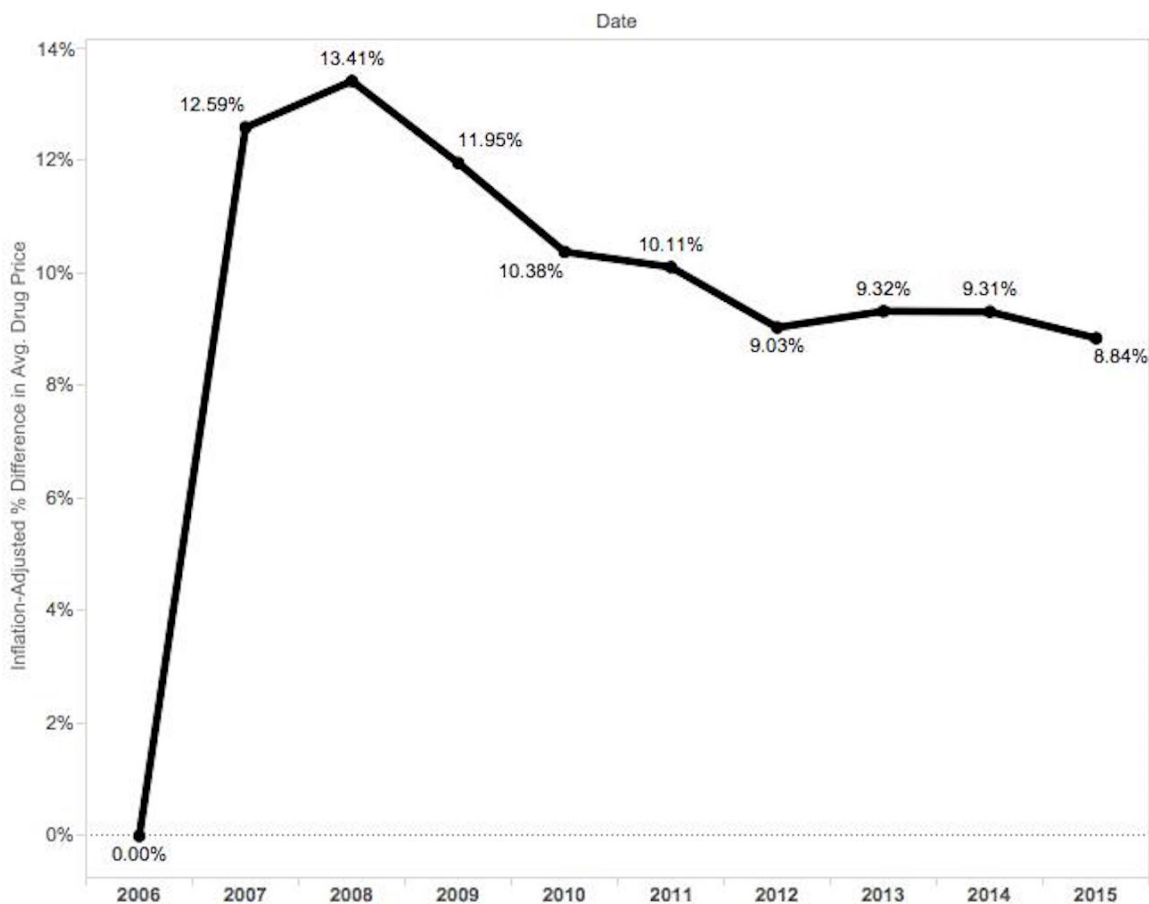
The Novartis case in India raises a broader question. What explains the corporation’s reluctance to lower the price of anticancer drugs and compete with generic manufacturers of their own accord, especially in middle-income countries when such a lowering of costs for on-patent anticancer drugs is a potential win-win for *both* corporations and patients (Reddy, 2013). In

middle-income countries with large populations and lower purchasing power, price reductions increase the potential market size, thereby increasing total revenues for corporations, while at the same time getting the drug to patients that can benefit from the breakthrough in treatment.

The real reason for the corporate reluctance to lower drug prices in middle-income countries cannot be found in a concern for profit margins within middle-income countries. The answer lies in a broader pharmaceutical global strategy. In high-income countries, branded anticancer drugs seem to have escaped the limitations of both state regulation as well as market-based forms of cost control (cf. Bach, 2009; Howard, Bach, Berndt, & Conti, 2015; Kantarjian, Steensma, Sanjuan, Elshaug, & Light, 2014; Leukemia, 2013; Malin, 2010). Controlling for all inflation and survival benefits, Bach and Howard suggest that the determinant factor for the rise in prices is simply unencumbered corporate will, and the failure of market and state controls.

(Howard et al., 2015) Figures 1 illustrate the dramatic increase in the price of a class of anticancer drugs – tyrosine-kinase inhibitors (TKI) over the last fifteen years. It is clear from Figure 1 that the prices of certain classes of anticancer drugs are not only high at launch but continue to rise significantly thereafter. The failure of the US market in controlling the prices of these drugs is having far-reaching implications beyond the cost to Americans—it puts the drugs out of reach of health systems in most countries.

Annualized Growth Rate of Tyrosine-Kinase Inhibitor Prices



The trend of % Difference in Avg. Drug Price for Date Year. The view is filtered on Date Year, which has multiple members selected.

Figure 1¹

As we have argued elsewhere, the real reason behind litigations such as the one by Novartis in Indian courts is to protect this poorly regulated US pricing (Banerjee, 2016). In a conversation on building public trust in Big Pharma, Bayer Pharma CEO Marijn Dekkers responded to a question about the unaffordability of Bayer's anticancer drug Nexavar in India with unexpected candidness: "We did not develop this product for the Indian market, let's be honest. I mean, you know, we developed this product for western patients who can afford this product" (Cassedy, 2014). Wary of generic exports, pharmaceutical corporations have repeatedly

¹ Data collated from RED BOOK™

expressed their concern about licit generics leaking into their primary Euro-American markets. In 2013, these fears led to 29 of the world's largest pharmaceutical corporations striking a three-year deal with INTERPOL to fund a US \$5.8-million-dollar program to stop pharmaceutical crimes. While the illegal sale of counterfeit drugs is certainly cause for legitimate concern, some commentators have expressed concern about how the term 'counterfeit' is applied indiscriminately to generics of on-patent drugs, as well as to fake drugs sold on the illicit market without any therapeutic benefit (Gopakumar & Shashikant, 2010). These commentators are troubled by how the issue of drug smuggling has been defined primarily by pharmaceutical interests. We suggest here that corporate fears and concerns about drug smuggling in relation to anticancer drugs is a symptom of a deeper malaise: the unaffordability of such drugs in high-income countries that receive such drugs. Evidence of high-volume anticancer drug smuggling is scant. However, even if anticancer drug smuggling were found to be pervasive, the phenomenon would serve as proof that drugs are being priced inappropriately, that comprehensive cancer insurance coverage is failing, and that universal access to cancer treatment is failing not only in lower and middle income countries, but also in high-income regions.

International Trade Pressure and the TPPA (please write the full name)

Since signing the WTO, the United States government has renewed its commitment to enforcing a uniform, global intellectual property regime. In recent years, motivated in part by the Novartis case, the Office of the United States Trade Representative— a crucial advisory body to the President now at the center of TPPA debates – has kept India on a priority watch list for countries with inadequate intellectual property protection. India has appeared on this priority watch list for over two decades; the justifications in the more recent reports focus on pharmaceutical intellectual property as further evidence of lax regulation and enforcement in the

region. Further, such responses in US policy circles are riddled with inaccuracies. The 2013 Special Report of the US Trade Representative Office (USTRO) is a prominent example (Office of the United States Trade Representative, 2013). This USTRO report took the Novartis judgment as exemplary of a failing intellectual property regime in India:

The United States is concerned that the recent decision by India's Supreme Court with respect to India's prohibition on patents for certain chemical forms absent a showing of "enhanced efficacy" may have the effect of limiting the patentability of potentially beneficial innovations. Such innovations would include drugs with fewer side effects, decreased toxicity, or improved delivery systems. (38)

This statement was a misreading of the Indian Supreme Court's judgment on the Novartis case. The Indian Supreme Court had delinked increased efficacy from increased bioavailability; it had explicitly left its relation to safety or toxicity open. Thus, the Court's judgment had left open possible future claims that increased efficacy may be measured through increased safety and decreased toxicity. The only precedent that the court had set with regard to the adjudication of efficacy in the Novartis judgment was to disallow increased bioavailability as a criterion for evergreening old drugs into new ones.

Since 2013, India has re-appeared on the Priority Watch List of the Special 301 Report in 2014 and 2015. In another historical echo, Indian trade policies were put under a special review in 2014, a tactic that the US government deployed against South Africa in 1999 and against Brazil in 2007.

The Trans-Pacific Partnership Agreement (TPPA)

After many years of controversial secret negotiations, the text of the Trans-Pacific Partnership Agreement (TPPA) was released on 5th November, 2015. Ever since the first WikiLeaks release of the treaty, the TPP has attracted strong media criticism and public activism on patent protections for new drugs. In January 2017, the new US president Donald Trump withdrew from the agreement, responding to public opinion against its provisions. At this time of writing, the remaining signatory countries are in the process of re-evaluating the deal, promising to implement it even without the United States as a partner. While the fate of the TPPA is unclear, the space vacated by the US exit will almost certainly be filled by new agreements. Among one such agreement is the still nascent Regional Comprehensive Economic Partnership (RCEP) that could include China, Japan, Australia and South Korea, among other countries. Examining the WTO and TPPA together helps consider the impact of such treaties on drug patent protection, and to better understand the validity of political and activist fears that they might prove detrimental to global public health.

At present, in accordance with Trade Organization's Trade-Related Aspects of Intellectual Property Rights (WTO-TRIPS), most global drug patents last for 20 years after the date of filing. This period is designed to allow pharmaceutical corporations to recuperate the cost of innovative research and development through exclusive control over a drug, allowing them to unilaterally setting prices that suit their profit margin. Exclusivity rights refer to provisions within the TPPA designed prolong patent protections beyond the current 20 year period and extend monopoly protection to many new corporate pharma products, including some remarkable new cancer therapies.

Extending Drug Monopolies

While the 20 year period has already been criticized for its length, The TPPA allows pharmaceutical corporations to extend this period even further through a proviso known as ‘exclusivity rights’. In brief, exclusivity rights delay generic manufacturing by denying safety and efficacy data to prospective generic manufacturers, and thereby preventing them from readying a drug for market release, even if such a drug had run its course of patent protection. In other words, data exclusivity protections require the expensive and time-consuming duplication of clinical trials whose outcomes are already known. Such repeated trials also raise concerns about the ethical care for clinical-trial subjects. Figure 2 shows how such exclusivity provisions extend monopolies over drugs even *after* their patent expiration. TPPA extends exclusivity rights for all drugs under the following conditions.

1. At the end of the 20-year period, if the pharmaceutical corporation submits that its product now covers a new indication, new formulation or new method of administration, it may extend exclusive control over such a drug of **at least three years**.
2. If it adds a new chemical entity to its product, the pharma corporation may extend its exclusive control over the drug for a period of **at least five years**. Further, the corporation is not required to publically disclose whether this new compound makes any difference to the safety and efficacy of the original drug.
3. If the drug in question is a biologic (i.e. contains a protein produced using a biotechnological process), such protections extend to a period of **at least eight years**.

These TPPA provisions are a direct result of controversies surrounding a pharmaceutical practice of ever-greening. The most prominent amongst these controversies was the Gleevec case in

India from 2007-2014, where Novartis sought to extend its patent over its bestselling cancer drug in India in order to block generic competition (Chaudhuri, 2013; Rajan, 2015). The Indian Supreme Court turned down Novartis' extension request, partly on the grounds that just enhancing the bioavailability of the compound did not really change the efficacy of the drug, as the corporation had claimed. This decision met severe criticism from the US Pharma lobby and the US Trade Representative's Office, that has been the guiding force behind the TPPA. Now however, under the TPPA exclusivity regulations, Novartis would have had no trouble in continually extending its monopoly over Gleevec, and delaying generic competition well beyond the 20-year mark. It could make use of a range of tactics – declaring a new indication, changing the dosage or the method of administration, or by claiming new safety and efficacy findings. As another example, in the United States, Roche-Genentech has continually extended its exclusivity over Herceptin (trastuzumab) – the most successful breast cancer drug currently on the market. It is also one of the biologic therapies now part of the WHO List of Essential Medicines. In bringing Herceptin into the global public health list of drugs, the WHO considered the high incidence of patients that the drug could treat; currently, 276,000 women are newly diagnosed with HER-2 positive breast cancer annually. Alongside chemotherapy, Herceptin is known to increase the chances of 10-year disease-free survival by 40% (Perez et al. 2014). In the United States, Roche-Genentech has continually extended its hold over Herceptin by patenting new methods of use and combinations with chemotherapy agents (Adler, Grauschopf, Mahler, & Stauch, 2016; Berry, Phillips, & Sliwkowski, 2014). Exclusivity provisions then might be understood as an additional global delay mechanism to already existing patent-protections. In effect, they are another strategy through which cost-lowering generic competition might be further postponed.

Further, Figure 3 shows that the exclusivity periods in a particular market begin from the time that a company introduces the drug in that country. Pharmaceutical corporations have been slow to introduce drugs to global markets, recognizing that many such populations are unable to afford them. However, in order to prevent generic competition from such markets, US and European pharmaceutical corporations routinely gain local approval for drugs and establish patent rights. Pre-TPPA, these corporations have faced resistance from local courts (India and the UK examples above) in extending patents. Now with the lowered bar of extension under exclusivity rights, there are very few regulatory pathways through which middle-income countries could deny indefinite extensions of exclusivity rights. This would bar generic manufacturers in such countries from using safety and efficacy data from the original drug trials, thereby effectively barring them from establishing the equivalence of their generic drug. Of course, they could start the trial process from scratch, but that would take a decade on its own, and would be prohibitively expensive for most generic manufacturers. **In effect, this means that an entire generation of global cancer patients might be deprived of the benefits of cancer research over the last two decades.** The highest impact of these regulations might be *off-patent* drugs. Exclusivity provisions are actionable regardless of the patent status of the drug. There is nothing in this treaty that prevents pharmaceutical corporations from taking a cheaply available life-saving drug and declaring a new indication (for example, for use in children rather than adults), and then guarding it with extended exclusivity rights to charge monopoly prices.

Biologics

The TPPA has attracted severe criticism for its special protection of a category of drugs called Biologics. Biologics, by the TPPA's definition, are any drugs that include a protein

produced using biotechnology processes. Currently, bestselling biologics include infliximab, etanercept and adalimumab primarily for arthritis, pegfilgrastim, rituximab, bevacizumab and trastuzumab used for cancer treatments, and insulin glargine used for diabetes. In 2014, these drugs alone accounted for over 65\$ billion in sales (Philipidis, n.d.).

Typically, biologics are far more expensive than traditional drugs, since they are complex large molecules that require biotechnological sophistication to produce. For this reason, pharmaceutical corporations have been slow to introduce these drugs to markets outside United States and Europe, anticipating that too few in lower-income and middle-income countries will be able to afford the drug to constitute a profitable market. However, middle-income countries and emerging economies are now beginning to appear as potential markets. The TPPA provisions allow pharmaceutical corporations to wait until the time they find such markets to be ripe before introducing the drug, even in such drugs are nearing the end of patent protections. Once they decide that such markets are ready for entry, they will be able to have exclusive monopoly for even **off-patent** biologics in such markets for an *additional 8 years*.

While India is not part of the proposed TPPA, the US withdrawal from the TPPA opens up the possibility of other regional alignments. Amongst these, the Regional Comprehensive Economic Partnership (RCEP) stands to gain strength in the void left by the TPPA, as does WTO-TRIPS which the TPPA would have eclipsed. As new regional treaties and alignments come into focus, intellectual property watchers and health activists would do well to learn lessons from the imminent failure of the TPPA, and guard against deals that hurt public health. Further, data exclusivity rights are under legislative and legal scrutiny in India, with little clarity regarding where policies regulating them (Chakrabarti, 2014; Reddy, 2016). India have vacillated over whether maintained that the WTO-TRIPS regulations require exclusivity

provisions (Barooah, 2011, 2015). Early analyses of the negotiations around the Regional Comprehensive Economic Partnership indicate that it carries exclusivity provisions very similar to those in the TPPA (Subramanian, 2016). Our argument has been that exclusivity rights delay the generic pipeline of drugs, especially as they are manipulated to allow for new practices of ever-greening. This is a matter of public health concern, especially to drugs that could serve large potential patient pools with convincing therapeutic benefits. At the least, as discussions coalesce around new treaties, stakeholders should consider including provisions that would protect a class of essential public health drugs from extended exclusive monopolies. In a global context where a large population of patients are either under-insured or cannot afford medicines as they are priced on the market, the further easing of competitive price-controls on drugs can only be understood as a threat to universal public health. As political and activist challenges gather momentum in the wake of the release of the TPPA text, they would do well to keep in mind both the limits and possibilities of public health safeguards such as compulsory licenses that are already part of the current text.

Compulsory Licensing: A Possible Solution

A possible solution that has emerged in recent years in response to the shortage of third-line HIV-AIDS drugs is the United Nations backed Medicine Patent Pools. Simply put, pharmaceutical corporations owning the IP of life-saving drugs may choose to place their patent in a collective pool, while a set of generic manufacturers compete to license such a patent, paying a royalty to the original corporation for the rights of use (Satyanarayana & Srivastava, 2010; Ulrich, 2015). While this solution holds some promise, its voluntary nature and antitrust concerns are reasons for caution (Gaule, 2006). For example, Johnson & Johnson – which is a key patent-holder over third-line ARVs – has refused to join any patent sharing arrangements,

jeopardizing the notion of a viable patent pool for HIV-AIDS treatments. Further, licenses are negotiated without transparency, and originator corporations unilaterally decide which generic manufacturers are allowed to compete for their patent and where they are allowed to sell the drug. In effect, originator corporations succeed in dictating the extent and nature of competition, and by extension, maintain control over global drug pricing. In other words, patent pools rely upon a core belief in the potential of corporate social responsibility. Indeed, Novartis and other corporations have repeatedly argued in Indian courts that they run philanthropic patient access programs that give away drugs for free to whoever needs them. This raises the question: how viable are corporate philanthropic models such as patent pools and patient access programs towards ensuring access to care, and can they substitute state-based public health programs? If we are to look at past studies of the alcohol and tobacco industries, it becomes clear that such programs often work against the goals of public health. Rather, CSR appears as a strategy to erode evidence-based regulation of industries, while aiding indirect brand marketing to gain access to emerging markets (see for example Fooks, Gilmore, Collin, Holden, & Lee, 2013; Yoon & Lam, 2013). Thus, it remains to be seen whether voluntary patent pools will indeed broaden drug access.

Here, following from the first author's work published elsewhere (Banerjee, 2016), as well as that of several scholars of pharmaceutical intellectual property (e.g., Chaudhuri, 2015), we suggest that provisions of *compulsory licensing* promise a more enforceable public-private solution. Any agreement on free trade should have an escape clause that allows the country to manufacture a drug that is deemed essential to the public health if that drug is priced on the international market in such a way so as to make it unavailable to the public. Such an escape clause already exists within the rubric of the WTO, as the following case illustrates.

In March 2012, the Indian Patent Controller, P H Kurien, issued the first *compulsory drug license* in Indian history. In his order, Kurien described compulsory licenses as an “involuntary contract between a willing buyer and an unwilling seller, imposed and enforced by the state” (Kurien, 2012). In effect, his order unilaterally allowed a domestic drug maker Natco Pharmaceuticals, to copy and sell sorafenib within the Indian market. Sorafenib is a generic version of Bayer’s highly profitable liver and kidney cancer drug Nexavar. This was not the first time that the Euro-American pharmaceutical industry had confronted this tool of sovereign state assertion. At the height of the HIV-AIDS controversy, South Africa, India and Brazil invoked compulsory licensing provisions combat pressure from Euro-American governments to block the sale of generic HIV-AIDS therapies between countries in the global south.

To receive a compulsory license for Nexavar under the Indian Patents Act, Natco Pharma had to prove that Nexavar was not available in India in the quantity that it was required; or that it was not affordable to the average consumer. Natco’s petition claimed that 16,000 patients in India required Nexavar on an annual basis and that the monthly cost of Nexavar was 36 times the average monthly salary of an Indian government employee. In response, Bayer declared that they were willing to set a special philanthropic price for those in India that could not afford the drug. This price would come close to matching the generic cost, but only after patients had demonstrated financial need to the extent of the corporation’s liking. No clear criteria were set as regards this demonstration of financial need. Bayer’s proposal to substitute public health with corporate philanthropy did not win any traction in the Indian courts. In the end, the effect of the compulsory license on Nexavar prices in India was dramatic. While Nexavar treatment in the United States costs about \$180,000 per patient per year, compared to \$1,332 in India.

To enforce further compulsory licenses will not be an easy task. Indeed, in the 2016 USTRO Special Report, the US government made clear that it “continues to monitor India’s application of its compulsory licensing law. The United States requests clarity from the Government of India regarding the compulsory license decision-making process, as it affects U.S. stakeholders” (Office of the United States Trade Representative, 2016). Recently, reports and concerns have been expressed that the Indian government has privately assured the United States – India Business Council that such licenses will be sparingly used, if at all (Chandra, 2016). Yet, we believe that if judiciously used, compulsory licensing provisions should not only be allowed, but encouraged, in the case of particular anticancer drugs with demonstrated public health relevance and magnitude of benefit. While they are stigmatized in current trade policy documents such as the USTRO report, discussions around the WTO and now the TPP agreement, compulsory licenses have the potential of dramatically aiding anticancer public health programs in middle-income countries where facilities exist for their disbursement.

Conclusion

In the recent literature on anticancer drugs, several physicians and policy analysts have shown how regulatory mechanisms over anticancer drug pricing have been systematically weakened in the United States (cf. Howard et al., 2015; Kantarjian et al., 2014). While pharmaceutical corporations continue to cite high R&D costs as the rationale for high prices, recent studies have debunked their estimates, as well as demonstrated the dependence of such research on National Cancer Institute funds (Light & Kantarjian, 2013; Light & Warburton, 2011). In the past, especially in relation to the HIV-AIDS crisis, generic alternatives to expensive branded drug were made available to global public health through generic manufacturing. However, in a post WTO-TRIPS world, we have seen how this makeshift

arrangement has been jeopardized. The work of global public health then is increasingly dependent on the corporate social responsibility of Euro-American corporations and their philanthropic initiatives.

In conclusion, drawing upon the research in this paper, we present three policy suggestions that could remedy this situation to a great degree.

- 1 Courts should recognize ever-greening as a threat to public health, when it means a generic cannot be produced without violating free trade. They should require that the new patent for an old drug must imply greater efficacy (widely defined), larger indications and significantly novel and inventive steps in their development, for it to be honored.
- 2 Countries should be wary of signing free trade agreements that threaten their domestic drug supply and allow multinationals to gain economic control over an important national industry. More specifically, legislators should more carefully scrutinize provisions in such agreements that contradict or modify existing domestic laws regarding patent exclusivity, expiry and protection. As a principle, if such modifications imply a narrowing of drug access and an increase in public health cost, legislators should favor existing regulations while negotiating the precise terms of such free trade agreements.
- 3 Any agreement on free trade should have an escape clause that allows the country to manufacture a drug that is deemed essential to the public health if that drug is priced on the international market in such a way so as to make it unavailable to the public. The Nexavar compulsory license issued in India is one such example of a successful escape clause. This is not to say that the originator companies lose all rights over the drug.

Compulsory licenses come with attached royalty provisions that in fact boost the revenue streams of Euro-American corporations in middle and low-income countries.

We believe that these steps are urgent and necessary preconditions for the continued availability of low-cost generic medications, especially in the anticancer drugs market.

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