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International Economic Law Practicum

INTELLECTUAL PROPERTY AND ACCESS TO MEDICINES: IMPLICATIONS OF NAFTA RENEGOTIATIONS

May 13, 2018, Washington D.C.

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International Economic Law Practicum

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Executive Summary

Mexico is considered a developing country, but its medicine prices tell a different story. Medicine prices in Mexico are some of the highest in the world. For example, the price for a pack of 30 Cataflam painkillers in Mexico in 2014 was $30.77, while in Ireland it was $2.12. At the same time, many households in Mexico do not have health insurance and must pay for medicine out of pocket. High prices accompanied by inadequate health insurance coverage and high rates of obesity with attendant health complications have resulted in a public health crisis.

Mexico pays twenty times more than other Latin American countries for medicines, yet was one of the first countries in the world to sign a free trade agreement with an intellectual property chapter and continues to sign on to trade agreements with strong intellectual property (IP) chapters. Its peers like Chile and Brazil have resisted strong intellectual property chapters and fought for flexibilities in their IP regimes. They also happen to have the cheapest prices medicines in South America. In spite of this evidence that stricter IP regimes may be hurting access to medicines for most Mexican citizens, Mexico has agreed to NAFTA renegotiations, including a renegotiation of the IP chapter. Mexico wants to remain part of NAFTA to eliminate tariffs, increasing trade with the United States and Canada. However, it should be wary of a renegotiated IP chapter, which will likely enhance IP protection at the expense of public health, decreasing access to medicines.

The North American Free Trade Agreement (NAFTA) between the United States, Canada, and Mexico, which came into force in 1994, was the first free trade agreement (FTA) to address IP rights. One year after NAFTA, the 1995 Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) of the World Trade Organization (WTO) became the most comprehensive multilateral agreement on IP. Since NAFTA was concluded, a number of FTAs have been negotiated that include IP protections. The U.S. position on IP has become more comprehensive over time, causing many U.S. stakeholders to view NAFTA as outdated and overdue for renegotiation. Official NAFTA renegotiations, or "NAFTA 2.0", began on August 16, 2017. The negotiations are comprehensive and cover all NAFTA chapters, but the U.S. Trade Representative (USTR) has highlighted increased IP protection as a particular negotiating objective.

As the U.S. position on IP has strengthened, a number of other stakeholders have challenged the inclusion of stronger IP protections in trade agreements. Strong objections to

stricter IP provisions arose in the context of the Trans-Pacific Partnership (TPP) trade agreement, for example, due to the increasing difficulty many countries are facing ensuring access to medicines. The Comprehensive and Progressive Trans-Pacific Partnership (CPTPP) was amended to reflect these concerns, and the IP language was scaled back to include more flexible IP provisions.

Although the TPP has transitioned to the CPTPP with new, more flexible IP provisions, the IP discussions under the original TPP negotiations highlight how NAFTA renegotiation might progress. It is likely that the U.S. will press for IP text in the NAFTA similar to the text it had negotiated in the TPP before withdrawing from the agreement, because the TPP text aligns with the USTR's goals of expanded IP coverage and stronger protection for patent holders. The positions of Canada and Mexico following U.S. withdrawal from the TPP are also telling. Because the United States was the strongest advocate for an enhanced IP chapter in the TPP, most IP provisions were suspended after its withdrawal. Canada, for example, wanted most of the IP chapter suspended after the United States left negotiations and may reject TPP-like provisions in NAFTA, even though it was already substantially in compliance with most of the proposed TPP IP chapter. Mexico may go along with Canada in the NAFTA renegotiations as it did in TPP negotiations.[1]

Since the U.S. will press for increased IP protection in the renegotiated NAFTA, it is helpful to examine the costs and benefits of potential changes to NAFTA. This paper draws upon past models, including the TPP, as an example of heightened IP standards. It then evaluates the effect these provisions will have on access to medicines in Canada, Mexico, and the U.S. Overall, this analysis shows that an enhanced NAFTA IP chapter would threaten public health and access to medicines, create significant costs for national governments, and limit the actions that governments may take to protect public health.

While an enhanced IP chapter in NAFTA 2.0 is likely, it is not necessary or desirable. An IP chapter valuing increased access to medicines over increased protection for drug companies would make medicine more affordable, foster innovation, and give countries greater regulatory leeway. In order to improve access to medicines, several considerations should factor into the NAFTA renegotiation:

[1] Andy Blatchford, Canada leans on Mexico to ease TPP pressure from Japan, Australia Global News (2017), *available at* https://globalnews.ca/news/3857943/canada-mexico-tpp-japan-australia/.

1. **Longer periods of data exclusivity delay market entry of generics, keeping prices high for consumers and slowing innovation.**

Data exclusivity protects the confidentiality of clinical data submitted to regulatory authorities to obtain market approval of a pharmaceutical product. This provision effectively delays entry of generic medicines onto the market, forcing consumers to pay brand-name drug prices for longer. The only alternative for generic producers in the face of long data exclusivity periods is to repeat clinical trials to prove the safety and efficacy of their drugs. Repeating clinical trials wastes time and money. It also raises ethical concerns by putting at risk the health of patients in clinical trials. In the case of biologic medicines, each unit of which often costs thousands of dollars, delayed market entry means a delay in public accessibility to life saving drugs. For biologics that treat cancer or other deadly illnesses, even minimal delays in affordable alternatives may mean the difference between life and death.

To increase access to medicines, NAFTA 2.0 should not include any provisions expanding data exclusivity. If NAFTA 2.0 includes a data exclusivity provision, it should be limited to drugs and not include biologics. Because TRIPS does not include a data exclusivity provision, biologic producers would be able to use the originator's studies immediately. This would decrease the amount of time spent getting approval, allowing faster market entry for generics and biosimilars, which reduces prices for consumers.

2. **Lower thresholds for patentability criteria delay generic market entry by making it easier to get secondary patent protection and would limit the diversity of medicines available.**

In order to receive a patent, inventions must be new, useful, and non-obvious, vague categories that countries define as they see fit. It is likely that the U.S. government will propose a lower threshold for patentability in NAFTA 2.0. A low threshold for what is "non-obvious" or "useful" could allow new mixtures of the same drug to be patented, extending patent protection well beyond the original twenty years. A low threshold for "new" could also allow for the patenting of traditional medicines, even though such medicines have been known within certain communities for centuries. By allowing the patenting of traditional medicine and the extension of patent protection for essentially the same drugs, a low threshold of patentability criteria would

limit the diversity of medicines available and create significant challenges for accessing medicines in the market.

3. **Defining IP rights as "investments" allows pharmaceutical companies to challenge democratic legislation enacted for public health and welfare.**

The original NAFTA text defines intellectual property as a right, not an investment. An enhanced IP chapter would broaden the definition of "investments" to include intellectual property. This would allow any company with a patent to bring an action through Investor State Dispute Settlement (ISDS). Unlike domestic courts, ISDS allows companies to sue for violations of their legitimate expectations, leading to expensive litigation in courts that are not bound by national precedent. This means that countries could be liable for a variety of actions traditionally within their power. A rush of expensive litigation could follow and intimidate countries from passing legislation or making actions that investors, including IP companies, don't like, for fear that a suit will be brought against them. To keep IP litigation in domestic courts, NAFTA renegotiations should either limit the definition of legitimate expectations to specific circumstances or remove ISDS entirely.

4. **Adding a "safe harbor" Bolar exemption would allow generic companies to conduct research without fear of patent infringement suits and would hasten the entry of generics into the market.**

Bolar exemptions are exceptions to patent infringement that allow a drug producer to use a patented drug for research and testing in order to obtain regulatory approval of a generic version. This means that generic drug makers will not have to replicate studies already done by patent holders, saving money, resources, and unnecessary human testing. This exemption allows manufacturers to get through the regulatory approval process for generics quickly so that they are ready for market entry upon patent expiration. NAFTA 2.0 should add a Bolar exemption similar to the exemption read into TRIPS as a result of a case brought before the WTO dispute settlement body.[2]

[2] Canada Patent Protection of Pharmaceutical Products: Complaint by the European Communities and their member States. WTO Panel Report, 2000.

Contents

I. Introduction

As a result of bilateral negotiations between the United States, Canada, and Mexico beginning in 1991, NAFTA entered into force on January 1, 1994. NAFTA resulted in the progressive elimination of a large majority of tariffs, duties, and quantitative restrictions among the parties over the next fifteen years. On May 18, 2017, following consultations with relevant Congressional committees, U.S. Trade Representative Robert Lighthizer informed Congress that the President intended to commence NAFTA renegotiations with Canada and Mexico. Through these negotiations, the United States seeks to support higher-paying jobs and grow the economy by improving opportunities to trade with Canada and Mexico.[3]

As part of the original NAFTA, Canada, Mexico, and the United States agreed to meet certain IP standards. NAFTA was the first FTA to create an obligation for countries to protect IP rights and initially served as a template for U.S. IP negotiations with countries around the world. The WTO TRIPS Agreement came into force in 1995, just one year after NAFTA, and sets forth minimum standards of IP protection that WTO members must meet in their domestic laws.

NAFTA includes, among other things, provisions covering the protection of intellectual property rights, investment, and dispute settlement. The chapters dealing with intellectual property, international investment, and dispute settlement are perhaps the three most influential provisions on access to medicines within the three countries. While the protection of IP rights is essential to a wide variety of U.S. industries, the issue is perhaps most critical to the innovative pharmaceutical industry.

[3] USTR Press Release, May 2017, *available at* https://ustr.gov/about-us/policy-offices/press-office/press-releases/2017/may/ustr-trump-administration-announces.

Internationally, concerns about enhanced IP rights and decreasing access to medicine have made strengthening IP provisions at the WTO level increasingly difficult to achieve. As a result, the United States began to focus on enhancing IP provisions in FTAs. In bilateral and regional FTAs, the United States has pushed aggressively for levels of IP protection beyond TRIPS requirements, known as TRIPS-plus rules. Although these agreements are not binding upon other parties, successive FTAs from the U.S. continue to build upon each other, steadily increasing IP protection.[4] This concerns all countries, because TRIPS Article 4 requires any WTO member that agrees to a higher standard of IP protection in a treaty to "immediately and unconditionally" extend that enhanced protection to all other members of the WTO.[5]

The most recent example of the United States' aggressive stance on IP protection can be found in the TPP. Twelve prospective member states took part in the IP chapter negotiations for the TPP, including the United States, Canada, and Mexico. After the United States' withdrawal in January 2017, the TPP transformed into the Comprehensive and Progressive Trans-Pacific Partnership (CPTPP). With the support of Canada and Mexico, A Ministerial Agreement in November 2017 suspended most of the more aggressive IP provisions championed by the U.S.

Recently, reports of Novartis charging higher prices for medicines in specific jurisdictions brought the issue of drug pricing into the national conscious. Internal company data showed that the drug maker charged higher prices for medicines in Mexico and several other Latin American countries, than it charged in many wealthy nations. In 2014, Novartis charged 29 percent to 548 percent more for 30 tablets of the Co-Diovan blood pressure pill in Mexico than

[4] Gaëlle Krikorian & Dorota Szymkowiak, "Intellectual Property Rights in the Making: The Evolution of Intellectual Property Provisions in US Free Trade Agreements and Access to Medicine POST data" (2007), *available* at https://onlinelibrary-wiley-com.proxygt-law.wrlc.org/doi/10.1111/j.1747-1796.2007.00328.
[5] *Id.* pg. 389.

in 20 other countries, including several high-income nations. For instance, the price for a pack of 30 was $63.06 in Mexico, compared to $35.51 in Germany, $30.04 in the UK, and $9.73 in Italy.

Similarly, Novartis charged anywhere from 6 percent to 135 percent for 30 tablets of the Cataflam painkiller. The cost in Mexico was $30.77, while the price was $28.90 in Chile, $11.41 in Sweden, $10.08 in the UK, and $2.12 in Ireland. The same pattern existed for three others — the Diovan blood pressure pill, the Tegretrol anticonvulsant and the Sirdalud muscle relaxant.[6]

Novartis charged these high prices in spite of the fact that Mexico is considered a developing country. According to the World Bank, it was ranked 91st among more than 200 countries when measured by gross national income per capita in 2016.[7] The public share of health care financing in 2014 in the country was about 50 percent, well below the average of 72 percent among 35 countries in the Organization for Economic Co-operation and Development. Additionally, about half of all health spending in Mexico is paid directly by patients. This combination of high drug prices in Mexico with low levels of public health care financing has created a public health crisis, all in the name of profit for Novartis.

This paper examines the effects of the protection afforded by intellectual property rights in international agreements, most notably NAFTA and TPP (including the most recent versions of both). The protection afforded affects access to medicines in general, and has a significant impact on lower-middle income economies like Mexico.

[6] Ed Silverman, "Not just Colombia: Novartis has charged more for some drugs in Mexico, too", March 28, 2017, *available at* https://www.statnews.com/pharmalot/2017/03/28/novartis-mexico-drug-prices/.
[7] World Bank, "Gross national income per capita 2016, Atls method and PPP", *available at* http://databank.worldbank.org/data/download/GNIPC.pdf.

Issue Summary				
Issue	NAFTA	TRIPS	TPP	Recommendation
Data Exclusivity	5 years	5 years	8 years/ or 5 years +3 years equivalent market protection.	Limit data exclusivity to the minimum TRIPS requirement
Biologic Data Exclusivity	5 years	5 years	8 years/ or 5 years +3 years equivalent market protection. (US advocated for 12)	Limit data exclusivity to the minimum TRIPS requirement
IP Rights/ ISDS Jurisdiction	Fair and Equitable Treatment, does not control compulsory licensing, generally limits "legitimate expectations" as a factor in the majority of tribunals.	None	More expansive interpretation	Remove ISDS Explicitly limit "legitimate expectations" as a factor

II. Data Exclusivity

Data exclusivity refers to the protection of clinical trial data submitted to a regulatory agency to prove safety and efficacy for a new drug. This provision requires generic producers to either replicate studies in order to create their own data for regulatory authorities, or wait for the specified time period to elapse before gaining access to the protected information, hindering the registration and marketing approval process for generic medicines. It also creates an additional system of monopoly protection entirely independent from patents, further delaying generic competition.

Another concern with data exclusivity periods is that drug developers will use research and development funds to generate more data for minor modifications drug products to increase the exclusivity period, often called 'me too' drugs because they add little if any therapeutic value

to existing drugs. This opportunity "risk[s] over-investment in well-tilled areas" at the expense of developing new medicines.[8] During that period of exclusivity, generic producers cannot use data from the patent holder to prove the efficacy of its own drug even though it is exactly the same, increasing costs and wasting resources while adding no research benefit.

Table 2: TPP IP provisions, consistency with existing national IP law in TPP parties and transition periods to implement changes:

TPP party	Exclusivity on undisclosed test data (small- molecule drugs) (Article 18.50)	Exclusivity on undisclosed test data (biologics) (Article 18.51)
United States	NLAR	NLAR
Canada	NLAR	NLAR
Mexico	May require legislative action with 5 years transition period (Art. 18.83.4c(iv)	May require legislative action with 5 years transition period (Art 18.83.4c(v))

*NLAR- no legislative action required

Small molecule medicines

The first and weakest, data exclusivity provision comes from the TRIPS Agreement. TRIPS Article 39 requires Member States to protect undisclosed test data or other confidential information "contrary to honest commercial practices" and against "unfair commercial use." The information covered by this protection requires effort to create and is submitted in order to get marketing approval. The wording of this article suggests that countries could theoretically meet this obligation by protecting data from dishonest use rather than keeping data strictly confidential. Furthermore, the text does not stipulate a specific time period for data exclusivity and does not articulate any methods of protection. Subsequent agreements provide for more sophisticated levels of protection, graduating from simple confidentiality to exclusive data rights for specific lengths of time.

[8] United States Trade Representative, 2006 Special 301 Report, *available at* https://ustr.gov/sites/default/files/2006%20Special%20301%20Report.pdf.

Both the draft TPP and NAFTA include heightened data exclusivity provisions. Article 18.50 of the draft TPP provides for data exclusivity for a minimum period of five years. Sub-section 2 further provides that the protection will apply for a minimum of three years for evidence "covering a new indication, new formulation or new method of administration" for an already patented drug. This means that the original drug already received five years of data exclusivity, so the additional stipulation of a minimum three years for "new" versions of this drug effectively creates 8 years of data exclusivity.

Articles 1711.5 and 1711.6 of NAFTA grant exclusivity for data used to determine the safety and effectiveness of a drug, where creating the data involved "considerable effort." The data remains confidential, "during a reasonable period of time after their submission," which the text specifies will be at least five years.

Large molecule medicines: Biologics

Over the past two decades, pharmaceutical innovation has shifted from chemically synthesized small molecule drugs toward more complex, bioengineered treatments grown from living tissue, known as biologics. Biologics are derived from biological sources like microorganisms, and are generally larger and more complex than small molecule drugs. Because of their complexity, biologics often treat severe diseases that do not have effective small molecule treatments. Additionally, biologic drugs are expensive. For example, a biologic drug for arthritis costs $26,537 yearly, and two biologics taken in combination for breast cancer cost $126,000 yearly.[9] Follow-on biologics (FOBs) are the equivalent of generic drugs, competing in

[9] Tao Gu et al., *Comparing Biologic Cost Per Treated Patient Across Indications Among Adult US Managed Care Patients: A Retrospective Cohort Study Advances in pediatrics.* (2016), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5127933/; Living and Dying Might Depend on Cost, Cure

the market after patent protection expires and offering a relatively cheaper alternative to name-brand biologics.

An increased period of data exclusivity for biologics is unnecessary and would be harmful for a number of reasons. Because of the complexity of biologics, they are easily patentable and are often covered by multiple patents relating not only to the biologic but its uses and the processes used to make it.[10] This complexity also makes it difficult for FOBs to prove similarity, which delays market entry and increases the cost to enter the market such that few FOBs will compete.[11] FOBs are likely to only capture between 10-30% of the biologic's market, compared to nearly 100% market capture by generic drugs.[12] Additionally, they will likely sell FOBs at a 10-30% discount, compared to an 80% discount when multiple generics enter the market. Because they are patentable, high-priced, and face little competition, biologics do not need data exclusivity.

Most FTAs do not specifically address biologic drugs due to their relatively recent development. TRIPS does not make any express mention of biologics or data exclusivity pertaining to them. However, a requirement for biologic data exclusivity could be read in under its broad provision allowing for protection of test data submitted for the purpose of obtaining regulatory approval. Biologic drugs were a sticking point in the TPP negotiations, with United States Senate Finance Chairman Orrin Hatch advocating for twelve years of exclusivity. The

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Today (2015), *available at* https://www.curetoday.com/community/susan-f/2015/09/whose-life-is-worth-saving-when-the-patient-has-cancer.

[10] Biologics may also be protected by process patents and technology platform patents, and extra layer of patents that drugs generally do not receive.

[11] Federal Trade Commission Report, *supra note 8,* pg. iii-iv. Unlike generics, which do not have to complete their own studies, FOBs will have to perform their own studies, increasing their cost and slowing their entry into the market. Most biologics are delivered by medical staff in hospitals, which will be more hesitant to switch to FOBs because it will require new inventory and training for healthcare workers. Because of high market entry costs accompanied with uncertainty in market share, biologic manufacturers will likely be able to maintain market share for years after FOB entry. Even then, because of costs of entry, only large, well-financed companies will enter into the market, creating less competition for biologics.

[12] *Id.* pg. v.

Draft TPP Article 18.51 requires biologic data exclusivity for at least eight years, or five years followed by three years of equivalent market protection.

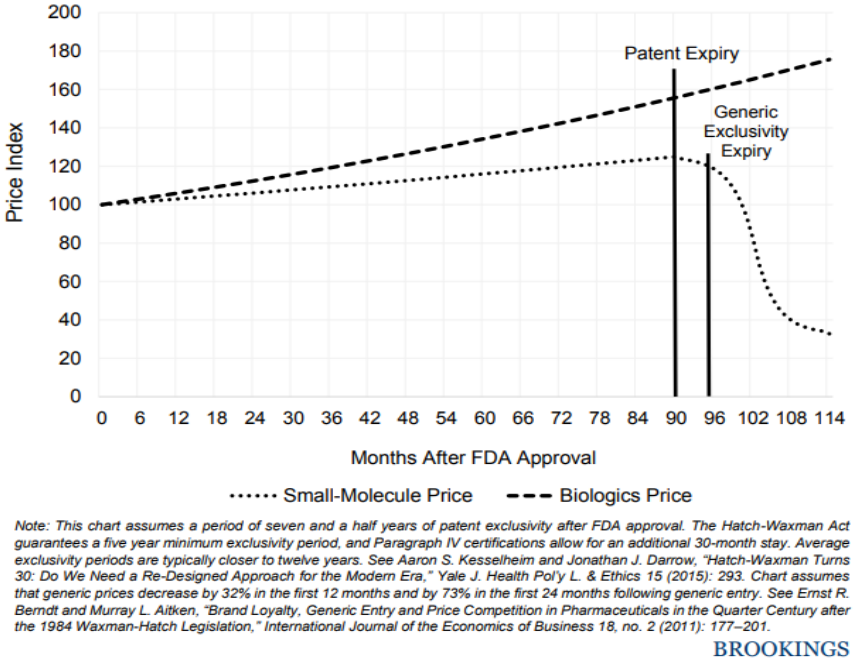
Likewise, NAFTA does not make any express mentions of biologics or a data exclusivity requirement for them, but it accords a minimum five years of protection for undisclosed test data submitted for the purpose of obtaining market approval of "pharmaceutical…products that utilize new chemical entities" which has traditionally been the data exclusivity threshold under this Agreement. However, it could be argued that because biologics are biological entities rather than chemical entities, they are not covered by this provision. Biologic data exclusivity remains a point of contention in the NAFTA 2.0 negotiations, with the U.S. pushing for a term of 12 years.[13] Canada, which operates a single-payer, publicly funded healthcare system, is not likely to cave to U.S. demands because a longer protection period for generics and biologics would raise drug prices, costing the Canadian government more. Mexico went into TPP talks offering zero years of biologics protection and agreed to the deal's five-plus-three model during the talks only after negotiation and compromise. Mexico's preferred baseline exclusivity period for biologics going into the NAFTA renegotiation was again zero years.

Table 3: Data exclusivity provisions for small molecules and for biologics in domestic legislation

State	Data Exclusivity for Small Molecules	Data Exclusivity for Biologics
United States	5 years	12 years
Canada	8 Years	8 years
Mexico	No domestic provision, although 5 years has been unchallenged.	No domestic provision

[13] Michael Grunwald et al., "Under Trump, U.S. Companies Face a Rough Road on Trade About Us" (2017), *available at* https://www.politico.com/magazine/story/2017/11/21/trump-nafta-trans-pacific-partnership-companies-trade-215851.

Figure 1- Patent cliff: biologics versus small molecule drugs. The ability of biologic prices to persist beyond generic entry contrasts greatly with the experience of small molecule branded drugs, which typically experience drastic price declines after generic entry.



Note: This chart assumes a period of seven and a half years of patent exclusivity after FDA approval. The Hatch-Waxman Act guarantees a five year minimum exclusivity period, and Paragraph IV certifications allow for an additional 30-month stay. Average exclusivity periods are typically closer to twelve years. See Aaron S. Kesselheim and Jonathan J. Darrow, "Hatch-Waxman Turns 30: Do We Need a Re-Designed Approach for the Modern Era," Yale J. Health Pol'y L. & Ethics 15 (2015): 293. Chart assumes that generic prices decrease by 32% in the first 12 months and by 73% in the first 24 months following generic entry. See Ernst R. Berndt and Murray L. Aitken, "Brand Loyalty, Generic Entry and Price Competition in Pharmaceuticals in the Quarter Century after the 1984 Waxman-Hatch Legislation," International Journal of the Economics of Business 18, no. 2 (2011): 177–201.

BROOKINGS

a. United States of America

i. Small molecule drugs and generics

In 1984, the Drug Competition and Patent Term Restoration Act (Hatch-Waxman) introduced the "Abbreviated New Drug Application" (ANDA) for generic drugs, allowing regulatory approval to be based on evidence that a generic drug is bioequivalent to the original.[14] To compensate, the Hatch-Waxman introduced a five-year period of data exclusivity.[15] Consequently, a generic producer cannot use the originator's data to obtain marketing approval for five years. In order to marketing approval during that five-year period, a generic competitor needs to submit independently generated clinical data or delay its application. Besides five years of data exclusivity for all new chemical entities, specific categories of drugs and clinical data

[14] 21 U.S.C. Sect. 355(j)(2)(A)(iv) (1984).
[15] *Id.* 355(c)(3)(E)(ii).

were given additional protection. Where a new drug is treats of rare conditions (an orphan drug), a period of seven years of data exclusivity applies. For data that supports changes to products already on the market (such as new indications, new dosages, and new delivery methods), "clinical investigation exclusivity" limits market authorizations for three years.[16] The submission of data to support the pediatric use of an existing drug lengthens the period of data exclusivity by six months.[17]

ii. Biologics and Biosimilars (Follow-on Biologics):

The Biologics Price Competition and Innovation Act (BCPI) of 2009 was enacted on March 23, 2010, as part of the Affordable Care Act. It includes two different pathways for approval: one for new biologics and one for follow-on-biologics (FOBs). The FDA will issue a license for a new biologic if it is "safe, pure, and potent."[18] FOBs have an abbreviated pathway, and are able to receive a license if they prove that the FOB is "highly similar" to a specific biologic and that there are no "meaningful differences" between the biologic and the FOB in "safety, purity, and potency."[19] In order to prove this, FOBs must provide data from their own analytical studies, animal studies, and at least one clinical study, unless the FDA decides that certain studies are unnecessary. While this process is more arduous than the process for generics because of biologic complexity and a current inability to perfectly replicate biologics, it still saves time, resources, and unnecessary human testing.[20] Most importantly, the FOBs are labeled as interchangeable and may be substituted by a pharmacist without a doctor's consent.[21] This

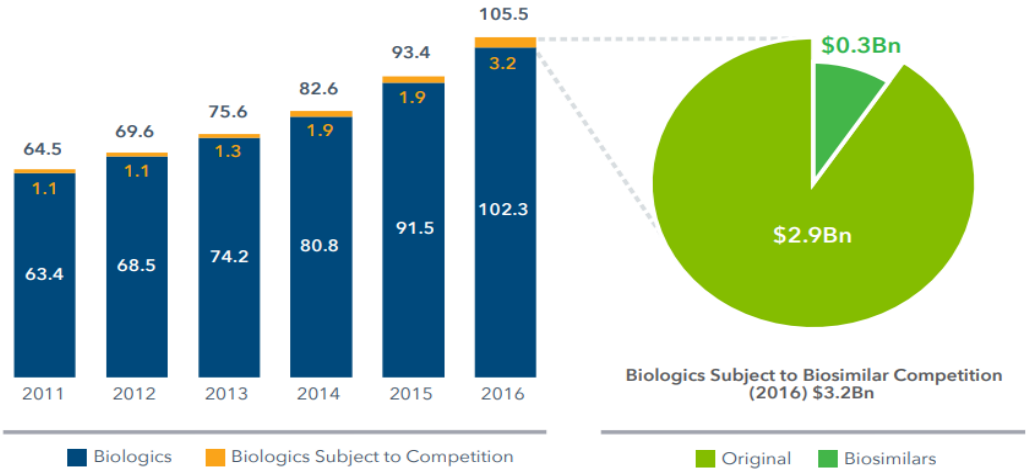
[16] *Id.* §262(a)(2)(C)(i)(I).
[17] *Id.*
[18] *Id.*
[19] BPCI Section 351(i) defines biosimilarity. This is similar to the Hatch-Waxman Act, which allows generic drugs to be approved upon a showing that the generic is the same as the brand version without having to perform its own studies.
[20] Federal Trade Commission Report, *supra note 8*, pg. 4.
[21] Public Health Services Act, 42 U.S.C. § 351(i)(3) (last amendment Aug. 2017).

mechanism grants FOBs market share without having to expend more resources on advertising. These domestic provisions are laudable, as they increase access to medicines.

However, BCPI also erects barriers in access to medicines through exclusivity provisions. An FOB applicant cannot submit an application until four years after the licensing of the original biologic and the FDA cannot issue a license to an FOB for twelve years.[22] The first FOB to enter the market also receives at least one year of exclusivity before another FOB is allowed to enter the market.[23] After twelve years of data exclusivity, FOBs are allowed to rely on the FDA's approval of the biologic to prove that their own FOB is safe, but they do not gain access to that data. These data exclusivity provisions go beyond the TPP model by requiring twelve years of data exclusivity rather than eight years. Because the USTR negotiates FTAs so that they align with already existing law, it is unlikely that it will push for exclusivity beyond 12 years in NAFTA 2.0, but with the shorter periods of exclusivity in both Canada and Mexico, the issue is whether the U.S. will agree to a lesser period of exclusivity. Ultimately, the U.S. will likely not be affected by data exclusivity provisions in NAFTA 2.0.

[22] *Id.* at 351(k)(7).
[23] *Id.* at 351(k)(6).

Figure 2- Biologics spending in billion USD. Biologics grew by 13% in 2016, and over 10% per year for the last five years, as a variety of biologic treatments for autoimmune disorders, immunology, and cancer came to the market. FOBs have been slow to emerge since the creation of a FOB pathway in the Affordable Care Act in 2010.



Source: IQVIA, National Sales Perspectives, Dec 2016; IQVIA Institute of Human Data Science

Chart notes:
Biologics are defined by IQVIA as clearly identifiable molecules of biologic origin, including but not limited to products created with recombinant DNA technology and without necessarily adhering to classifications by regulatory bodies which are sometimes inconsistent with this approach. Biosimilars are abbreviated biologic approvals made with reference to an original biologic and demonstrating similarity to the reference product. Non-original products approved outside the official biosimilar pathway have been noted as "biosimilar."

b. Canada

i. Small molecule drugs and generics

Canada currently provides eight years of data exclusivity for an innovator drug.[24] This data exclusivity period applies to both biologics and conventional small molecule drugs. It is enforced through a six-year "no filing" period and a two-year "no approval" period.[25] A manufacturer may not file a drug submission referencing an innovator drug within six years of

[24] Eligibility for data protection is governed by the definition of "innovative drug" under the Food and Drug Regulations. The definition sets out what is not an innovative drug: an innovative drug contains a medicinal ingredient that is not (1) previously approved in a drug by the Minister and (2) a variation of a previously approved medicinal ingredient, such as a salt, ester, enantiomer, solvate or polymorph. The Food and Drug Regulations do not provide further guidance regarding the meaning of "previously approved" or "a variation." Therefore, these terms are left for the Minister and the Courts to interpret and apply. Since 2006, a series of decisions from the Federal Court and Federal Court of Appeals have tackled the meaning of these terms. Three of the most important judgments of the Federal Court and Federal Court of Appeals address the meaning of "previously approved:" *Epicept* (Federal Court), *Teva* (Federal Court of Appeals), *Celgene* (Federal Court of Appeals). As a general trend, the interpretation of "innovative drug" has been restrictive. Food and Drug Regulations, section C.08.004.1, C.R.C., c. 870. Drug products authorized prior to June 17, 2006 receive a five-year data exclusivity period (Food and Drug Regulations, section C.08.004.1(1), C.R.C. 1978, c. 870).

[25] Section C.08.004.1(3) of the Food and Drug Regulations

the initial authorization of the innovator drug. Comparisons may be made in a drug submission after six years. However, an additional two-year period remains before generic or biosimilar marketing authorization can be granted.[26] An additional six months of exclusivity may be added to the eight-year term where a pediatric clinical trial has been conducted.[27] These long periods of data exclusivity lengthen the patent holder's monopoly in the market, and the Canadian single-payer public health system would be harmed if NAFTA 2.0 included longer protection periods.

ii. Biologics and biosimilars

There are different paths of approval for generics and FOBs. Because FOBs are not identical to biologics, they must go through Health Canada's approval process as a new drug. To be approved, the FOB manufacturer must identify the comparable biologic. The active substances, dosage, strength, and route of administration must be similar to the biologic in order for an FOB to be approved. To meet this burden, the FOB manufacturer must provide human clinical studies.[28]

An FOB must also prove that its product does not infringe the biologic's patent. Canada does not differentiate between biologics and drugs in its exclusivity regime. Therefore, like drugs, biologics are subject to a six-year period of exclusivity where an FOB applicant cannot submit an application until six years after the licensing of the original biologic, and cannot receive a license until eight years of exclusivity for the original biologic.[29] The biologic maker

[26] Guidance Document: Data Protection under C.08.004.1 of the Food and Drug Regulations, *available at* https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/guidance-document-data-protection-under-08-004-1-food-drug-regulations.html.
[27] *Id.*
[28] Government of Canada, "Fact Sheet: Biosimilars," (2017), *available at* https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/fact-sheet-biosimilars.html.
[29] Yoo Kang & Daphne Laison, "Pharmaceutical patents in Canada: key issues for life sciences companies," IAM, *available at* http://www.iam-media.com/Intelligence/IAM-Life-Sciences/2017/Articles/Pharmaceutical-patents-in-Canada-key-issues-for-life-sciences-companies. There is an extra 6 months of exclusivity if pediatric extension applies.

can sue for infringement, and during the trial the FOB cannot be approved by Health Canada.[30] The maximum length of the proceeding is twenty-four months, so even if there is no patent infringement by the FOB, its market entry may still be delayed for two years by lawsuits. This means that biologics in Canada have up to ten years of de facto exclusivity.

If NAFTA 2.0 includes the twelve-year exclusivity provision endorsed by the United States and included in the draft TPP, FOB manufacturers will be unable to gain access to valuable data for four extra years, further slowing their research and development. FOB market entry will be delayed, leaving Canada's government to pay the high cost of biologics in the meantime.[31]

c. Mexico

i. Small molecule drugs and generics

Although the Mexican Constitution treats international treaties as national law, the Mexican Congress has amended many laws to adjust them to NAFTA provisions. In August 1994, several amendments to the Industrial Property Law were enacted. This includes the addition of Article 86*bis* on data exclusivity. This article states that "the information required by the special laws to determine the safety and efficacy of pharma-chemical and agro-chemical products that use new chemical compounds shall be protected in the terms provided in the international treaties that Mexico is a member of."[32] However, national legislation does not explain how the Mexican government will protect research data, the minimum or maximum term of data exclusivity, or

[30] Government of Canada, "Guidance Document: Information and Submission Requirements for Biosimilar Biologic Drugs", (2017), *available at* https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/information-submission-requirements-biosimilar-biologic-drugs-1.html#app; Daphne C Lainson & Nancy Pei, "When it comes to biologics, Canada dances to a different tune", *available at* https://www.expertguides.com/articles/when-it-comes-to-biologics-canada-dances-to-a-different-tune/aryxabqr.

[31] "The drug landscape is changing...Say Hello to Subsequent Entry Biologics", Greenshield Canada, (2016), *available at* https://www.greenshield.ca/en-ca/news/post/the-drug-landscape-is-changing. For example, one FOB, Infectra, costs 47% less than a similar biologic.

[32] NAFTA Article 86*bis*

when the term starts; it just refers to the provisions of the international treaties. Therefore, the scope of the data exclusivity protection depends upon the international treaty from which a party benefits.

Articles 1711.5 and 1711.6 of the NAFTA, which have been in force in Mexico since January 1994, are the first provisions regarding data exclusivity in Mexico. For confidential information about the safety and efficacy of a new medicine that took considerable effort to create, Articles 1711.5 and 1711.6 of the NAFTA stipulate that regulatory authorities receiving the information must do two things. First, they must refrain from disclosing such information unless it is necessary to protect the public. Even then, measures must be taken to avoid unfair commercial use of such information.[33] Second, they must take measures to avoid the unfair commercial use of such information.[34] NAFTA explicitly provides that authorities must avoid relying on the research data filed by the innovator to approve a third party's marketing authorizations without originator authorization for at least five years from the date the authorities granted the marketing authorization to the originator.[35]

A 2006 USTR Special Report criticizes Mexico's lack of compliance with the data exclusivity requirements laid down in NAFTA and "encourages Mexico to make further efforts to provide protection for patents and against unfair commercial use of undisclosed test and other data submitted by pharmaceutical companies seeking marketing approvals for their products."[36] In 2012, the Commission for Protection against Sanitary Risks (COFEPRIS) published an internal memorandum on its website providing guidelines on regulatory data exclusivity.[37]

[33] NAFTA Article 1711
[34] NAFTA Article 1711.5
[35] NAFTA Article 1711.6
[36] "2006 Special 301 Report." USTR. found at https://ustr.gov/sites/default/files/2006%20Special%20301%20Report.pdf.
[37] Erwin Cruz and Alejandro Luna, "Key issues for biotech products in Mexico", *available at* http://www.iam-media.com/Intelligence/IAM-Life-Sciences/2015/Articles/Key-issues-for-biotech-products-in-Mexico.

According to these guidelines plus a minimum term set by NAFTA, any entity that has obtained market approval has a five-year exclusivity period during which its information cannot benefit or be used to support a third party application for registration of a generic drug.[38] These guidelines do not preclude generics from conducting their own clinical trials to obtain market approval.[39]

ii. Biologics and biosimilars

Because of free trade agreements, including NAFTA, a de facto exclusivity period of five years has been granted to biologics.[40] Biologic manufacturers have challenged this five-year period and would like to see it extended. In the case of biologic manufacturer Janssen Cilag, a Mexican Federal Circuit Court held that data exclusivity could be granted for longer than five years if the clinical data was difficult and time-consuming to produce.[41] This ruling could substantially increase periods of data exclusivity if courts interpret it to mean that five years is the minimum period of protection for data exclusivity rather than the default.[42]

Because FOBs do not have the same structure as biologics, Mexico requires clinical trials to prove their safety and efficacy. The Sanitary Authority determines the number of trials on a case-by-case basis. This is different from the generics process, where generic manufacturers can use trials by the pioneer drug to gain access to the market.[43]

An extended period of data protection would prove especially harmful for an economy like Mexico where access to medicines does not have the same connotations as in the

[38] *Id.*
[39] *Id.*
[40] Data Protection for Innovator Biologic Drugs in South America: the Case of Mexico, Moeller IP(2017), *available at* http://www.moellerip.com/data-protection-for-innovator-biologic-drugs-in-south-america-the-case-of-mexico/.
[41] *Hospira Healthcare Corporation v. Kennedy Institute of Rheumatology, Janssen Biotech, Inc., Janssen Inc., and Cilag GmbH International*, 2016 FCA 215 (Court File No. A 303 15, on appeal from T-396-13).
[42] Lisa Mueller, "In Mexico: Can the Minimum Period of 5 Years Established by NAFTA for Regulatory Data Exclusivity be Extended for Biological Medical Products?", The National Law Review (2015), *available at* https://www.natlawreview.com/article/mexico-can-minimum-period-5-years-established-nafta-regulatory-data-exclusivity-be-e.
[43] "Biological and Pharmaceutical Patents in Mexico", AIPLA.org, (2013), *available at* http://www.aipla.org/committees/committee_pages/IP-Practice-in-Latin-America/Committee Documents/AIPLA 2013 Spring Meeting - Eugenio Perez - Mexico.pdf.

significantly more developed Canada and U.S. Such enhanced protection would only push prices up and reduce access to medicines where it is most needed.

III. Patentability Criteria

The rationale of patents is to reward development of new drugs by restricting competition. This rationale is distorted when secondary patents are given because the inventors have already been rewarded for such development with one period of exclusivity.[44] Another rationale of patents it to allow companies to recoup the expenses of developing a new drug. But this rationale doesn't apply to secondary patents because research and development costs for medicines that are already proven safe are significantly lower because "the search for new indications is more a function of routine, plodding investigation than 'inventive-step' science."[45] Secondary patents do not fulfill the policy reasons behind patenting and should be minimalized.

The best way to minimalize secondary patenting is to define patentable subject matter narrowly. TRIPS defines patentable subject matter as inventions that are "new, involve an inventive step, and . . . [are] capable of industrial application.[46] In countries like the United States and Canada, "non-obvious" and "useful" are synonymous with "inventive step" and "capable of industrial application." These are vague terms that allow for a wide range of interpretations. These terms may be interpreted narrowly to create a high threshold for patentability, resulting in fewer patents. Conversely, they may be interpreted broadly to create a low threshold for patentability, resulting in more patents. Narrow patentability thresholds are more desirable as they curb the granting of meritless patents, making it possible for other drugs to enter the market without having to wait for a patent to expire. Broad patent thresholds, on the

[44] Receiving secondary patents is known as "evergreening" which is discussed further in Annex IV.
[45] Brook K. Baker, "Trans-Pacific Partnership Provisions in Intellectual Property, Transparency, and Investment Chapters Threaten Access to Medicines in the US and Elsewhere", *Medicine* 13.3 (2016): e1001970. *PMC*, *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4783061/.
[46] Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), art. 27, Apr. 15, 1994.

other hand, can have extreme consequences in price and patent duplication. For example, the antiretroviral booster, Ritonavir, has been under patent protection for decades and has over 800 different families of patents. [47] In one study, the costs of secondary patents like those used to extend the patent life of Ritonavir totaled 14.4 million euro over 8 years for hospitals and pharmacies in Geneva.[48]

The United States and Europe have some of the broadest patentability standards. In both places, patents cover the particular use of a compound rather than the compound itself.[49] This allows for multiple different uses of a compound to be patented. If the only patentable subject matter were the compound itself, new patents would not be given to protect particular uses. Any protection for the compound would end after the original patent expired in 20 years, rather than be extended indefinitely due to new uses of the compound. In the United States, new forms of known substances are also patentable and considered new and non-obvious even though creating new forms is a "straightforward, trial-and-error process" that pharmacists have engaged in for decades.[50] Both of these techniques for getting secondary patents are practiced widely throughout the U.S. and Europe and result in lower access to medicines, as generics cannot be placed on the market due to patent term extensions.

In contrast, India has adopted the narrowest patentability thresholds and is often lauded for its relatively high access to medicines. It has a high threshold for inventive step and excludes

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[47] Amin T Kesselheim, "Secondary Patenting of Branded Pharmaceuticals: a Case Study of How Patents on Two HIV Drugs Could be Extended for Decades", Health Affairs. 2012; 31:2286-94.

[48] Vernaz N, Haller G, et al., "Patent Drug Extension Strategies on Healthcare Spending: a Cost-Evaluation Analysis", PLoS Med., (2013) *available at* http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1001460.

[49] Amy Kapczynski, "Harmonization and its Discontents: a Case Study of TRIPS Implementation in India's Pharmaceutical Center", pg. 1591 citing John Thomas, Pharmaceutical Patent Law, 44-49 (2005); see also Int'l Center for Trade &Sustainable Dev. (ICTSD) & United Nations Conferences on Trade & Dev (UNCTAD), Resources Book on TRIPS and Development 356-57 (2005).

[50] *Id.* at p. 1591.

most new uses and new forms of known substances from patentability. Because of this, India routinely invalidates meritless patents that jurisdictions like the U.S. would grant. India has implemented these standards entirely through its Patent Act, but these regulations could also be implemented in NAFTA 2.0. The table below examines these measures and contrasts them with the TPP draft that the U.S. took part in before giving a recommendation as to which text NAFTA 2.0 should mirror.

Table 4: Patentability thresholds and recommendations for the NAFTA 2.0 patentability requirements.

	India Patent Act	2015 TPP Draft	Recommendations	Changes to Domestic Law
New uses of known substances	Art. 3 the following are not inventions . . . (d) the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a known substance or of the mere use of a known process . . . unless such known process results in a new product or employs at least one new reactant. *Explanation*- . . . other derivatives of known substances shall be considered to be the same substance, unless	Art. QQ.E.1(2) . . . each party confirms that patents are available for inventions claimed as at least one of the following: new uses of a known product, new methods of using a known product, or new processes of using a known product. Art. QQ.E.21 for the purposes of Article QQ.E.16.1, a new pharmaceutical product means a pharmaceutical product that does not contain a chemical entity that has been previously approved in the Party. QQ.E.16.1 is about data protection of test data about the safety or efficacy of the product.	If the TPP draft text is implemented, the definition found in Article 21 should apply beyond Article 16 so that the definition of new products extends to patents rather than just data protection. This is a high standard of protection banning any new compounds of a drug regardless of efficacy or new uses. Therefore, if the qualifier is removed, NAFTA 2.0 should use the TPP's draft text. However, using the India text would also result in a high level of protection. The only difference between the India text and the TPP is that the India text allows for new forms of a substance if they enhance effectiveness, and new forms of a process if it results in a	Implementing either the TPP draft text or the India Patent Act text would require a change in U.S. law, as it current only requires a "new and useful improvement" to issue a patent even if the invention is in reality a new form of a known substance.[51] Mexico is a monist system so whatever text is implemented will automatically be incorporated into Mexico's domestic law. Mexico is therefore less concerned with whether a treaty provision matches its current domestic law or not. Canada is a dualist system so it will have to implement NAFTA 2.0 into its domestic law through legislation. It has a low threshold of

[51] 35 U.S.C. § 101 (1952).

	they differ significantly in properties with regard to efficacy	Because art. 16 qualifies art. 21, it seems that this narrow definition only applies to data protection. The parties would only give data protection to new pharmaceutical products that match 21's definition, but they still may grant patents to products that don't match article 21's definition, meaning that they contain a previously approved chemical entity.	new product or employs at least one new reactant. These qualifiers make it possible, but still difficult, for new uses of known substances to be patented. This middle ground may be best because it still encourages some experimenting with known drugs and processes but prevents most cases of evergreening.	patentability, allowing patents on "any new and useful art, process, machine, manufacture or composition of matter, or any new and useful improvement in any art, process, machine, manufacture or composition of matter."[52] Because both Canada and the U.S. would have to change their patent laws to implement either recommendation, it is unlikely that either will be implemented in NAFTA 2.0.
Inventive step	Art. 3 the following are not inventions . . . (e) a substance obtained by a mere admixture resulting only in the aggregation of the properties of the components thereof or a process for producing such substance	No similar provision	This prohibition should be incorporated in NAFTA 2.0 because it precludes patents for slightly different combinations of already patented medicines.	35 U.S.C. § 103, and Mexico's Patent Act art. 12(3), and Canada's Patent Act art. 28.3 have inventive step thresholds. All three generally require that subject-matter of an invention not be obvious to a person skilled in the art or science to which it pertains. The Statement of Administrative Action (SAA) for NAFTA 2.0 could direct countries to interpret an inventive step threshold so as to prevent the patenting of admixtures, as they are obvious to a "person having ordinary skill in the

[52] The Patent Act R.S.C. 1985 c. P-4 Section 2.

				art." This would not require any changes in domestic law.
Traditional knowledge	Art 3 the following are not inventions . . . (p) an invention which in effect, is traditional knowledge or which is an aggregation or duplication of known properties of traditionally known component or components.	Art. QQ.B.xx calls on parties to recognize the relevance of traditional knowledge in intellectual property and cooperate to enhance the understanding of issues between IP and traditional knowledge with regards to genetic resources. Art. QQ.B.xx.3 calls on parties to conduct quality patent examination which includes (a) in determining prior art, relevant publicly available documented information related to traditional knowledge associated with genetic resources may be taken into account" (b) an opportunity for third parties to cite, in writing, to the competent examining authority prior art disclosures that may have a bearing on patentability, including prior art disclosures related to	India's traditional knowledge criteria should be implemented into NAFTA 2.0. If patent evaluators find that an alleged invention is traditional knowledge, then it is not an invention and as a result cannot be patented. NAFTA 2.0's text should not be similar to the TPP draft text. While it devotes a lot of text to traditional knowledge, a determination that something is traditional knowledge is only a factor to be considered in patent evaluations. Furthermore, only traditional knowledge "with regards to genetic resources" is relevant in this consideration. WIPO defines genetic resources as "any material of plant, animal, microbial or other origin containing functional units of heredity."[53] Traditional medicine generally uses plants, animals, or other natural sources for healing so it this qualifier does not seem to limit the scope of traditional medicine. Regardless, this qualifier unnecessarily	Neither Canada, Mexico, nor the U.S. include any provisions acknowledging traditional medicine in their patent acts. As signatories to the CPTPP, Canada and Mexico will be subject to the CPTPP text on traditional medicines, which is the same as the TPP draft text, calling on countries to take traditional medicine into consideration. A way to get strong traditional medicine considerations into NAFTA 2.0 is through the SAA. The SAA could require patent offices to consider applications of traditional medicines as "otherwise available to the public before the effective filing date of the claimed invention"[54] and therefore not patentable.

[53] WIPO, "Genetic Resources", http://ww. Wipo.int/tk/en/genetic/.
[54] 35 USC § 102(a)(2) (1952).

		traditional knowledge associated with genetic resources. Sections c and d call for the use of databases containing traditional knowledge associated with genetic resources and training patent examiners about traditional knowledge associated with genetic resources.	complicates what should be a straightforward analysis of traditional medicine. The relevant question should be whether the medicine has been traditionally used, not whether it is genetic based.	
Inventive Step Threshold	Art. 2(1)(ja) 'inventive step' means a feature of an invention that involves technical advance as compared to the existing knowledge or having economic significance or both and that makes the invention not obvious to a person skilled in the art	Art. QQ.E.1 Footnote 33- In determinations of inventive step, each party shall consider whether the claimed invention would have been obvious to a person skilled or having ordinary skill in the art having regard to the prior art.	Preferably, India's inventive step threshold would be adopted in NAFTA 2.0. The requirement that an invention not be obvious to a person skilled in the art is standard, but the requirement that an invention also makes a technical advance or has economic significance adds a unique criteria. This heightened standard would give patent offices in each country the opportunity to narrow the types of inventions that receive patent protection. For example, this provision would likely disqualify slightly different combinations of drugs from patent protection.[55] If language similar to the draft TPP is adopted, obviousness	As shown two rows above, 35 U.S.C. § 103, Mexico's Industrial Property Act Art. 12(3) and Canada Patent Act 28.3 all contain similar inventive step provisions. CPTPP contains the same provision as the TPP text. The SAA should require agencies to interpret inventive step so as to require that the product make a technical advance in order to qualify as an invention. This will prevent a lot of secondary patents that simply create new mixtures of the drug.

[55] Kapzyncski, *supra note 49*, at p. 1593.

			should not be determined by a person "having ordinary skill in the art." Instead, it NAFTA 2.0 should only allow determine obviousness based upon what a "skilled" person standard. Ordinary skill is a lower threshold because the person need not be an expert. What is obvious to an expert is likely nonobvious to anyone else, so more meritless inventions could be patented.	

IV. Investment and Legitimate Expectations in Investor-State Dispute Settlement

An enhanced IP chapter along the lines of the TPP Draft would define investment broadly to include IP rights,[56] meaning that any company with a patent could seek private arbitration through Investor-State Dispute Settlement (ISDS). ISDS allows companies to sue for unfair or inequitable treatment that violated their legitimate expectations. Countries could be liable for denying patents, granting a compulsory license, capping the sales price of a medicine, or any other changes to a country's regulatory scheme.

[56] TPP Draft Chapter 9 "Investment" art. 1 https://ustr.gov/sites/default/files/TPP-Final-Text-Investment.pdf.

Table 5: Legitimate expectations recognized by NAFTA and TPP and recommended solutions for such provisions.

Issue	NAFTA	TPP Draft	CTPP Changes	TRIPS	Problem with TPP provisions	Recommendation
Revoking / Nullifying Patents	Art. 1107 "This Article does not apply to the issuance of compulsory licenses granted in relation to intellectual property rights, or to the revocation, limitation or creation of intellectual property rights, to the extent that such issuance, revocation, limitation or creation is consistent with Chapter Seventeen (Intellectual Property)."	Art. 18.40 Companies may sue government restriction on use of patent right if it "unreasonably conflict [s] with a normal exploitation of the patent and do not unreasonably prejudice the legitimate interests of the patent owner…" for loss of their "legitimate expectations" due to regulatory or judicial decisions, including "denials or revocations of pharmaceutical patents; granting of compulsory licenses; denials or restrictions on marketing rights…"	None	Articles 8 and 40 allows government to prevent patent holders from abusing intellectual property rights, "unreasonably" restraining trade, or hampering the international transfer of technology.	Allows for challenges to revoking/nullifying patents if considered to undermine "regulatory stability."	Limit legitimate expectations to explicit guarantees and contracts made to investors by the government. If possible, it would be best to remove ISDS protection for IP rights.

Excessive Pricing	No provision	Companies may sue for loss of their "legitimate expectations" due to regulatory or judicial decisions.	None	None	Potential litigation for disagreement on application or enhancement of price control regulations.	Remove ISDS provision or limit legitimate expectations to written assurances made by the government.
Compulsory Licensing	Art. 1107 "This Article does not apply to the issuance of compulsory licenses granted in relation to intellectual property rights…"	Art. 18.40 allows suits if the government action ""unreasonably conflict[s] with a normal exploitation of the patent and do not unreasonably prejudice the legitimate interests of the patent owner…" Companies may sue for loss of their "legitimate expectations" due to regulatory or judicial decisions regarding "granting of compulsory licenses"	None	Art. 31: requires "adequate remuneration" to the patent owner, unless there is a national emergency (Art. 31b)	An issuance of a compulsory licenses may lead to a violation of legitimate expectations if payment is not "adequate." Also, may lead to forum shopping between WTO and ISDS tribunals	Extreme positions: Remove ISDS from this entirely. Alternatively, bring it back to TRIPS requirement for "adequate remuneration" and remove language regarding "normal exploitation."

NAFTA was the first trade agreement among developed countries to include investor-state dispute settlement provisions, although these provisions currently do not extend to IP.[57] NAFTA subjects all protected investments found in the three NAFTA countries to the International Center for Settlement of Investment Disputes, a forum for investor-state dispute settlement. It also includes a minimum treatment standard requiring countries to give investors "fair and equitable treatment" (FET).[58] NAFTA stipulates that legitimate expectations should only be applied as a "factor" when assessing whether or not FET has been breached.[59] In spite of this, in *Bilcon v. Canada*, the tribunal ruled that an environmental decision in Canada frustrated an American investor's legitimate expectations by denying its proposed quarry by making a discriminatory decision to deny its proposal in spite of the approval of other quarry applications by Canadian firms. The tribunal ruled that this violated NAFTA's FET obligation although NAFTA does not expressly include this obligation.[60] The tribunal's ruling is concerning because it shows ISDS tribunals' willingness to ignore the text of a treaty regarding ISDS in favor of following precedent.

NAFTA's investment chapter also specifies that the article on revoking patents "[does] not apply to the issuance of compulsory licenses granted in relation to intellectual property rights, or to the revocation, limitation or creation of intellectual property rights, to the extent that

[57] "NAFTA ISDS Platform", Stop Investor-State Dispute Settlement, *available at* https://isds.bilaterals.org/?-isds-nafta-.
[58] The North American Free Trade Agreement (NAFTA): a Guide to Customs Procedures. Washington, DC :Dept. of the Treasury, U.S. Customs Service, art. 1105, 1994. Print.
[59] Patrick Dumberry, Michael McIlwrath & Luke Eric Peterson, "The Emergence of a Consistent Case Law: How NAFTA Tribunals have Interpreted the Fair and Equitable Treatment Standard", Kluwer Arbitration Blog (2013), *available at* http://arbitrationblog.kluwerarbitration.com/2013/10/30/the-emergence-of-a-consistent-case-law-how-nafta-tribunals-have-interpreted-the-fair-and-equitable-treatment-standard/.
[60] Ronald Labonté, Ashley Schram & Arne Ruckert, The Trans-Pacific Partnership: Is It Everything We Feared for Health? International Journal of Health Policy and Management (2016), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4968252/.

such issuance, revocation, limitation or creation is consistent with Chapter Seventeen (Intellectual Property)."[61]

Recent events suggest that NAFTA 2.0 will not enhance ISDS, although it will be enhanced under the CPTPP. The most recent CPTPP draft reaffirms legitimate expectations as a factor when determining whether there is indirect expropriation."[62] It is important to note that the CPTPP currently only applies to Canada and Mexico. USTR head Robert Lighthizer has spoken against the inclusion of an ISDS provision in NAFTA 2.0, arguing that these protections effectively subsidize US companies to invest abroad.[63] Though this has been met with opposition within the U.S. Senate, this makes the expansion of existing ISDS provisions to patents unlikely in NAFTA 2.0.[64]

The TPP draft investment chapter gives considerable rights to investors at the expense of each country's policy autonomy. TPP Article 9.1 includes IP rights as protected investments, subject to and protected by the International Center for Settlement of Investment Disputes (ICSID), a forum for investor-state dispute settlement. Under Article 9.8, investors are protected against direct and indirect expropriation unless properly compensated. Annex 9-B to TPP Chapter 9 further defines indirect expropriation as "an action or series of actions by a Party [that] has an effect equivalent to direct expropriation without formal transfer of title or outright seizure."[65] To determine indirect expropriation in a dispute, a tribunal must consider "the extent to which the government action interferes with distinct, reasonable investment-backed

[61] NAFTA, *supra note 58*, art. 1107.
[62] Comprehensive and Progressive Trans-Pacific Partnership (CPTPP), Ch. 9, Annex 9-B, footnote 36, *available at* http://www.trungtamwto.vn/sites/default/files/tpp/9.-investment-chapter.pdf.
[63] Carlos Vejar & Laura Yvonne Zielinski, "U.S. Investors Face Possible Loss of Investment Treaty Arbitration Under NAFTA", Lexology (2018), *available at* https://www.lexology.com/library/detail.aspx?g=71ec448b-c207-4c3f-b61d-e88ce029c979.
[64] *Id.*
[65] TPP, Annex 9-B, 3)

expectations."[66] Within a footnote it is clarified that "[f]or greater certainty, whether an investor's investment-backed expectations are reasonable depends, to the extent relevant, on factors such as whether the government provided the investor with binding written assurances and the nature and extent of governmental regulation or the potential for government regulation in the relevant sector."[67] The language of the footnote, including "factors such as," implies that this is not intended to be an exhaustive list. This ambiguity is troubling because it give each tribunal considerable discretion to determine what additional factors to consider in its legitimate expectations analysis.[68] This means that legitimate expectations could potentially expand to include compulsory licensing, revocations, or price controls. *Eli Lilly v. Canada* litigated in ISDS as a result of NAFTA's investment chapter, when the patent owner claimed a violation of its legitimate expectations regarding regulatory stability under Canada's new promise utility doctrine.[69] Though the firm lost, it still shows that there is a potential for damaging and costly litigation, especially since the litigation went on from 2012 to 2017.[70]

Legitimate expectations presuppose that an agreement or a promise generates a certain level of expectations to the investor.[71] It is a vague term that remains undefined, but arbitral

[66] *Id.* at Annex 9-B, 3 (a) (ii).
[67] *Id.*
[68] Ronald Labonté, Ashley Schram & Arne Ruckert, "The Trans-Pacific Partnership: Is It Everything We Feared for Health?" International Journal of Health Policy and Management (2016), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4968252/.
[69] "This doctrine comprises three elements: (i) the identification of a 'promise' in the patent disclosure, against which utility is measured; (ii) the prohibition on the use of post-filing evidence to prove utility; and (iii) the requirement that pre-filing evidence to support a sound prediction of utility must be included in the patent."); Thomas Musmann & Thorsten Bausch, Eli Lilly v. Canada – The First Final Award Ever on Patents and International Investment Law Kluwer Patent Blog (2017), *available at* http://patentblog.kluweriplaw.com/2017/04/04/eli-lilly-v-canada-the-first-final-award-ever-on-patents-and-international-invest-ment-law/.
[70] *Eli Lilly and Company v. Government of Canada*, GAC (2017), *available at* http://www.international.gc.ca/trade-agreements-accords-commerciaux/topics-domaines/disp-diff/eli.aspx?lang=eng.
[71] Michele Potesta, "Legitimate Expectations in Investment Treaty Law: Understanding the Roots and Limits of a Controversial Concept," Levy Kaufmann Kohler (2013), p. 2, *available at* https://lk-k.com/wp-content/uploads/potesta-legitimate-expectations-inv.-treaty-law-2013.pdf.

tribunals have gradually limited its scope.[72] There are three different situations where "legitimate expectations" may be created: by contract, by promises and assurances by the government, and by the stability of the existing regulatory framework.

1. Contractual commitment

This situation is the most straightforward and arises after a state and company conclude a contract.[73] In this situation, the company can only argue that a government violation of the contract breached its legitimate expectations. Tribunals will not rule on normal contract law, which only domestic courts have jurisdiction over.[74] In order for a tribunal to have jurisdiction, the investor must claim that the government has done more than just failed to fulfill the contract. Though tribunals do not precisely agree, in general there must either be "a breach involving sovereign power," an "outright and unjustified repudiation of the transaction," or a "substantial breach...under certain limited circumstances."[75]

2. Assurances made by the government

The second situation is less formal, because unilateral declarations by the host state such as promises, assurances, representations, etc., are enough to create legitimate expectations.[76] If a government administration were to make promises or assurances that a company's investment would be safe or would bring certain returns, then the company could claim that the country's failure to fulfill its promises violated its legitimate expectations. In *SPP v. Egypt*, the tribunal found that investors could rely upon expectations created by decisions and representations made by high-ranking officials.[77] A number of other tribunals agree with this interpretation.[78]

[72] *Id.* at p. 15
[73] *Id.* at 15.
[74] *Id.* at p. 18.
[75] *Id.* at p. 17-18.
[76] *Id.*
[77] *Id.* at p. 19.
[78] *Id.* at p. 20.

However, tribunals have also stated that the assurances must be sufficiently specific.[79] The difficulty here lies in determining whether statements are specific and fact-bound or whether they are political in nature, which is not enough to provide sufficient assurance."[80] Generally, however, the threshold for these assurances is high.

3. Stability of the regulatory framework

The third situation occurs where the company invests in the host state at a time when a specific regulatory framework is in place, creating a legitimate expectation that the regulatory framework will remain.[81] In this scenario, if the country were to change its regulations or laws in a way that harms the investment of the parties relative to its position when it made its investment, then it would have a claim.

This is the most controversial situation because it encroaches upon state sovereignty by forcing states to pay companies for regulatory changes. Case law from tribunals does not give a fixed answer and seems to rely heavily on a country's context in making this determination by looking at its level of development, the frequency with which it changes rules and regulations, and the country's rule of law in general.[82] For example, the tribunal in *Occidental Exploration & Production Co. v. Ecuador* concluded that, "there is certainly an obligation not to alter the legal and business environment in which the investment has been made."[83] In *Enron v. Argentina*, the tribunal held that a "stable framework for the investment," is crucial to protect legitimate

[79] *Id.* at p. 22-23. Wälde in his Separate Opinion in Thunderbird, though adopting a broad notion of protection of legitimate expectations, concedes that 'a legitimate expectation is assumed more readily if an individual investor receives specifically formal assurances that display visibly an official character.
[79] *Id.* at p. 23, quoting *International Thunderbird Gaming Corporation v. Mexico, NAFTA/UNCITRAL,* Award, 26 January 2006, Separate Opinion Thomas Wälde.
[80] *Id.* at p. 24.
[81] *Id.* at p. 26.
[82] *Id.* at p. 34-35.
[83] *Id.* at p. 28.

expectations.[84] Conversely, a more recent tribunal stated, "it would be unconscionable for a country to promise not to change its legislation as time and needs change, or even more to tie its hands by such a kind of stipulation in case a crisis of any type or origin arose."[85] Depending upon the tribunal, a country's regulatory changes could be enough for a company to bring a successful claim that its legitimate expectations were breached.

After one of the three situations discussed above establishes legitimate expectations, a company can sue a state for a breach of those legitimate expectations. This exposes countries to a high risk of litigation if they attempt to regulate the drug industry, making countries hesitant to alter their existing regulatory framework in a way that disfavors pharmaceutical companies. There are numerous ways for an investor to argue that its legitimate expectations have been breached, so this paper will examine the three most common in the pharmaceutical context: abuse of patent, excessive pricing, and compulsory licensing.

1. Abuse of Patent Remedies

Abuse of patent occurs when a company uses its patent in an illegitimate manner, and can be used by defense or prosecution in court.[86] Successful abuse of patent claims prevent companies from anticompetitive practices like buying all relevant patents to prevent competition, attempting to enforce a patent that the holder knows is invalid, or selling goods only to a buyer that agrees not to buy from a competitor, all of which potentially drive up prices for customers. The precise definition depends upon the country's laws and cases, but can include using a patent to harm competition by threatening litigation or unreasonably refusing to grant a license to

[84] *Id.* at p. 29.
[85] *Id.* at p. 29 quoting *Continental Casualty Company v. Argentina*, ICSID Case No. ARB/03/9, Award, 5 September 2008.
[86] Michelangelo Temmerman, "The NCCR Trade Regulation" (2011), *available at* http://www.nccr-trade.org/fileadmin/user_upload/nccr-trade.ch/wp3/3.5/The Legal Notion of Abuse of Patent Rights.pdf.

generic companies.[87] While TPP Article 9.8(5) gives countries the ability to apply compulsory licenses and revoke patents, this is only allowed if it "is consistent with Chapter 18 (Intellectual Property) and the TRIPS Agreement." TPP Article 18.39 allows countries to revoke or render patents unenforceable for "fraud, misrepresentation or inequitable conduct." However, this remedy would likely give companies a legitimate expectations claim in ISDS. Furthermore, any attempts to reform the abuse of patent laws can also risk a legitimate expectations claim that the country undermined the stability of the regulatory framework.

Finally, this creates a new forum that may allow investors to forum shop. Under TRIPS, companies could not appear by the WTO on their own behalf. Their host company would have to sue on their behalf at the WTO. Now, investors have the ability to sue on their own and may be able to forum shop between the ISDS or the WTO tribunals, based on which tribunal they believe would bring them the better results.[88]

A. Canada

Per paragraph 127 of the Patent Act, anyone may apply for relief to the Commissioner of Patents by alleging abuse of patent three years after the grant of a patent.[89] There is an abuse of patent if "the demand for a patented article in Canada is not being met to an adequate extent or on reasonable terms." This occurs when:

a. the refusal of the patentee to license at all or on reasonable terms causes prejudice to an existing trade, industry or class or persons in trade or by blocking the establishment of any new trade or industry and it is in the public interest that a license be granted;

[87] See description on Canada below.
[88] KEI Staff, "KEI TPP Briefing note 2015:1 Compulsory licenses on patents and the 3-step test, Knowledge Ecology International" (2015), *available at* https://www.keionline.org/22768.
[89] The Patent Act R.S.C. 1985 c. P-4 127(1),(2).

b. the conditions attached to the purchase, hire, license or use of a patented article or the use or working of a patented process are such that a trade or industry, or persons therein is unfairly prejudiced; and

c. Process patents using unpatented materials or patents for substances produced by such processes, are used by the patentee so as to unfairly prejudice the manufacture, use or sale of any materials.[90]

The guidelines for determining how the patent may be licensed are based on three goals: 1) to secure the widest possible use of the invention in Canada consistent with the patentee deriving a reasonable advantage or earning a reasonable profit; 2) to secure the maximum advantage to the patentee consistent with the invention being worked by the licensee at a reasonable profit in Canada; and 3) to secure equality of advantage among several licensees, including, where due cause is shown, reducing the royalties or other payments accruing to the patentee under any license previously granted. If satisfied that a case of abuse has been established, the Commissioner may order a compulsory license or revoke the patent.[91]

As proven by *Eli Lilly v. Canada*, the potential for litigation on revoking patents is possible. Possible bases for suits can come in situations where 1) the government made assurances that the use of the patent in this way was perfectly legal leading to the revocation, or 2) the courts revoke patent based on a new criteria that was not there when the original patent was made, thus undermining the "regulatory stability." A pharmaceutical company could therefore sue Canada in ISDS based on its abuse of patent regime for the revocation of a patent.

B. Mexico

[90] *Id.* at 127(3).
[91] Constance Too, Xiang Lu & John Norman, "Canada: Abuse Of Patents In Canada" Gowling WLG (2012), *available at* http://www.mondaq.com/canada/x/191256/Patent/Abuse Of Patents In Canada.

While there is no law explicitly against the abuse of patent, in theory, an action could be brought against activities falling outside the scope of a patent, such as: non-competition agreements for products that are not covered by patents; product-tying within that scope, such as a seller refusing to license its product to a buyer unless it consents to buy other goods that the company sells; unfair competition activities, such as advertising that a product is better than an alternative for the sole reason of it having a patent. Actions could also be brought before the ECFC for other forms of abuse of patent rights, such as clearly unfounded attempts to enforce a patent.[92] In 2010, the ECFC imposed a fine on six pharmaceutical companies for anti-competitive practices in public tender proceedings by IMSS.[93] In theory, the agency would be able to do the same for the misuse of a patent. However, due to the lack of case law on the matter, it is unclear what the proper remedy would be.

If fines, compulsory licensing, or patent revocation are used as a remedy for either the abuse of a patent or using a patent that is later found to be inapplicable, the parties would be able to sue the government for preventing the "normal exploitation" of the patent, and would go to the ISDS to determine the validity of either their patent or the use of the patent. Because of the lack of clarity regarding abuse of patent and the remedy, there is an additional risk that there would be a suit that the government undermined "regulatory stability" by introducing new criteria or remedies that were not previously employed, even if it might have been possible in theory.

C. United States

[92] Alejandro Luna, Armando Arenas & Karla Paulina Olvera Acevedo, "Pharmaceutical IP and competition law in Mexico: overview," Thomson Reuters Practical Law, *available at* https://uk.practicallaw.thomsonreuters.com/4-560-6346?transitionType=Default&contextData=(sc.Default)&firstPage=true&bhcp=1.
[93] *Id.*

In the United States, abuse of patent claim can only be used in court as a defense. As such, patent abuse only leads to the temporary unenforceability of the patent, which may be enforced once the misuse has stopped.[94]

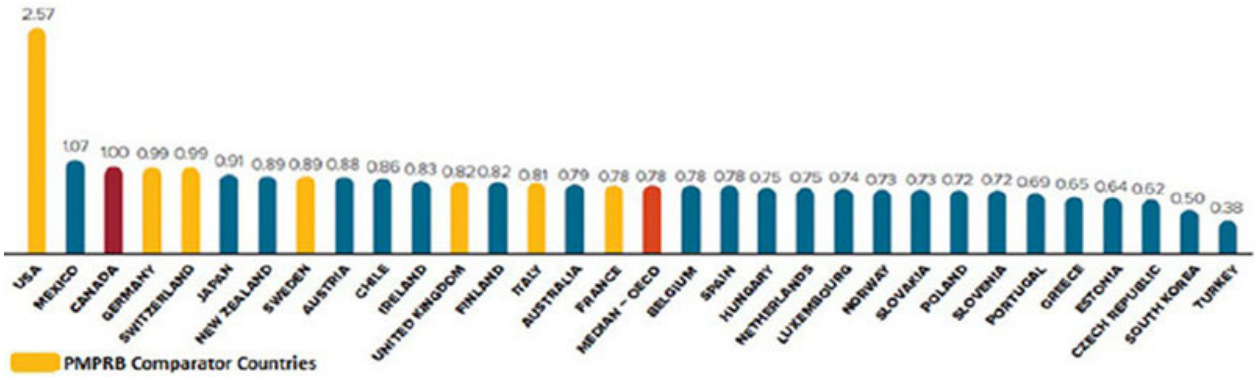
If NAFTA renegotiations result in language similar to the original TPP provisions, there would likely be little effect on the existing regulatory framework. However, this might have a chilling effect on future legislation and regulations regarding abuse of patent, as the most likely way a legitimate expectation would be created is through the regulatory framework. If, for instance, the United States were to apply a new law that created a broad definition for an abuse of a patent, raised the bar for getting a patent, or severely limited the scope of the patents, then the foreign investors would have a claim under international arbitration. Additionally, if a government organization were to assure a foreign investor that, in their professional opinion, their use of a patent would not be considered an abuse of a patent, then the parties would likely have a claim.

2. Excessive pricing

Excessive pricing controls is a form of antitrust law that is meant to prevent firms from using their dominant market power from excessively pricing consumers. This can be very important in the pharmaceutical industry because people often need the drugs to function and may not have alternatives, especially if they are patented.

[94] Temmerman, *supra note 86*.

Figure 3: PMRPB Comparator Countries Pharmaceutical Prices[95]



a. Canada

Canadian patented drug prices are among the highest in the world. Amongst all 35 member countries of the Organization for Economic Co-operation and Development (OECD), only the United States and Mexico have higher patented drug prices than Canada. In 2015, median OECD prices for patented drugs were on average 22% below those in Canada, as seen in Figure 3.[96]

Canada may curb drug prices through its Patented Medicine Prices Review Board (PMPRB), which determines whether patented medicines are being sold at excessively high prices and may order companies to decrease excessive medicine prices.[97]

More specifically, under Canada's *Patent Act*,

> [w]here the Board finds that a patentee of an invention pertaining to a medicine is selling the medicine in any market in Canada at a price that, in the Board's opinion, is excessive, the Board may, by order, direct the patentee to cause the maximum price at which the patentee sells the

[95] "Protecting Canadians from Excessive Drug Prices: Consulting on Proposed Amendments to the Patented Medicines Regulations", Health Canada, (2017), *available at* https://www.canada.ca/en/health-canada/programs/consultation-regulations-patented-medicine/document.html.
[96] *Id.*
[97] Patented Medicine Prices Review Board (PMPRB) (2018), *available at* http://pmprb-cepmb.gc.ca/home.

medicine in that market to be reduced to such level as the Board considers not to be excessive and as is specified in the order.[98]

Factors to consider when evaluating excessive pricing include 1) the prices at which the medicine has been sold in the relevant market; 2) the prices at which other medicines in the same therapeutic class have been sold in the relevant market; 3) the prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada; 4) changes in the Consumer Price Index (CPI); and 4) such other factors as may be specified in any regulations made for the purposes of this subsection.[99]

Based on the above criteria, the Patented Medicine Prices Review Board (PMRPB) in 2017 ordered Alexion, a U.S. Drug manufacturer, to slash prices for the drug, Solaris, meant to treat a rare disease.[100] This was done even though the company had not changed prices since 2009.[101]

While this framework is laudable, it includes many limitations. For instance, the existing framework only allows the PMRPB to use price comparisons and Consumer Price Index (CPI), to assess whether a price is excessive. The PMRPB cannot consider whether the price of a drug reflects its value to patients or other relevant factors that influence drug prices in different markets, such as market size or the relative wealth of a country.[102] Canadian prices for new drugs are also pegged to countries with high drug prices. Moreover, under the guidelines, once a new drug enters the market, prices can remain high as long as they do not increase by more than CPI

[98] Protecting Canadians, *supra note 95*.
[99] *Id.*
[100] Kelly Grant, "U.S. drug maker ordered to slash prices in Canada, pay back millions", The Globe and Mail (2017), *available at* https://www.theglobeandmail.com/news/national/canadian-regulator-orders-price-cut-of-expensive-us-drug-soliris/article36418703/.
[101] Protecting Canadians, *supra note 95*.
[102] *Id.*

and the highest international price.[103] Finally, the regulations do not require patentees to provide information to the PMPRB on rebates provided to Canadian customers beyond the first point of sale, despite their widespread use. The absence of this information leaves the PMPRB with a limited understanding of actual market prices.[104]

If an ISDS provisions is added to NAFTA 2.0, Canada's excessive pricing provisions may be limited in application for fear of breeching a companies' "legitimate expectations." If Canada's PMPRB ordered a company to slash prices on a pharmaceutical good, this could be viewed as "price control." A company could make the case to ICSID that it had legitimate expectations that it would be able to price the drug however it wanted. If the tribunal accepted such arguments, Canada could be liable for millions of dollars in revenue lost by forcing the company to cut its prices.

The greater risk is that a company's "legitimate expectations" of regulatory stability may chill significant reforms in Canada. Though the reforms would be unlikely to significantly affect the regulatory stability of the regime, the lack of a clear definition of "regulatory stability" may encourage some investors to threaten to bring suit. If Canada decided to implement stronger regulations or laws regarding price controls, then the patent holder could sue for violations of legitimate expectations. If the government actively encouraged expectations that incentivized companies to invest or sell within Canada and then set regulations that cut down on expected revenue the patent owner would have a case.

b. Mexico

In Mexico, excessive pricing determinations are based on a scheme of self-regulated maximum retail price (MRP) covering patented products, overseen by the Ministry of Economy.

[103] *Id.*
[104] *Id.*

Pharmaceutical companies' participation is voluntary. Under the price control system, each product's MRP must not exceed an international reference price, estimated as the average price in six major markets, plus a market factor. There are no established sanctions for violations of the MRP.[105] The fact that most, if not all, manufacturers choose to participate suggests that manufacturers perceive that the system is ineffective. If the regulation had an impact by resulting in prices lower than what would otherwise be set in the absence of regulation, manufacturers would face strong economic incentives not to participate. A second indicator of ineffectiveness is that the pharmaceutical manufacturers association has set up its own price monitoring system in an effort to ensure that individual manufacturers do not take advantage of the system by setting high prices and causing political pressure that would jeopardize the current arrangements.[106] If the self-regulated MRP system were effective, a secondary price monitoring system would be unnecessary.

As it stands, Mexico does not seem to have strong pricing regulations for the private sector and so would not likely face significant breech of legitimate expectation claims regarding pricing. The concern here is that "legitimate expectations" would have a chilling effect that would deter the Mexican government from attempting to make significant reforms, such as making the MRP program mandatory, or trying to make the existing program mandatory and enforceable. If Mexico does this, a foreign investor would then be able to initiate litigation by claiming that Mexico's reforms undermined regulatory stability that the investor had relied on, breeching its legitimate expectations. The risk of this kind of claim being brought in litigation

[105] Alejandro Luna, Armand Arenas. "Medicinal product regulation and product liability in Mexico: overview" Thompson Reuters Practical Law (2017).
[106] Pierre Moïse, Elizabeth Docteur, "Pharmaceutical Pricing and Reimbursement Policies in Mexico", OECD Health Working Paper (2007), ¶ 35, *available at* https://www.oecd.org/mexico/38097348.pdf.

may be enough to dissuade Mexico from making its MRP program mandatory and enforceable or creating another price monitoring mechanism.

c. United States

Unlike Canada and Mexico, the U.S. does not have any excessive pricing statute or price control regulations.[107] It will likely be extremely difficult to create a regulatory pricing regime out of nothing. As Judge Learned Hand aptly put it: "[t]he successful competitor, having been urged to compete, must not be turned upon when he wins."[108] It should come as no surprise that the United States has the highest prices for pharmaceuticals among developed nations (see graph above). Any attempts at change in this area would likely cause a breech of legitimate expectations claim, further dissuading the U.S. from legislating in this area.

3. Compulsory licensing

A compulsory license allows companies to produce a patented product without the consent of the patent owner. This is only allowed after the government has "made efforts to obtain authorization from the right holder on reasonable terms and conditions and that such efforts have not been successful within a reasonable period of time" or there is a "national emergency or other circumstances of extreme urgency or in cases of public non-commercial use."[109] The government must also pay the patent holder "adequate remuneration" for its infringement.[110] The threat of compulsory licensing can be an effective way to force companies to license their product to generics producers or other competitors, both preventing a monopoly on the product and providing access to generic medicines.

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[107] "Excessive Prices- United States", Working Party No. 2 on Competition and Regulation, OECD (2011), *available at* https://www.ftc.gov/sites/default/files/attachments/us-submissions-oecd-and-other-international-competition-fora/1110excessivepricesus.pdf.
[108] *U.S. v. Aluminum Co. of America*, 148 F.2d 416, 430 (2d Cir. 1945).
[109] TRIPS art. 31.
[110] *Id. a*rt. 31(h).

TPP Article 9.8(5) gives countries the ability to apply compulsory licenses and revoke patents, but this is possible only if there is a compulsory license, and follows the requirements of TRIPS article 31, as discussed above, and TPP Chapter 18. TPP Article 18.40 allows compulsory licensing as long as the government "do[es] not unreasonably conflict with a normal exploitation of the patent and do not unreasonably prejudice the legitimate interests of the patent owner…" Because these terms are so vague, they expose countries to ISDS litigation from companies claiming that the compulsory licensing "unreasonably prejudiced" their "legitimate interests."

a. Canada

In 1993, the federal government eliminated compulsory licensing. Brand-name drugs thus enjoyed all the protections afforded under the Patent Act. It is worth noting that compulsory licensing continued to be used in antitrust cases under the violation called "abuse of patent right."[111] In this regime, the generic would have to pay a royalty to the original patent owner as determined by regulations and the court.[112] The Patent Act defines a formula for calculating the royalty payable to the patent-holder when issuing a compulsory license for export. It uses a sliding scale based on the importing country's UN Human Development Index ranking with the maximum royalty at 4% of the total value of the contract between the generic manufacturer and the purchaser[113]

Even with this compensation regime in place, the draft TPP provisions might leave open potential ICSID litigation. TPP Article 18.40 allows parties to issue a compulsory license as long as it does not "unreasonably conflict with a normal exploitation" or "prejudice the legitimate

[111] Constance Too, et al. *supra note 77*.
[112] Parliament of Canada, "An Act to Amend the Patent Act and the Food and Drugs Act (The Jean Chrétien Pledge to Africa)", Article 21.80 (1)-(4), (2004), *available at* http://www.parl.ca/DocumentViewer/en/37-3/bill/C-9/royal-assent/page-19#ida1tyoh.
[113] Richard Elliot, "Global Access to Medicines: Canada's law on compulsory licensing for export", Canadian HIV/AIDS Legal Network *available at* http://www.aidslaw.ca/site/wp-content/uploads/2013/04/RE_compulsorylicensing.pdf.

interests of patent owners." These vague terms may encourage foreign patent owners to claim that current royalty rates "conflict with a normal exploitation" and undermine their "legitimate interests," especially if the foreign patent owner planned to export its patent to a developing country with higher returns than what they receive through royalties.

b. Mexico

Any person can request a compulsory license from the Mexican Institute of Industrial Property (IMPI),[114] when a patent has not been used within three years starting from the date of grant of the patent or four years from the filing date, whichever is later, unless there are justified reasons for the non-use.[115] A party applying for a compulsory license must have the technical and economic capacity to efficiently work the patented invention.[116] Before the grant of the first compulsory license, the IMPI will provide the patentee with the opportunity to begin working the patent within one year from the date of personal notification provided.[117] Following a hearing with the parties, the IMPI will decide whether to grant a compulsory license. If the IMPI grants one, it will set out its duration, conditions, field of application, and the amount of royalties to be paid to the patent holder. The royalties must be fair and reasonable, and are established by the IMPI after a hearing with the parties. No compulsory licenses have been given in recent years.[118]

If Mexico were to being issuing compulsory licenses again, the government would risk challenges through ICSID for not providing sufficient payment if the investor considered it interfering with its "normal exploitation" of the patent rather than just "adequate remuneration" as required by TRIPS within the WTO.

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[114] Alejandro Luna, Armando Arenas, and Karla Paulina Olvera Acevedo, "Pharmaceutical IP and competition law in Mexico: overview," Thompson Reuters Practical Law (2017).
[115] *Id.*
[116] *Id.*
[117] *Id.*
[118] *Id.*

c. United States

When issuing compulsory licenses, the United States waives its sovereign immunity so that patent holders can sue them in court for compensation because of a government taking. Under 28 U.S.C. § 1498, the government does not have to seek a license or negotiate for use of a patent or copyright. Any federal employee can use or authorize the use of a patent or a copyright. The patent owner is entitled to compensation, but cannot enjoin the government or a third party authorized by the government to prevent use of the patent. Any contractor, subcontractor, person, firm, or corporation who receives authorization from the federal government to use patents or copyrights cannot be sued for infringement.[119]

An enhanced IP chapter would likely create a chilling effect on any use of compulsory licenses. Furthermore, depending on the remedy made by local courts, the foreign investor could aim sue because the payment for the taking still sufficient interfered with the "normal exploitation" of the patent. As with Mexico, it would be open to ISDS from investors, rather than just States.

V. Regulatory review exceptions: Bolar Exemption

Bolar exemptions allow pharmaceutical manufacturers to research and perform tests in preparation for an application for regulatory approval while being exempt from liability for infringing on a patent. This allows manufacturers to create generics before patents expire. Otherwise a generic competitor would only be able to start its bioequivalence and other testing after patent expiry, which would result in the de facto extension of patent protection.

NAFTA does not include a regulatory review (Bolar exemption), but all three countries have such exemptions in their domestic laws. TPP Article 18.49 says that "Without prejudice to

[119] 28 U.S.C. § 1498(a).

the scope of, and consistent with, Article 18.40 (Exceptions), each Party shall adopt or maintain a regulatory review exception for pharmaceutical products." By using the word *shall*, TPP makes Bolar exemptions mandatory in domestic law, a positive measure that enables faster market entry for generics.

In a landmark WTO case, the European Union challenged the Canadian Patent Act article 55.2 that stated, inter alia, that "[i]t is not an infringement of a patent for any person to make, construct, use or sell the patented invention solely for uses reasonably related to the development and submission of information required under the law of Canada, a province or a country other than Canada that regulates the manufacture, construction, use or sale of any product."[120] The European Union argued that this exception violated Article 28.1 of TRIPS, which gives patent owners exclusive rights "to prevent third parties not having the owner's consent from the acts of: making, using, offering for sale, selling, or importing for these purposes that product."[121] Canada defended Article 55.2, arguing that it is a "limited exception" to the exclusive rights conferred by a patent within the meaning of Article 30 of the TRIPS Agreement.[122] Article 30 says that, "Members may provide limited exceptions to the exclusive rights conferred by a patent, provided that such exceptions do not unreasonably conflict with a normal exploitation of the patent and do not unreasonably prejudice the legitimate interests of the patent owner, taking account of the legitimate interests of third parties."[123]

The Panel found that as long as the exception is confined to conduct needed to comply with the requirements of the regulatory approval process and no commercial use is made of resulting final products, the regulatory approval exception is a "limited exception," even though

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[120] Canada Patent Protection of Pharmaceutical Products: Complaint by the European Communities and their member States. WTO Panel Report, 2000.
[121] *Id.*
[122] *Id.*
[123] TRIPS art. 30

the approval processes may require substantial amounts of test production to demonstrate reliable manufacturing.[124] This is also a crucial finding because it deters countries from bringing breach of legitimate expectation claims to ISDS for Bolar exemptions, as the WTO has found that such exemptions do not breach legitimate expectations. Having been firmly grounded in WTO law, the Bolar exception has been maintained by many countries in their patent legislation. With such an exemption being read into TRIPS, it is important for the legacy to be carried forward and formally codified in NAFTA 2.0, the old text of which did not have a regulatory review exemption. Although the three countries have their own domestic legislative (or in the case of Mexico, administrative) provisions governing this, it is important for it to be present in NAFTA 2.0 especially because of the certainty it would bring in the ambiguous space it currently occupies in Mexico.

a. United States

The United States' Bolar exemption is found in §271(e)(1) of the Hatch-Waxman Act: "it shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or biological products."[125]

The scope of this exemption fluctuates, but most recently has been interpreted expansively. In 2012, the Federal Circuit held that the exemption applies to post-approval "submissions that are required to maintain FDA approval."[126] This holding extends the

[124] Canada Patent Protection of Pharmaceutical Products: Complaint by the European Communities and their member States. WTO Panel Report, 2000.
[125] Hatch-Waxman Act § 271(e)(1).
[126] *Momenta Pharmaceuticals, Inc. And Sandoz, Inc. v. Amphastar Pharmaceuticals, Inc., International Medication Systems, Ltd., Watson Pharmaceuticals, Inc., And Watson Pharma, Inc.,* US Court of Appeals for the Federal Circuit, decided August 3, 2012.

exemption beyond its text to protect acts that are not necessary for regulatory approval of generic drugs. While this is a win for public health advocates, the parameters of this exemption are often challenged. The lack of clarity around this rule constantly exposes manufacturers to litigation. Therefore, NAFTA 2.0 should include a Bolar exemption with clear limits, putting an end to the constant stream of litigation regarding this issue in the United States.

b. Canada

Under Section 55.2(1) of the Patent Act, "[i]t is not an infringement of a patent for any person to make, construct, use or sell the patented invention solely for uses reasonably related to the development and submission of information required under any law in Canada, a province or a country other than Canada that regulates the manufacture, construction, use or sale of any product."[127] Canadian courts have interpreted this exemption to apply only when a patented invention is used for the development and submission of information required by a regulatory authority.[128] As in the United States, Canadian courts have extended the Bolar exemption to encompass material that is not submitted to a regulatory authority but is subject to potential inspection, including samples and data stored pursuant to regulatory requirements.

c. Mexico

The IMPI (abbreviation for the Mexican Institute of Industrial Property, which is the patent and trademark administration body of Mexico) has applied the Bolar-like exemptions with some flaws in its interpretation and scope. For example, the IMPI determined that if brokers or third parties imported the patented products, the Bolar-like exemption does not apply and there will be a finding of patent infringement. In contrast, if the manufacturer imports the product, the

[127] Canadian Patent Act § 55.2(1).
[128] Anthony Tridico, Partner, Jeffrey Jacobstein, Associate, and Leythem Wall, "Facilitating generic drug manufacturing: Bolar exemptions worldwide" WIPO Magazine, June 2014, *available at* http://www.wipo.int/wipo_magazine/en/2014/03/article_0004.html.

exemption applies and there will be no finding of patent infringement. In both situations, the IMPI disregards the amount of the imported product. Currently, these cases are under debate at the Mexican Supreme Court. The few cases in which this exemption has been litigated have some flaws in terms of the understanding of the facts and applicable procedural rules. For example, IMPI determined that the burden was on the plaintiff in a patent infringement action to prove that the amount of patented product exceeded amount needed to obtain regulatory approval. Given the fact that the Bolar Exemption is meant as an exception to patent infringement, the burden would typically be on the defendant to show that the exemption has not been misused, but these interpretations of the Mexican authorities have led to some debate about the content as well as scope of the exemption.

COFEPRIS (which is the abbreviation for the Federal Commission for the Protection against Sanitary Risk which is a regulatory body of the Mexican government) is in charge of granting approval of imports of active pharmaceutical ingredients (APIs), which is mandatory before Mexican Customs. However, neither the wording of the exemption nor the rules governing the importation of APIs clearly address the amount of API that can be imported by an applicant of a follow-on product for the purposes of conducting the tests needed to obtain marketing approval. Neither IMPI nor COFEPRIS have published their opinion regarding whether the Bolar exemption allows for the importation of only small quantities of APIs for the purposes of conducting the tests and trials necessary obtain market approval. This has led to circumstances where unauthorized parties received approval from COFEPRIS to import large amounts (e.g., 4 kilograms) of patented APIs far beyond the small amounts necessary to conduct pilot production and testing.

In most instances, the approvals by COFEPRIS for importation of large amounts of patented APIs are for those APIs where the patents are close to expiry. However, during the last four years, this trend has increased because parties manufacturing medicinal products in Mexico no longer have to have a facility physically located within Mexico. The removal of this requirement has significantly changed the pharmaceutical business in Mexico. Now, many small and medium foreign companies start their business in Mexico by: (1) entering into partnerships with pharmaceutical companies already established in Mexico; and (2) introducing their products via brokers and distributors.

Annex I Mexico Background

a. Economic Standing

Mexico is the second largest economy in Latin America, with a population of about 127.5 million and a per-capita income of approximately $9,040.[129] As of 2014, about 40% of the country lives below the poverty line.[130] Mexico is generally regarded as a developing country.

Box 1: Health-related TRIPS-plus rules and obligations in Mexico's IP code

Industrial Property Law

- Article 86-bis requires data exclusivity periods for as long as its treaty obligations require. Currently, this is five years.
- Article 70 allows applications for compulsory license applications three years after the date of grant of the patent or four years after the patent application and only where the patent has not been used.

b. Access to Medicines

In the 1990s, about half of Mexico's population lacked health insurance. Policymakers responded to this problem by establishing the Sistema de Protección Social en Salud (Seguro Popular). Seguro Popular sought to increase public funding by 1% each year for seven years in order to provide universal health insurance starting in 2010.[131] This goal has not been met, and 48.49% of the Mexican population is effectively unable to access health services.[132] Indigenous people are especially hard-hit, accounting for 20% of the extreme poor and suffering higher

[129] Poverty & Equity Data Portal, "Mexico", World Bank, *available at* http://povertydata.worldbank.org/poverty/country/MEX.
[130] *Id.*
[131] Julio Frenk, Octavio Gómez-Dantés and Felicia Marie Knaul, "The democratization of health in Mexico: financial innovations for universal coverage", World Health Organization (2011), *available at* http://www.who.int/bulletin/volumes/87/7/08-053199/en/.
[132] Juan Pablo Gutiérrez et al., "Advances in pediatrics", (2014), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4006670/.

levels of deprivation in health status and access to medical services.[133] In spite of a high poverty level, Mexico pays twenty times more than other Latin American countries for drugs, and even pays more than Canada and certain other OECD countries. This is arguably not so much a direct result of NAFTA as it is a result of domestic legislation implementing several TRIPS-Plus protections for the pharmaceutical industry.

c. Historical Position on IP Protection, and the impact of NAFTA 2.0

Mexico implemented NAFTA in 1994 and TRIPS in 1995. Despite originally implementing most public health safeguards to control the price of medicines in the 1990s, these safeguards have been rolled back due to domestic legislation implementing several TRIPS-plus provisions. Mexico has traditionally been keen to implement enhanced IP measures befitting a more developed country, hoping to increase pharmaceutical investment in its economy. However, there is no evidence that stronger IP rights in developing countries incentivize pharmaceutical companies to invest in developing treatments for diseases that are endemic in these countries.[134] Moreover, for developing countries, there is no relationship between patent protection and investment in research and development (R&D),[135] or between the adoption of data exclusivity and the amount of investment by the pharmaceutical industry in that country.[136]

The phenomenon of ever-increasing patent protection is a legacy of early pharmaceutical patents. The early and retroactive introduction of patents, along with broader economic policies introduced by NAFTA, fundamentally restructured the pharmaceutical industry in Mexico. Local

[133] "Poverty in Mexico : An Assessment of Conditions, Trends and Government Strategy", World Bank, (2004), *available at* http://documents.worldbank.org/curated/en/598621468050981885/pdf/311150ENGLISH0ME0Poverty0see0also0286120.pdf.
[134] Margaret Kyle and Anita McGahan, "Investments in pharmaceuticals before and after TRIPS", The National Bureau of Economic Research Working Paper No. 15468, (2009).
[135] Walter G. Park, "Intellectual Property Rights and International Innovation" Frontiers of Economics and Globalisation. Amsterdam: Elsevier, pg. 289–327 (2012).
[136] Mike Palmedo, "Do Pharmaceutical Firms Invest More Heavily in Countries with Data Exclusivity?" Currents International Trade Law Journal 21: 38–47 (2013).

firms closed, capabilities generated in the pre-TRIPS/NAFTA era were eliminated, and firms that survived were eventually taken over by foreign firms.

Early in the 2000s, the transnational sector engineered reforms to patent and health policies, strengthening their ability to control pharmaceutical markets. Yet as data exclusivity became a more pressing part of the international agenda, Mexican health authorities remained opposed. The transnational sector consistently complained about "insufficient" data protection in Mexico, asserting that this was an implicit violation of NAFTA and TRIPS, but the Health Secretariat and COFEPRIS refused to revise their regulations and practices. Unable to secure data exclusivity through either legislative or regulatory channels, AMIIF pursued a legal case, arguing that the grant of marketing authorization based on an originator firm's data violated constitutional law, and eventually secured an injunction against COFEPRIS. The judicial order essentially established a five-year period of data exclusivity, and in 2012 the health surveillance agency subsequently revised its regulations to comply. Later, when there seemed to be a wave of reform coming on to introduce pre-grant opposition for patents, the transnational sector was able to make sure that the most disagreeable proposals were taken off the table, significantly diluting the final version. The local pharmaceutical sector in Mexico, or what is left of it, is too weak to either secure revisions to the patent system or stand in the way of the transnational sector's efforts to further strengthen the benefits they enjoy. Policies have consequences; after the first changes in the 1990s, Mexico became a country in which tailoring the patent system became exceptionally difficult.

d. Relationship with the United States and Canada

While NAFTA itself cannot be said to be the reason for the increased standards of IP protection that Mexico has consistently adopted, it is a contributing factor. Much of Mexican

politics was different after the end of seventy years of single-party rule, but in the area of pharmaceutical patents, continuity was the order of the day. This period witnessed the consolidation of an "internationalist" pharmaceutical patent system in Mexico, featuring consistent catering to the demands of the transnational pharmaceutical sector and seemingly open-ended adoption of global "best practices." One seemingly obvious explanation for Mexico's policy trajectory, for example, may be the country's relationship with the United States. After all, Mexico's northern neighbor has not only been the principal leader of the global campaign to increase IP protection, but the U.S. is also Mexico's most important economic partner and its main export market. The close economic relationship between the two countries is solidified in the form of NAFTA, which includes a chapter dedicated to IP.

Annex II Canada Background

a. Economic Standing

Given its abundant natural resources, highly skilled labor force, and modern capital stock, Canada enjoyed solid economic growth from 1993 through 2007. The global economic crisis of 2007-08 moved the Canadian economy into a sharp recession by late 2008, and Ottawa posted its first fiscal deficit in 2009 after twelve years of surplus. Canada's major banks emerged from the financial crisis of 2008-09 among the strongest in the world, owing to the financial sector's tradition of conservative lending practices and strong capitalization. Since the fall in world oil prices in 2014, Canada has achieved modest economic growth."[137]

b. Access to Medicines

Access to medicine in Canada is overall quite high, with almost 80% of the public enrolled in either private or public health insurance. Public health plans have programs to cover individuals who are not normally able to receive affordable health insurance, such as patients with cancer or diabetes.

Prices are regulated by the Patented Medicines Prices Review Board, which sets out the maximum price for all patented medicines by comparing suggested prices with the price of existing medicines, and the price of the medicine in other countries, as well as the therapeutic value of the medicine. Health insurers are then able to further negotiate the cost with drug companies. In spite of this regime Canada pays more than all other OECD countries besides the United States and Mexico. In 2015, the average cost per-person for prescription medication was

[137] The World Factbook: CANADA, Central Intelligence Agency (2018), *available at* https://www.cia.gov/library/publications/the-world-factbook/geos/ca.html.

$158, and Canadians pay on average three to five times the price as other high-income countries for the same drugs.[138]

c. Relationship with the United States and Mexico

Canada's economy is heavily intertwined with the United States. Canada is the United States' second largest trading partner and its largest export market.[139] U.S. goods and services trade with Canada totaled an estimated $673.9 billion in 2017. Exports were $341.2 billion; imports were $332.8 billion. The U.S. goods and services trade surplus with Canada was $8.4 billion in 2017.[140]

The 1989 Canada-US Free Trade Agreement and the 1994 NAFTA dramatically increased trade and economic integration between the United States and Canada. They enjoy the world's most comprehensive and highly balanced bilateral trade and investment relationship, with merchandise trade of $544 billion in 2016, services trade of over $80 billion, and two-way investment stocks of nearly $700 billion. Over three-fourths of Canada's exports are destined for the United States each year. Canada is the largest foreign supplier of energy to the United States, including oil, natural gas, and electric power, and uranium imports.[141]

Canada and Mexico are each other's third largest trading partner, with two-way merchandise trade reaching over $37.8 billion in 2015. Canadian direct investment in Mexico reached over $14.8 billion (stock) in 2015, while Mexican direct investment in Canada totaled $1.4 billion (stock).[142]

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[138] "Canada pays more for prescription drugs than comparable countries: study", CTVNews (2017), *available at* https://www.ctvnews.ca/health/canada-pays-more-for-prescription-drugs-than-comparable-countries-study-1.3454056.
[139] *Id.*
[140] Canada United States Trade Representative, Countries & Regions | United States Trade Representative (2017), *available at* https://ustr.gov/countries-regions/americas/canada.
[141] "Foreign Affairs Trade and Development Canada", Embassy of Canada, (2016), http://www.canadainternational.gc.ca/mexico-mexique/canmex.aspx?lang=eng.
[142] *Id.*

d. Historical Position on IP Protection

"Canada took the lead on seeking amendments to the TPP's deeply problematic intellectual property chapter," wrote Michael Geist, a Canadian law professor. "The IP chapter largely reflected U.S. demands, and, with its exit from the TPP, an overhaul that more closely aligns the agreement to international standards was needed." These issues were included in the deal because major American companies rely on strict intellectual property rules to make money, and their interests set the terms for the American negotiating team. Without America making those demands in exchange for access to its markets, it no longer made economic sense for other countries to accept them, said Malcolm.[143] While Canada has vocally opposed certain provisions in TPP, it was already substantially in compliance with many of the provisions. Therefore, it is likely that Canada will agree to enhanced IP provisions in NAFTA renegotiations.

[143] Matt Peterson, "A Glimpse of a Canadian-Led International Order", The Atlantic, (2018), *available at* https://www.theatlantic.com/international/archive/2018/01/new-tpp/551405/.

Annex III United States of America Background

The U.S. domestic position on pharmaceutical patents:

The United States encourages high-risk research and development in the pharmaceuticals industry by ensuring strong intellectual property protection of pharmaceutical technologies domestically through a range of measures, including: (1) a relatively low standard of non-obviousness for patentability, and (2) the ability to extend the life of a patent beyond the standard term, and (3) data exclusivity.

Important legislations:

- Federal Food, Drug and Cosmetic Act
- Drug Price Competition and Patent Term Restoration Act (The Hatch-Waxman Act)

The US holds a very protectionist position as far as patent protection is concerned, and has several legislative carve-outs allowing for effective extension of the monopoly rights granted by IP rights:

1. Exclusivity periods: Exclusivity refers to certain delays and prohibitions on approval of competitor drugs available under the statute that attach upon approval of a drug or of certain supplements. Prospective generic manufacturers can submit an Abbreviated New Drug Application, an "ANDA", to seek approval of a drug equivalent to a reference drug already approved by the FDA.[144] The use of a patent holder's data and trial information, as well as samples of the actual drug to test for bioequivalence, are all exempt from an assertion of patent infringement when used for ANDA development.[145] When a generic drug maker files an ANDA, it must make one of four "certifications" to each of the

[144] 21 U.S.C. § 355(j) (2012).
[145] 35 U.S.C. § 271(e)(1) (2012).

patents the brand-name drug maker has listed for the medication in the Orange Book. The most contentious of these is the Paragraph IV certification, which alleges that the listed patent is either invalid or would not be infringed by the generic drug making the filing. This provision was intended for generic manufacturers to challenge weak patents and is treated as an artificial act of patent infringement. The patent holder must initiate litigation within 45 days of receiving notification from the ANDA applicant or risk the application being approved by the FDA. The incentive that the generic producer gets out of filing this application and having to fight the infringement suit brought by the patent holder is that if the generic producer does not lose the case, they will be entitled to 180 days of market exclusivity alongside the brand-name drug. This creates a duopoly consisting of the patent holder and the first generic applicant, and the exclusivity period is extremely lucrative, representing the large majority of the potential profits to be gained from generic entry. If the patent holder chooses to initiate litigation, a thirty-month stay is placed on generic approval, with the goal of allowing the infringement litigation to work through the courts while the FDA is reviewing the generic application. The generic application cannot be approved during the following thirty months, unless a court enters a final order declaring the patents at issue invalid, unenforceable, or not infringed.

2. Secondary patenting: Secondary patenting involves obtaining patents on features other than the original active drug ingredient, including secondary patents on alternate formulations of the drug or on methods of administration. Independent secondary patents on average add substantial time to the nominal patent terms enjoyed by drugs.[146] For

[146] For instance, the US patent on the active ingredient in the proton-pump inhibitor omeprazole (Prilosec) expired in April 2001, but the manufacturer received later-issued patents on the pill's coating that lasted until 2007 and beyond. Manufacturers seeking to market competing generic versions had to challenge these patents in court. The litigation

drugs that have chemical compound patents, secondary patents add on average between 4 and 5 years of additional nominal patent term.[147] Drugs that do not have chemical compound patents rely much more substantially on secondary patents for exclusivity: here, when there are secondary patents, they generate an average of 9 and 11 years of patent term beyond the standard data exclusivity period.

3. Patent linkages: Patent linkage is defined as "the practice of linking the granting of . . . any regulatory approval for a generic medicinal product to the status of a patent for the originator reference product."[148] For a generics manufacturer to overcome claims of infringement when seeking regulatory approval, the manufacturer must demonstrate that each patent listed in the register is invalid.[149] Thus, a company's ability to list many patents on a register imposes a significant burden on the generics manufacturer. This results in the delayed release of generics into the market as the manufacturers wait for the patents to expire before initiating the regulatory approval process. The US attempts to balance the consumer and industry interests through this, but this is frustrated by the patent term extension mechanism.
4. Patent term extensions: The Hatch-Waxman Act favors patent holders through a provision that provides for a form of patent-term extension for pioneer drugs known as patent-term restoration, which allows a pharmaceutical company to extend the term of its

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process helped further delay the release of competing versions. *See Astra Aktiebolag v. Andrx Pharmaceuticals*, 222 F. Supp. 2d 423 (S.D.N.Y. 2002).

[147] Amy Kapczynski, Chan Park, Bhaven Sampat, "Polymorphs and Prodrugs and Salts (Oh My!): An Empirical Analysis of "Secondary" Pharmaceutical Patents", *available at* https://doi.org/10.1371/journal.pone.0049470.

[147] Mabel Tsui, "Access to Medicine and the Dangers of Patent Linkage: Lessons from Bayer Corp. v. Union of India", 18(3) J. Law & Med. 577, 582 (2011).

[148] Mabel Tsui, "Access to Medicine and the Dangers of Patent Linkage: Lessons from Bayer Corp. v. Union of India", 18(3) J. Law & Med. 577, 582 (2011).

[149] Ron A. Bouchard et al., "The Pas de Deux of Pharmaceutical Regulation and Innovation: Who's Leading Whom?", 24 Berkeley Tech. L.J., 394-395 (2009).

patent for up to five years to compensate for lost time during the investigational new drug period and the new drug application review period.[150]

The US international position on pharmaceutical patents:

In the late 1990s, the US and other developed nations sought to negotiate higher levels of WTO IP. These efforts were met with organized resistance from developing countries, which not only contributed to the collapse of the Seattle Ministerial but later also prevented the confirmation of the flexibilities built into TRIPS via the Doha Declaration on TRIPS and Public Health and a prolonged Doha Round (including the failure of the Cancun Ministerial in 2003).

As a result of the strong and unwavering resistance, the US shifted its negotiating focus and sought to use bilateralism/regionalism to increase IPR by requiring FTA partners to implement TRIPS-Plus provisions in the following form:

(a) inclusion of new areas of IPRs; or

(b) implementation of more extensive levels or standards of IP protection than is required by TRIPS; or

(c) elimination of an option or flexibility available under TRIPS.

TRIPS-plus elements in US FTAs:

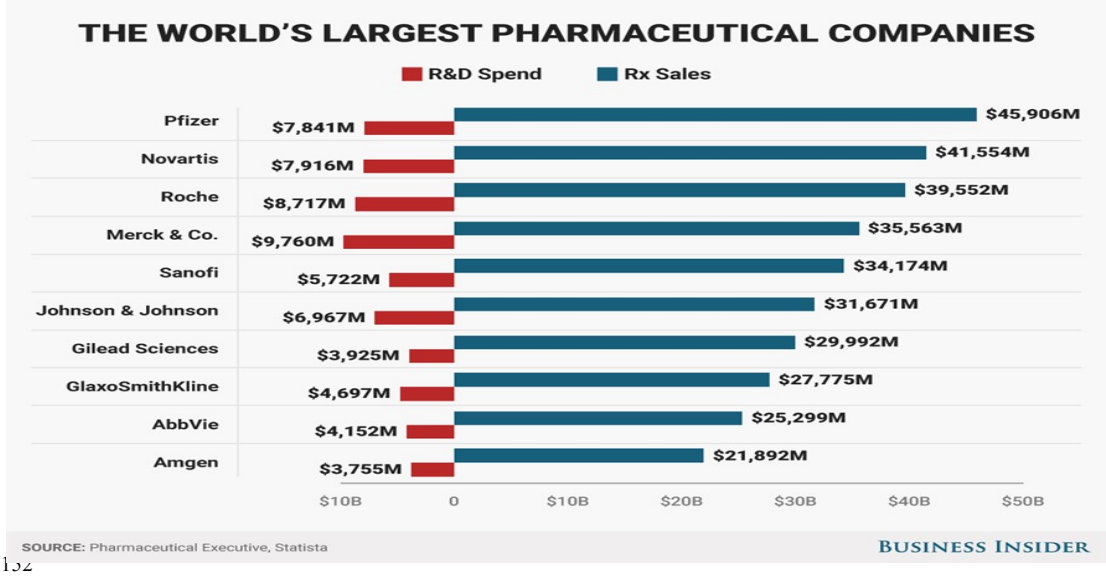
- Extensions to the scope of patentability
- Limits on patent revocation
- Patent term extension (restoration)
- Prohibition of parallel importation
- Linkage between patent status and regulatory approval
- Limitations on compulsory licensing
- Data protection, extended data protection and data exclusivity
- Obligatory accession to other multilateral IP agreements e.g. the Patent Cooperation Treaty

From the United States' standpoint, the switch to bilateralism has at least two benefits. By changing the forum and reducing the number of negotiating parties, the United States can

[150] 35 U.S.C. §156 (2006).

provide side payments that it would not be able to offer in a multilateral forum, given the diversity of interests the United States has vis-a-vis the contracting states. By switching to bilateralism, the United States can also prevent less developed countries from reopening the TRIPS negotiations with a better bargaining position.[151] Arguably, this has led to the US imposing its domestic standards of IP protection on other countries through its bilateral agreements, and the standards that it has typically held in such negotiations has been in line with its domestic standards.

Figure 4: The world's largest pharmaceutical companies



[152]

(Six of the world's ten largest pharmaceutical companies are American)

[151] P. Yu, "Intellectual Property at a Crossroads: The Use of the Past in Intellectual Property Jurisprudence: Currents and Crosscurrents in the International Intellectual Property Regime" 38 Loy LAL Rev, 323, 395, (2004).
[152] Lydia Ramsey, "Here's how much the 10 largest pharmaceutical companies spend on R&D", Business Insider (2017), *available at* http://nordic.businessinsider.com/largest-pharmaceutical-companies-by-prescription-sales-and-rd-2017-7/.

Annex V Cross-border Medicine Purchases

Due to fact that drug prices in Mexico and Canada are so much lower, one wonders whether it would be in the interest of American citizens to be able to buy similar pharmaceuticals as imports. If they could, this would have the potential of significantly reducing prices by both introducing low-priced competition into the United States and giving immediate relief from the low-priced foreign goods.

It is still illegal to order drugs from countries like Canada due to the Federal Food, Drug & Cosmetic Act (FDCA), 21 U.S.C. §§ 301-397, and the Medicare Prescription Drug, Improvement, and Modernization Act (MPDMA), 21 U.S.C. § 384, that prohibits the importation of prescription drugs from Canada by consumers.[153] Large volume importation of prescription drugs could be permitted under current law only if the Health and Human Services (HHS) Secretary was willing to certify that imported drugs "pose no additional risk to the public's health and safety, and result in a significant reduction in the cost of covered products to the American consumer."[154]

Most recently, Senator Bernie Sanders introduced a bill that would allow for the importation of prescription drugs from Canadian pharmacies, as long as they meet certain safety standards.[155] The Pharmaceutical Researchers and Manufacturers of America say drugs from other countries do not necessarily meet the U.S. safety standards and could "taint our medical supply."[156] The

[153] *Andrews v. U.S. Department of Health and Human Services*, Food Drug Cosm. L. Rep. P 3879228 USC 1498.
[154] 28 U.S.C. § 1498.
[155] Jessie Hellmann, "Sanders offers bill to allow purchase of prescription drugs from Canada", TheHill (2017), *available at* http://thehill.com/policy/healthcare/321597-sanders-introduces-bill-that-would-allow-the-purchase-of-drugs-from-canada.
[156] *Id.*

organization claims that "a large share of medicines that flow through Canada are counterfeit, and while it may seem safe to import medicines from developed countries like Canada and Western Europe, those medicines may have originated from countries all over the world."[157] This is somewhat suspect considering that those drugs would still need to meet approval within Canada's standards. Furthermore, if that is a concern, the bill can be altered to require approval by Canada's government. As such, regardless of where it originates, the drugs would still be up to the safety standards of developed nations.

[157] *Id.*