

An Evaluation of the Proposed PMPRB Amendments

Kristina M. L. Acri, née Lybecker



Contents

Special Note / i

Executive Summary / ii

1. Introduction / 1

2. Description of the Patented Medicine Prices Review Board (PMPRB) / 4

3. Description and History of the Proposed Changes / 6

4. Consequences for the Canadian Industry / 11

5. Consequences for Canadian Patients / 18

6. Global Consequences / 26

7. Conclusions / 33

References / 36

About the Author / 46

Acknowledgments / 46

Publishing Information / 47

Supporting the Fraser Institute / 48

Purpose, Funding, and Independence / 48

About the Fraser Institute / 49

Peer review—validating the accuracy of our research / 49

Editorial Advisory Board / 50

Special Note

On April 14, 2022, the Honourable Jean-Yves Duclos, Canadian Minister of Health, presented the most recent changes to the proposed Patented Medicines Prices Review Board (PMPRB) Amendments. The Statement (<https://www.canada.ca/en/health-canada/news/2022/04/statement-from-minister-of-health-on-the-coming-into-force-of-the-regulations-amending-the-patented-medicines-regulations.html>) announced that Health Canada will be moving forward with the implementation of a new basket of comparator countries, but that the government would not proceed with the Amendments related to the new price regulatory factors, nor with the requirements to file information net of all price adjustments. This is but the most recent change to the proposed changes that were first outlined in May 2017.

This study was originally written as an examination of the complete set of changes. It was authored shortly after the Patented Medicines Prices Review Board (PMPRB) announced a fourth delay in enacting the proposed changes to the new Guidelines which, like the amendments to the *Patented Medicines Regulations*, came into effect on July 1, 2022. The changes were designed and are expected to drastically reduce drug prices, potentially more than 60 percent for some medicines.

The original set of changes would have had significant consequences, for the Canadian market and for the international community. While the proposed Amendments are no longer being considered, it is still worth reflecting on the consequences they would have unleashed in Canada. Essentially, the now-shelved changes (1) would have provided additional price regulatory factors and reporting requirements related to the new factors of pharmacoeconomic value and market size, and (2) would have allowed the PMPRB to collect price and revenue information net of third party rebates. With this in mind, it is unsurprising that the majority of the proposed Amendments were scrapped in April. This study considers both the national impact and the global effect. In Canada, government policies and regulations implemented over many years have created an environment hostile to biopharmaceutical research and innovation. The new basket of comparator countries is current evidence of the continuation of these policies.

The COVID-19 pandemic brought this into sharp focus, highlighting the lack of domestic investment in the biopharmaceutical sector. Specifically, it is worth noting that Canadians had relatively rapid access to COVID vaccines and drugs because they were exempted from PMPRB scrutiny. The regulatory changes would have discouraged innovators from launching new products in the Canadian market, increased cost containment measures, and maintained the inadequate intellectual property protections in the biopharmaceutical sector. In the international context, Canada's efforts to reduce drug prices serve to reduce the incentives to innovate, develop, and manufacture new medicines, treatments, and cures. Arguably, these changes negate Canada's responsibility to bear a proportional fraction of global research and development financing for biopharmaceutical innovation.

The pandemic demonstrated that a thriving biopharmaceutical industry is more important than ever. For Canada to support and embrace the biopharmaceutical sector and establish Canada as a frontrunner in drug development and vaccine production, it must embrace an environment that encourages and incentivizes biomedical innovation. The revision of the PMPRB Amendments is a step in the right direction.

Executive Summary

In May 2017, Health Canada proposed an amendment to Patented Medicine Prices Review Board (PMPRB) regulations governing patented medicines. On December 23, 2021, for the fourth time, it was announced that changes to the PMPRB regime, contained in pending amendments to the *Patented Medicines Regulations*, would be delayed. The amendments that would have formed the basis for new PMPRB *Guidelines* would not have gone into effect until July 1, 2022. Then, on April 14, 2022, the proposed Amendments were changed again. Health Canada announced that they will be moving forward with the implementation of a new basket of comparator countries and reduced reporting requirements for those medicines at lowest risk of excessive pricing, [1] but that the government would not proceed with the Amendments related to the new price regulatory factors, nor with the requirements to file information net of all price adjustments. The proposed amendments had been designed to drastically reduce list prices of new medicines deemed unreasonable by the PMPRB and the government. However, the new price level would have been unsustainable and would have drastically diminished Canada's attractiveness as a market for new medicines.

The 1987 amendments to the Patent Act that created the PMPRB reflected a thoughtful balance across several policy objectives, protecting consumers from excessive patented medicines prices, while ensuring sufficient incentives for patentees to introduce new medicines to Canada. In striking contrast, the proposed changes were limited solely to lowering patented drug prices. As a result, the aforementioned policy balance is put at risk. The proposed amendments threaten to reduce investment in the Canadian biopharmaceutical industry and disincentivize innovative drug launches in Canada, potentially deprioritizing Canada in the global launch sequences for new drugs. In addition, the increasing reporting requirements represent an unnecessary regulatory burden and would increase the time to achieve public reimbursement.

Treatments and cures that benefit patients and society are valuable, but they don't come cheap. Innovative biopharmaceutical firms must cover their costs of production, development, and also of *failed* drug development programs. Innovation, from research and development to product testing, is expensive, difficult, risky, and time consuming. It requires incentives which profits provide. Fundamentally, the economics are straightforward: increased profit leads to an increase in investment which leads to an increase in

[1] Specifically, the reduced requirements are described as: "Reducing patentee reporting obligations for medicines at the lowest risk of excessive pricing, including all veterinary medicines, an expanded subset of medicines that do not require a prescription and certain 'generic' medicines, so that the PMPRB can focus its attention and resources on medicines at greater risk of excessive pricing." <<https://canadagazette.gc.ca/rp-pr/p2/2019/2019-08-21/html/sor-dors298-eng.html>>

research and development which leads to an increase in employment, innovation, and the creation of treatments and cures.

Reducing drug prices, as the proposed PMPRB regulations would have mandated, translates into reduced revenues and reduced innovation. Accordingly, the proposed changes would have reduced the financial capacity of patentees to invest in the Canadian life sciences sector and will result in reduced innovation and fewer drugs in development. The proposed changes to the PMPRB would also have the potential to exacerbate the launch delays already seen in the Canadian market.

Not only were the amendments unwarranted, but the consequences could inflict real harm. These changes had the potential to impact the trajectory and scale of biopharmaceutical research and development, global drug prices, international trade agreements, and the public good that is biomedical technology. The concern for undermining innovation in the Canadian biopharmaceutical industry is real and justified. While the modification in reference pricing comparator countries is a simple, albeit short-sighted, change, the totality of the proposed regulations would have been undeniably burdensome, adding greater complexity to a pharmaceutical policy environment that's already burdened with barriers that manufacturers must overcome to make their medicines accessible to a majority of Canadian patients.

This evaluation of the proposed PMPRB amendments and the potential consequences makes clear that the narrative that justified the changes was unfounded. Moreover, the proposed regulatory changes would have fundamentally altered the role and responsibilities of the PMPRB, in ways that would have been harmful to Canadian patients, the industry and innovation. The new policies would have likely reduced Canadian patients' access to medicine, stymied the biopharmaceutical industry's incentive to innovate and decreased the jobs and income generated in the life sciences sector. The regulations would have served to exacerbate the free riding problem that characterizes global research and development in the biopharmaceutical industry and the pharmaceutical pricing policies would have further complicated future negotiations of international trade agreements. Rather than bolstering the Canadian healthcare system, the proposed changes would only have served to undermine it. Accordingly, it is unsurprising that the majority of the proposed changes were abandoned.

1. Introduction

In May 2017, Health Canada proposed an amendment to Patented Medicine Prices Review Board (PMPRB) regulations governing patented medicines. On December 23, 2021, for the fourth time, it was announced that changes to the PMPRB regime, contained in pending amendments to the Patented Medicines Regulations, would be delayed. The amendments that form the basis for new PMPRB Guidelines would not go into effect until July 1, 2022. Then, on April 14, 2022, the proposed Amendments were changed again. Health Canada announced that they will be moving forward with the implementation of a new basket of comparator countries and reduced reporting requirements for those medicines at lowest risk of excessive pricing, but that the government would not proceed with the Amendments related to the new price regulatory factors, nor with the requirements to file information net of all price adjustments. The proposed amendments had been designed to drastically reduce list prices of new medicines deemed unreasonable by the PMPRB and the government. However, the new price level would have been unsustainable and would have drastically diminished Canada's attractiveness as a market for new medicines.

This study examines the complete set of original Amendments, which would have had significant consequences for the Canadian market and for the international community. While many of the proposed Amendments are no longer being considered, it is still worth reflecting on the consequences they would have unleashed in Canada. This study considers both the national impact and the global effect. In Canada, government policies and regulations implemented over many years have created an environment hostile to biopharmaceutical research and innovation. The new basket of comparator countries and the recently abandoned amendments are current evidence of the continuation of these policies.

At the federal level, Canada regulates the prices of all patented medicines to ensure that the prices of patented drugs are not “excessive”. This extends to every patented drug, whether covered on an insurer's formulary or not. It is important to recognize the scope of this regulation: the prices of off-patent branded medicines are not regulated, and the regulations do not grant jurisdiction to regulate the prices of patented medicines throughout the distribution chain (from wholesaler to pharmacy to patient). Despite significant changes in the biopharmaceutical market, the regulations have not markedly changed in more than 30 years. The proposed amendments included five important changes to the regulations: economics-based price regulation factors, an update of the reference country basket set used for international price comparisons (now set to go into effect in July 2022), establishment of a complaints-based system of oversight for patented generic products, the pricing information required of patentees, and requirements for the provision of rebate and discount information on domestic prices. This was the first time that the Canadian government moved to amend the drug pricing regulations, which were

intended to reverse the trend of recent increases in drug spending. According to CIHI, drug spending increased from 15.0 percent of total health expenditures in 1998 to 15.6 percent in 2017. The peak was reached in 2010 (16.8 percent). To put this in perspective, it is important to recognize the main source of increase in drug spending does not come from prices, but from the volume of prescriptions and the number of prescriptions per person.

The 1987 amendments that created the PMPRB reflected a thoughtful balance across several policy objectives, protecting consumers from excessive patented medicines prices, while ensuring sufficient incentives for patentees to introduce new medicines to Canada. According to the Patent Act, the PMPRB has a dual mandate:

- *Regulatory*: To ensure that the prices charged by patentees for patented medicines sold in Canada are not excessive; and
- *Reporting*: To report on pharmaceutical trends and on the research and development (R&D) spending by patentees.

In striking contrast, the proposed changes were limited solely to lowering patented drug prices. As a result, the aforementioned policy balance was put at risk. The proposed amendments threatened to reduce investment in the Canadian biopharmaceutical industry and disincentivize innovative drug launches in Canada, potentially deprioritizing Canada in the global launch sequences for new drugs. In addition, the increasing reporting requirements represented an unnecessary regulatory burden that would increase the time to achieve public reimbursement.

There was significant debate in Canada over the proposed changes, with both advocates and detractors taking strong positions. Those supporting the changes note that the new regulations would have forcefully and significantly lowered biopharmaceutical prices. This serves to remedy industry changes that have essentially usurped the PMPRB's management of the pharmaceutical marketplace. The collective, confidential negotiations between pharmaceutical suppliers and the federal and provincial governments have resulted in a shrunken pool of pricing data from which the PMPRB can draw its bureaucratic conclusions about what a drug "should" cost, not to mention untold delays in getting new drugs to Canadians. The proposed changes aimed to remedy this paucity of data by requiring disclosure of these confidential deals. Notably, they were found to be unconstitutional by both Quebec and federal courts (Owens, 2021). Advocates claimed that the proposed regulations would refocus the mandate of the PMPRB, to increase the affordability and access of drugs for Canadian patients.

In contrast, the Quebec government publicly (and fiercely) showed opposition to the reform. Reducing drug prices, as the proposed PMPRB regulations would mandate, translates into reduced revenues and reduced innovation. Treatments and cures that benefit patients and society are valuable, but they don't come cheap. Specifically, DiMasi, Grabowski, and Hansen (2016) report the average pre-tax development cost of 106 randomly selected new drugs to be about US\$2.9 billion per drug (2013 dollars). Innovative biopharmaceutical firms must cover their costs of production, development, and also

of failed drug development programs. Innovation, from research and development to product testing, is expensive, difficult, risky, and time consuming. It requires incentives and profits provide those incentives. Accordingly, the proposed changes would have reduced the financial capacity of patentees to invest in the Canadian life sciences sector and resulted in reduced innovation and fewer drugs in development. The proposed changes to the PMPRB also had the potential to exacerbate the launch delays already seen in the Canadian market.

This essay examines the potential consequences of many of the now-abandoned amendments as well as the new basket of comparator countries, focusing on the impacts on Canadian patients, the biopharmaceutical industry, and the global life science sector. The new policies would have likely reduced Canadian patients' access to medicine, stymied the biopharmaceutical industry's incentive to innovate, and decreased the jobs and income generated in the life sciences sector. The regulations would have served to exacerbate the free riding problem that characterizes global research and development in the biopharmaceutical industry and the pharmaceutical pricing policies would have further complicated future negotiations of international trade agreements. Rather than bolstering the Canadian healthcare system, the proposed changes would only have undermined it. While the changes announced in April 2022 will reduce the damaging impact of the changes, it is important to examine the new basket of comparator countries and its effects on the Canadian market.

2. Description of the Patented Medicine Prices Review Board (PMPRB)

The Patented Medicine Prices Review Board (PMPRB) describes itself as “an independent quasi-judicial body established by Parliament in 1987. The PMPRB has regulated prices of patented medicines in Canada for the last 34 years. The Board has a dual regulatory and reporting mandate: to ensure that prices at which patentees sell their patented medicines in Canada are not excessive; and to report on pharmaceutical trends of all medicines and on research and development spending by patentees” (PMPRB, 2021). Since its establishment, the PMPRB reflected a thoughtful balance between protecting Canadians from excessive patented medicines prices while simultaneously facilitating access to medicines by providing sufficient incentives [2] for innovators to introduce new drugs to Canada (Acri, 2021). At the federal level, Canada regulates the prices of *all* patented medicines, whether covered on an insurer’s formulary or not. The prices of off-patent branded medicines are not regulated, and the regulations do not grant jurisdiction over the prices of patented medicines through the distribution chain, from wholesaler to pharmacy to patient. A thorough description of the primary elements of the Canadian regulatory process for pharmaceuticals may be found in Acri (2018), including the role of the Patented Medicine Prices Review Board, the Board’s Regulatory Process, the Scientific Review Process, and the Price Review Process.

Canada’s Patented Medicine Prices Review Board carries out its mandate by conducting scientific and pricing reviews to determine the maximum list price at which a patented medicine may be sold. This scientific review is utilized to establish several important pieces of information: the primary indication, level of therapeutic improvement, and comparators of the patented medicine. With this, the PMPRB selects the appropriate maximum list price, while also comparing the Canadian price with the drug prices in seven OECD nations: Italy, France, Germany, Sweden, Switzerland, the United Kingdom, and the United States. The process aims to keep Canadian patented drug prices consistent with those in other countries (Humphries and Xie, 2019). The price ceiling in Canada is determined by the prices in these countries and the PMPRB’s assessment of the value of the medicine. It is worth noting that the PMPRB’s assessment of “value” is extremely restrictive, with few products being regarded as breakthroughs.

[2] The PMPRB sought to increase investment in biopharmaceutical research and development (to 10% of revenues) while simultaneously keeping prices affordable.

In 2016, the PMPRB began the process of modernizing its guidelines for regulating drug prices. Then in May of 2017, Health Canada presented the proposed update to the PMPRB regulations, noting that they have remained largely unchanged for more than 30 years. For the first time, the Canadian government was working to amend the drug pricing regulations and hoped to reverse the trend of increases in drug spending. According to CIHI, drug spending increased from 15.0% of total health expenditures in 1998 to 15.6% in 2017. The peak was reached in 2010 (16.8%). [3]

Health Canada acknowledged “the coupling of high Canadian patented drug prices and record low investment in R&D has many questioning the effectiveness of the PMPRB” (PMPRB, 2016). The agency recognized that while Canada’s pharmaceutical prices are at the median of the seven OECD countries used by the PMPRB as comparator nations, Canada currently has the third-highest global prices for drugs. In addition, Canada is second in per-capita spending on drugs, trailing only the United States. This, however, paints an incomplete picture of the situation. That is, true net pricing data is unavailable and the majority of what is known about pharmaceutical pricing is based on pre-rebate pricing data. “This is a fairly serious limitation that could significantly distort our view of the evidence. Indeed, it seems likely that rebates are, in many cases, correlated with other variables we care about, like quantity, value, manufacturer market power, payer market power, and other related variables. To date, there have been relatively few rigorous solutions proposed to this problem” (Lakdawalla, 2018). While Lakdawalla’s evidence brings into question the validity of the global price ranking, the argument should not affect the evidence of Canada’s high per-capita spending figures.

As further described by Boothe (2018), “[w]hen comparing drug prices internationally, we should understand that the PMPRB uses ‘list’ prices, similar to the ‘sticker’ prices on new cars. Like new cars, the price of drugs is negotiated between sellers and purchasers and is not transparent. Drug manufacturers offer purchasers confidential discounts in exchange for listing their drugs. Larger purchasers (such as governments purchasing for an entire country) can negotiate better prices. Confidential price negotiations likely widen the gap between drug prices in Canada and countries like the United Kingdom and Australia, because smaller provincial drug plans have less negotiating power and the discounts they get only apply to people who are covered by public plans.”

[3] It is important to recognize that CIHI includes ALL drugs – patented and generic Rx drugs as well as non-prescription drugs.

3. Description and History of the Proposed Changes

In May 2017, Health Canada proposed an amendment to PMPRB regulations governing patented medicines. As envisioned at the time, the amendment would include five major changes, listed below. With recent revisions, only two of the five proposed amendments will take effect on 1 July, 2022: the adoption of a new basket of comparator countries, and reduced reporting requirements for those medicines at lowest risk of excessive pricing^[4] (items 2 and 3 in the list below).

- A mandate that the PMPRB use economic factors in its regulatory determinations, including a medicine’s pharmacoeconomic value (that is, calculating the cost-per quality-adjusted life year (QALY) of the drug for comparison against an explicit cost effectiveness threshold), and price reductions based on market size to determine if a pharmaceutical price is excessive. ^[5] Patented drugs priced higher than their computed pharmacoeconomic value would be subject to dramatic price cuts.
- A change in the mix and the number of reference countries used for price comparison, amending the list of countries used for international price comparisons to include 11 countries (Australia, Belgium, France, Germany, Italy, Japan, the Netherlands, Norway, Spain, Sweden, United Kingdom) and remove the United States and Switzerland as comparator nations. This removes the high-cost countries, replacing them with low-cost countries, essentially lowering the price calculated by Canada for comparison.

[4] See <<https://www.canada.ca/en/patented-medicine-prices-review/services/consultations/notice-comment-price-review-approach.html>>.

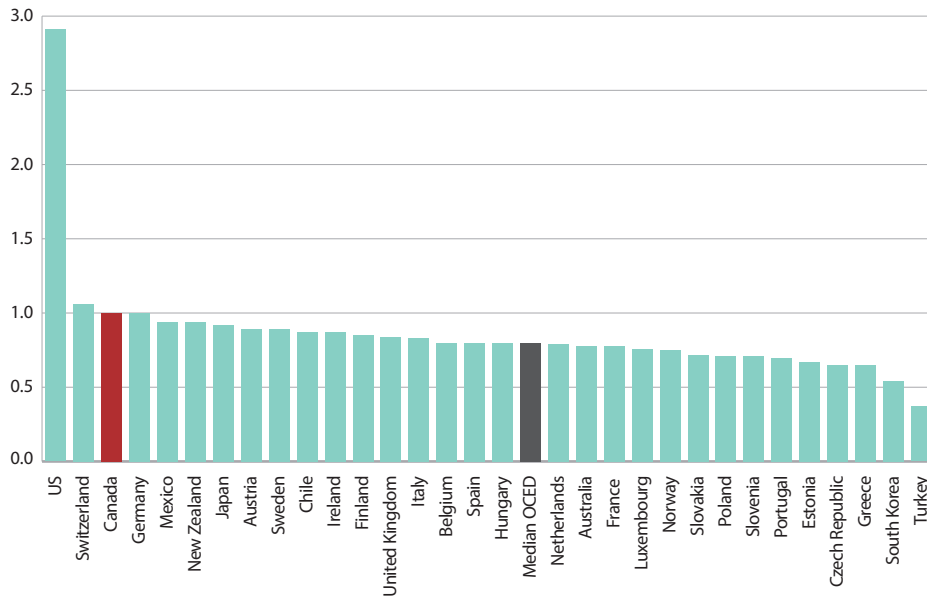
[5] Canada’s Patented Medicine Prices Review Board carries out their mandate by conducting scientific and pricing reviews to determine the maximum list price at which a patented medicine may be sold while also estimating its value. “In performing the delicate balancing act between these objectives, public plan administrators are increasingly appealing to some form of pharmaco-economic evaluation when justifying a decision to not cover a drug. The approach most commonly used today is cost utility analysis (CUA), a methodology that uses data from randomized controlled clinical trials and other sources to measure the health gains and costs of a new drug vis-a-vis that of the drugs (or other health interventions) currently used ... CUA remains controversial, especially with respect to how the PMPRB should use it in price regulation. As well, it has many methodological issues that are far from settled” (Blomqvist and Grootendorst, 2021).

- Reduce the regulatory burden for generic drugs by removing the requirement to systematically identify and report the price of these drugs, thus allowing the PMPRB to prioritize drugs at higher risk of monopoly pricing.
- Institute a reporting requirement to establish the information required on price, revenue, and research and development (R&D) expenditures.
- A requirement that patent holders disclose all third-party discounts and rebates rather than just the list price, providing the board the ability to assess whether the price of the medicine is reasonable when setting its ceiling. The guidelines also allow a 50% increase in the maximum rebate prices for drugs that treat rare diseases, to reflect the prevailing revenue premium these medicines currently realize over non-rare disease medicines. Rare diseases are those that are found in fewer than one in 2,000 Canadians.

The regulations would also impose profit controls on drug products with sales revenue exceeding defined thresholds (Skinner, 2021). Notably, the new legislation and regulations would have created two new drug categories, low priority drugs and high priority drugs. The PMPRB would classify drugs based on their anticipated impact on Canadian patients. The high priority drugs would be subjected to a more comprehensive price review (Paterson, 2020). On December 18, 2020, the Quebec Superior Court declared as unconstitutional the amendments that would have required price and revenue reporting to take into account confidential rebates provided to provincial payers. The PMPRB was hoping to use the MRP [Maximum Rebated Price] cap for drugs deemed at high risk of excessive pricing, taking into account the level of therapeutic improvement, and the pharmacoeconomic price. Mandating that companies disclose confidential rebates and discounts, considered “trade secrets” by biopharmaceutical companies, was a highly controversial strategy, essentially attempting to incorporate a value-based adjustment to setting price ceilings. A successful defense of the rebated price requirement would set a dangerous precedent for global International Reference Pricing programs (Labban, 2021). A more detailed description of the changes proposed by Health Canada in 2017 may be found in Acri (2018).

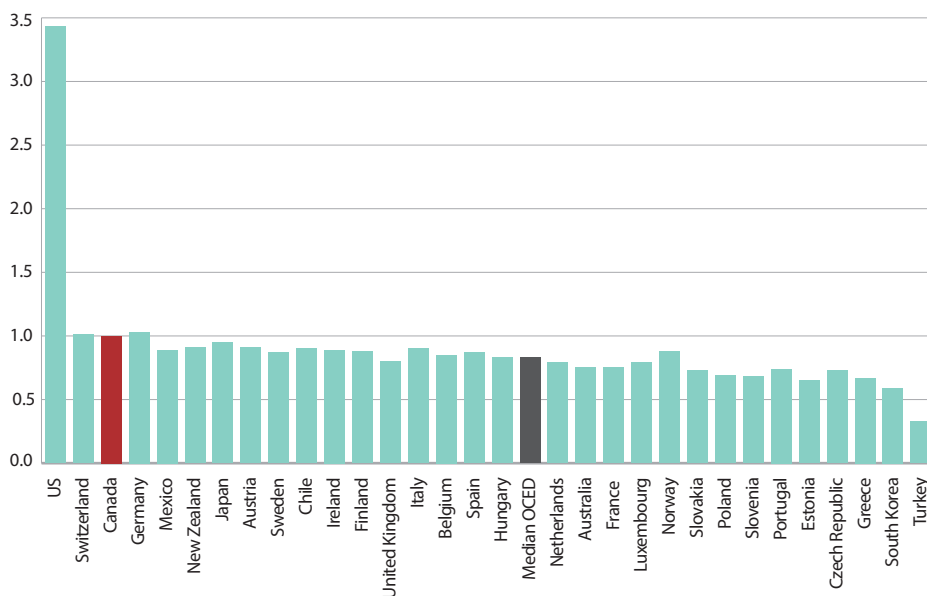
Historically, the PMPRB’s charge has been to work to ensure that Canadian drug prices are not excessive. Recent data from the seven (previous) and eleven (new) comparator countries indicates that Canadian prices are at the upper end of those price ratios, as depicted in **figures 1 and 2**.

Figure 1: Average Foreign to Canadian Price Ratios, Patented Drugs, OECD, 2016; PMPRB7 (previous comparator countries) listed in descending order



Source: Gastrointestinal Society, 2020.

Figure 2: Average Foreign to Canadian Price Ratios, Patented Drugs, OECD, 2018; PMPRB11 (new comparator countries)



Source: Gastrointestinal Society, 2020.

While this is what's presented in the 2020 annual report published by the PMPRB, these numbers should not be taken at face value, as there are many limitations with the PMPRB's price comparisons. Indeed, caution should be exercised when comparing the prices of pharmaceuticals between countries, especially when they differ in size and standard of living (as is the case among OECD countries). [6]

In August 2019 Health Canada introduced revised changes to the guidelines the PMPRB uses to set ceiling prices for new medicines. Health Canada estimated that under the new (2019) rules maximum prices allowed for some patented medicines could fall by 52%. [7] For a comprehensive description of how the amendments would be applied, please see the analysis provide by the Regulatory Affairs Professionals Society (Oakes, 2020).

On December 23, 2021, the Honorable Jean-Yves Duclos, Canada's Minister of Health, announced another delay in the coming-into-force of recent amendments to the Regulations Amending the Patented Medicines Regulations. The amendments to the Regulations were introduced in August 2019 and were set to take effect on July 1, 2020. The implementation was then pushed back until January 1, 2021, and then to July 1, 2021. They had most recently been scheduled to come-into-force on January 1, 2022. This most recent delay, the fourth, pushes that date back by six months, to July 1, 2022. The new Patented Medicine Prices Review Board Guidelines, which operationalize the Patented Medicines Regulations, were also expected to take effect at the same time.

Then, on 14 April, 2022, the Canadian Minister of Health presented additional changes to the proposed Patented Medicines Prices Review Board Amendments. The Statement announced that Health Canada will be moving forward with the implementation

[6] I am grateful to an anonymous reviewer for the information contained in this note. Researchers that have attempted to rank countries according to the magnitude of drug prices have encountered significant methodological difficulties and have very often found conflicting results. While the PMPRB concludes that Canadian prices are relatively higher than those in other developed countries, other studies show that Canada is among the most affordable countries in the world (Kanavos et al., 2013; Lichtenberg, 2011). There are multiple reasons for this phenomenon. International comparisons of pharmaceutical prices are complex because researchers must take into account many factors, including differences in the basket of pharma products in each country, the respective shares of generic and brand-name drugs, distribution and retail costs, exchange rate fluctuations and the purchasing power of different currencies, to name a few. In addition, information on real prices is limited in most countries. When it is available, this information paints a misleading picture that does not reflect true list prices for drugs, because of confidential rebates given to payers by drug companies. As a result, researchers are forced to acknowledge the limitations of their analyses and generally advice that their results on price comparisons be interpreted with caution.

[7] "One of the key amendments is changing the international reference pricing (IRP) formula for "grandfathered drugs" (or drugs already on the market before August 2019). Instead of setting a price ceiling based on the median international price (MIP), the PMPRB decided to use the highest international price (HIP) instead. This would still effectively lower list prices for grandfathered medicines by 5% on average and generate CAD4.6 billion in savings (a large bulk of the program's overall savings estimate)" (Labban, 2021).

of a new basket of comparator countries, but that the government would not proceed with the Amendments related to the new price regulatory factors, nor with the requirements to file information net of all price adjustments. While the proposed Amendments are no longer being considered, it is still worth reflecting on the consequences they would have unleashed in Canada.

4. Consequences for the Canadian Industry

Treatments and cures that benefit patients and society are valuable, but they don't come cheap. Innovative biopharmaceutical firms must cover their costs of production and development, and also cover the costs of *failed* drug development programs. Innovation, from research and development to product testing, is expensive, difficult, risky and time consuming. It requires incentives and profits provide those incentives. Fundamentally, the economics are straightforward: increased profit may result in an increase in investment which leads to an increase in research and development which leads to an increase in employment, innovation, and the creation of treatments and cures.

Put simply, firms introduce higher prices to induce greater profit which ultimately allows for more innovation and drug discoveries. [8] The protection of intellectual property rights granted by patents enables innovative pharmaceutical companies to temporarily raise prices above the level of production costs and realize economic profits to compensate for the tremendous investment—of time, talent, and funding—in pharmaceutical R&D, including R&D in failed drug development programs. According to a recent report published last year by the US Congressional Budget Office (2021), “[d]eveloping new drugs is a costly and uncertain process, and many potential drugs never make it to market. Only about 12 percent of drugs entering clinical trials are ultimately approved for introduction by the FDA.”

Reducing these prices, as the proposed PMPRB regulations would mandate, translates into reduced revenues and reduced innovation. Without this temporary protection, however, few if any pharmaceutical innovators would be willing to make these lengthy and risky investments. As described by Frank and Ginsburg (2017), “[t]here has been a variety of evidence assembled regarding the relationship between profitability and innovation in the pharmaceutical industry. One major strand of evidence involves natural experiments regarding industry responses to growth in the size of markets. The logic behind this quasi-experimental approach is simple: larger markets generate greater revenues that in turn create expectations of more profits to manufacturers, which expand investment in new drugs to pursue those profits.” Notably, a “recent study found that industry losses could be more than three times the government’s already worrisome estimate of an \$8.6 billion loss in revenue over 10 years (“net current value” so in fact much

[8] While firms will elect to raise prices to increase profits, it is not necessarily the case that higher prices generate more profits. It depends on the elasticity of demand, and available alternatives/competition. I am grateful to an anonymous reviewer for the suggestion to add this point.

higher when considering inflation and other factors)” (Critchley and Owens, 2018). [9] Accordingly, the proposed changes would have reduced the financial capacity of patentees to invest in the Canadian life sciences sector (Innovative Medicines Canada, 2018), the consequences of which would have resulted in reduced innovation and fewer drugs in development (Acri, 2018).

These potential outcomes are essentially driven by two sources of uncertainty: the uncertainty of the timing following the announcement of the proposal and the uncertainty surrounding the implementation of the regulatory changes and their consequences. Numerous industry executives warned the House of Commons health committee that “the regulations add an unreasonable administrative burden, leave companies mired in uncertainty about what they can charge for new medicines, and discourage investment in Canada” (Rabson, 2021). The uncertainty increases the stakes and risk faced by innovative firms, discouraging investment and product launches.

Biopharmaceutical price controls reduce investments in the research and development that generates new biopharmaceutical treatments and cures. Policies that reduce drug prices are attractive for consumers in the short run, making new products available at lower prices. However, this comes at the expense of innovators’ profits, which has long term consequences. Canadian patients are penalized when pharmaceutical research becomes unprofitable because it means that new innovations are not introduced. A drug that is *not launched* in Canada cannot be purchased at *any* price. The health benefits that are forgone can be extremely high. Philipson (2017) equates cost-containment strategies of public health care schemes to rate-of-return regulation, both with adverse implications for dynamic efficiency. That is, strict price regulations reduce the incentives for biopharmaceutical innovation. Consider that a 2005 study by Giacotto, Santerra, and Vernon demonstrates that biopharmaceutical research and development investment increases with real drug prices, holding constant the other determinants of R&D. The study estimates that a ten percent increase in the growth of real drug prices is associated with a nearly six percent increase in the growth of R&D intensity. [10]

[9] It is important to note that Critchley is a former executive director of the PMPRB (1990-2005).

[10] Admittedly, drugs are expensive, and their costs are increasing. Gliberman and Barua (2019) explore this at length: “Some note that this reflects the rising cost of developing new drug therapies, which should legitimately include the costs of development efforts that fail to produce new approved therapies. There are varying estimates of the costs associated with developing new drug therapies. For example, DiMasi, Grabowski, and Hansen (2016) report the average pre-tax cost of 106 randomly selected new drugs obtained from a survey of 10 pharmaceutical companies. They estimate pre- and post-approval R&D costs to be about US\$2.9 billion per drug (2013 dollars). Other industry experts argue that it now costs upwards of \$5 billion, on average, to invent a new medicine (Graham, 2014). Recent and prospective cost increases associated with developing new drugs reflect, in part, the emergence of personalized medicine. The latter is defined as the receipt of care conditional on the results of a biomarker-based diagnostic test (Garrison and Towse, 2017). To date, genetic-based therapies have been expensive to develop given the costs involved in identifying genetic markers and linking them to disease processes. Other features of the pharmaceutical industry have been implicated as factors contributing to increasing expenditures on drugs. For example, Bach (2015) highlights the fact that

This is nothing new. For many years, successive federal governments have created a pharmaceutical policy environment that discourages investment in innovations, pharmaceutical research, development, and manufacturing within Canada (Field, 2021; Lucas, 2020; Rawson et al., 2020). As described by Rawson and Adams (2021), the formative policies date back many decades. The proposed changes were just the most recent.

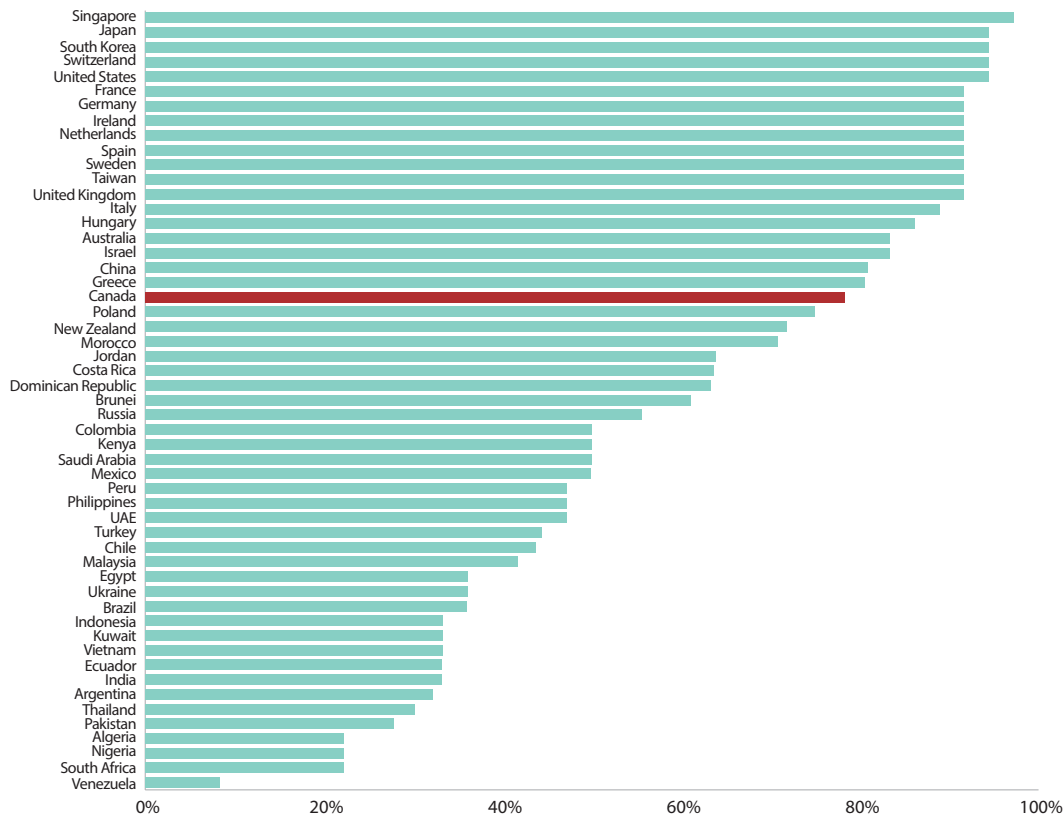
There have been and continue to be few Canadian world players in the pharmaceutical field. Most global companies have affiliates in Canada, but their footprint has decreased over many years, with manufacturing, research and high-paid jobs moving to other countries. The reasons for this brain-drain are numerous. They date back more than 50 years to the government of Pierre Trudeau and its move to eliminate pharmaceutical patents when it introduced compulsory licensing—a price control mechanism much-loved by anti-industry activists (Lexchin 2020)—with the aim of lowering drug prices and fostering a Canadian domestic industry. However, rather than encouraging a Canadian industry, this government policy choice resulted in the opposite. Several global brand-name companies closed their research centres in this country and the ill-considered policy of rewarding generic drug manufacturers led to the establishment of an oligopoly of these companies that perform little innovative research but accumulate great personal and corporate wealth by charging Canadians high generic prices. (Rawson and Adams, 2021)

The antipathy for the life science sector goes beyond research, development, and manufacturing. The would-be PMPRB guidelines and regulations would have disincentivized investment in a sector that already faces challenges. In particular, firms in the Canadian biopharmaceutical industry and life science sector take issue with Canadian intellectual property protections for the biopharmaceutical industry. As a summary measure, **figure 3**, places Canadian IP protections in a global context.

The problematic issues include: (1) the period of patent term restoration (also called “*sui generis* protection”); (2) weak enforcement of patents (e.g., no patent linkage right of appeal for innovators); (3) the duration and scope of regulatory data protection; and (4) the lack of an orphan drugs regime. Each of these is examined in turn in an earlier study by this author (Lybecker, 2017), which analyzes the specific weaknesses of Canadian legislation and how these elements measure up against other nations. These weaknesses have been documented and fully explored in numerous other studies as well (Owens, 2017; Raffoul, 2021; US Chamber of Commerce, 2021). The proposed Amendments only amplified the concerns of the industry.

expensive drugs are increasingly being introduced for conditions that affect large rather than small patient populations, thereby contributing to higher total costs incurred by insurers. He also mentions that the pace of conversion to generics or biosimilars (the generic version of biologic drugs) has been slowing in recent years, while the prices of many generic drugs have been increasing. A consequence is that drugs now account for upwards of 20 percent of health care expenditures (OECD, 2017).”

Figure 3: Patents, Related Rights, and Limitations, percentage available score



Source: US Chamber of Commerce, 2021: 47.

Unsurprisingly, the changes were derided by innovative pharmaceutical companies. Following the federal government's announcement of the changes, five multinational pharmaceutical companies filed a constitutional challenge to the changes to the Patented Medicines Prices Review Board (Merck & Co., Janssen Inc., Bayer, Boehringer Ingelheim Ltd, and Servier Inc.). As described in the previous section, the Quebec Superior Court declared as unconstitutional the amendments that would have required price and revenue reporting to take into account confidential rebates provided to provincial payers, though there is litigation that is still pending. Confidential rebates are important in this debate because of their impact on net prices. Behind the scenes, pharmaceutical companies, working with third parties, agree upon confidential rebates that reduce the price of the drug to insurers—called the net price—but rarely if ever do these rebates reduce the costs for the people actually buying medications. It clearly advantages the PMPRB to know what these rebates are, providing the board the ability to assess whether the price of the medicine is reasonable when setting its ceiling. However, forcing firms to reveal them could have, paradoxically, resulted in their elimination.

Those closest to the industry operations, and possibly in the best position to anticipate the impact of these new regulations, are the industry executives. As expected, they

had strong opinions about the multifaceted effects of the proposed changes. Life Sciences Ontario (LSO) commissioned a research study to explore the implications of the PMPRB changes on the pharmaceutical industry and life science organizations. The findings of the study confirmed that the changes would negatively impact business investments in Canada. All of the executives, 100 percent of them, believed that the PMPRB changes would negatively impact their overall business plans in Canada. The impacts would have been felt by firms of all sizes. According to one small Canadian company, “we have already been impacted, putting product extensions on hold because of the uncertainty. Our Global CEO visited Canada and articulated he doesn’t see Canada in the same way. There are trust issues ... Now we are seeing delays in decisions for Canada” (Research etc., 2020).

Of perhaps the greatest concern, industry executives repeatedly emphasized the impact on Canada’s global launch position. A variety of therapeutic areas would be impacted. While they noted that rare diseases immediately come to mind, they acknowledged that any patient that wants access to great new medicines would face the risk of waiting years to access them. The expected delay would be “potentially 1–3 years based on the impact of Canada’s price in other country’s reference-based pricing framework.” In addition, it is expected that “more decisions will be made to not launch at all vs delay because of the potential for broader harm to other larger markets.” This had the potential to also impact upcoming indications of currently approved products. That is, companies might elect not to launch in Canada. As evidence of this, one executive noted that “[w]e have delayed launch of two significant innovative products due to uncertainty around the regulatory environment and the lack of predictability and stability around establishing a fair price in Canada, planned significant expansion has been halted” (Research etc., 2020). This would play out through the industry’s revision of tiered launch waves. Historically, Canada was always considered a Tier 1 or Tier 2 nation, launched either with or just after US, Germany, and the UK. The proposed Amendments prompted an executive to state: “Now it will be several years later since there will be access challenges before you even get to reimbursement. We will move down to Tier 3 or 4, or even worse, not launched at all” (Research etc., 2020).

Patients would also feel the effects through the impact on clinical trials in Canada. The proposed regulatory changes would dismantle the world-class clinical trial network developed in Canada and limit the biopharmaceutical industry’s ability to invest. One executive noted that companies would “not do clinical trials for risk of having to keep patients on therapy in perpetuity without prospects of reimbursement at an acceptable price” (Research etc., 2020).

In addition, the structure of the Canadian industry would have been profoundly changed. Canada currently comprises 2–2.5% of the global biopharmaceutical market. It was estimated that this share would drop to 1–1.5%. The proposed changes prompted numerous concerns about the Canadian industry landscape. “There will be more layoffs, less investments, and fewer smaller companies going forward.” “We employ 250 high paying employees in Quebec alone, 35% are PhDs and 60% are Masters, all tax payers.

PMPRB threatens them plus another 300–400 suppliers which is 500–600 jobs in the next 3 years in Quebec alone, not to mention the impact on their families” (Research etc., 2020).

It is essential to recognize that these innovative therapies are life-changing for many patients and use a modest share of Canadian healthcare funding. Janssen (a pharmaceutical company of Johnson and Johnson) provided input to Health Canada noting the importance of innovation, stating “[t]he proposed PMPRB reforms may create barriers for multinational companies to maintain healthy levels of investment in Canada. This means that Canada would have less access to healthcare innovation; a key to leading to improvements in Canadians’ health. For example, innovative medicines help to extend patients’ lives and keep people out of hospitals, while using just 6.4% of overall healthcare spending in Canada” (Janssen, 2021).

While price controls are often cited as a contributing factor, Lexchin argues that “while there are drugs that are not sold in Canada, the reason is the relatively small Canadian market, not the price” (Lexchin, 2018). In reality, it is likely the combination of both price and market size that influence launch decisions. According to Suzanne Lepage, a private health plan strategist, “[g]lobally, we [Canadian patients] represent about two percent of the overall market and if the pricing model isn’t conducive to a company succeeding with their product they may just bypass Canada or delay Canada” (Rolfe, 2019).

The proposed changes would also have negatively affected other dimensions of the biopharmaceutical industry: investment in the life-sciences sector, employment, and clinical trials. The proposed regulatory changes would almost certainly have reduced investment in the pharmaceutical sector, Canada’s third leading industry in terms of R&D spending. Notably, this would reduce an already modest amount: pharmaceutical R&D investment in Canada is already comparatively low, 5% of sales in Canada as compared to 20% of sales in the UK (Boothe, 2018). [11] [12] The loss of revenue and investment would have a ripple effect on employment in the sector and clinical trials.

The heightened uncertainty and pending regulations impacted clinical trials as well. A recent Canadian Health Policy study (2021) found that the number of advanced

[11] It is important to recognize that the methodology used by the PMPRB is described as “outdated” by some analysts. A 2017 survey of Innovative Medicines Canada members (not all of whom reported) calculated that firms invested 9.97 percent of gross patented medicines revenue into a 21st century definition of R&D that is comparable to how R&D expenditures are reported in other OECD nations” (Field, 2021).

[12] Notably, the PMPRB only uses work eligible for the Scientific Research and Experimental Development (SR&ED) program. As Rawson and Owens (2022) point out, “[o]pponents, including the PMPRB, suggest that the current level of investment is less than four percent of revenues. Statistics Canada puts it as high as 9.5 percent; a more inclusive system would put it higher still. But squabbling over who’s right is an empty argument, pointless penny-pinching. What we need is not a primitive economy that extorts investment in exchange for political favours, but an attractive investment regime that would make Canada a welcoming host for innovation and economic growth.” Moreover, none take account of big pharma investing in star-ups that, if successful, they will buy.

clinical trials in Canada, which were consistent between 2015 and 2019, decreased by 26 percent in 2020. While this may have been impacted by COVID, the long planning horizon for such trials indicates this may be a sign that manufacturers were responding to the proposed legislation and do not intend to bring as many new medicines to Canada. These results confirm those of a study by Skinner (2019) that studied the correlation between industry-funded clinical trials and drug price levels across 31 OECD countries, controlling for differences in GDP and market size. Regression analysis found that price level was a statistically significant predictor of the number of industry-funded clinical trials. Further confirmation comes from a series of papers authored by Rawson (2020, 2021a, 2021b), who analyzed whether the pending introduction of the new PMPRB regulations and guidelines was associated with a decline in clinical trials activity in Canada. Results showed a striking decrease in Canadian clinical trials following the announcement of the regulatory changes.

In addition, industry executives candidly revealed significant concern surrounding the changes and the consequences that would follow for innovative firms and for patients. For the industry, the changes that would have been introduced with the proposed regulations would limit their financial capacity to invest in Canada while unnecessarily increasing the complexity of the regulatory mechanisms. In the context of the new basket of comparator countries that will be implemented, globally, the new reference country basket will significantly impact both the highest international price and the median international price comparison metrics. The change will lower the maximum allowable price, requiring pharmaceutical innovators to lower their prices in Canada in order to be in compliance, a factor that may be a further impetus for manufacturers to delay launches in Canada or decide not to launch at all. This is confirmed in a recent industry study that finds, “[b]ased on launch and reimbursement data from other countries, the changes would restrict access to new innovative medicines for Canadian patients. The proposed changes would greatly reduce patentee financial capacity to invest in Canada. They are also unnecessarily complex and would obstruct the effective functioning of mechanisms that Canadian payers already use to negotiate drug savings” (Innovative Medicines Canada, 2018). For patients, new product launches will likely be delayed even further than they already are (Barua, Westcott, and Vo, 2021). The impact felt by the industry may translate into real—potentially life or death—consequences for individuals and patients, as is explored more fully in the next section.

5. Consequences for Canadian Patients

While three of the five proposed regulations were abandoned, it is still essential to examine what the anticipated impact would have been for Canadian patients. Of particular interest are the ways in which patient access and affordability could have been affected. The proposed Amendments would have generated significant outcomes deserving tracking, and consequences that must be recognized and evaluated.

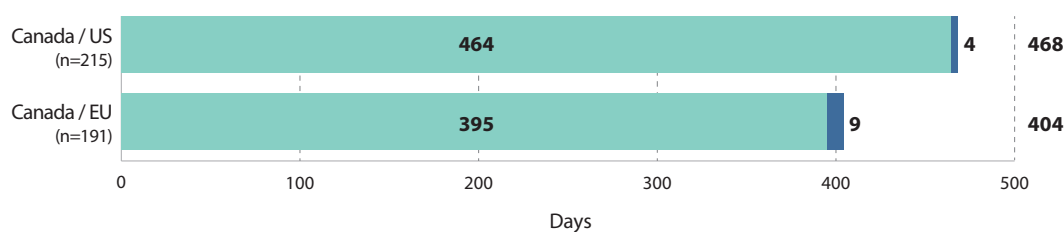
First, it is important to acknowledge that the proposed changes to the PMPRB would have exacerbated the existing launch delays seen in the Canadian market. A recent study from the Fraser Institute finds that new drug approvals in Canada currently lag behind both the United States (by 496 days) and the European Union (by 468 days). The delay in the availability of new drugs in one country in comparison with another will depend on two sources: a difference in approval time (efficiency) and a difference in when the drug was submitted for regulatory approval in the first place. These results are confirmed by Hoskyn (2020), establishing that the reason for delayed access in Canada can be traced to differences in the dates that manufacturers submitted new drugs to Health Canada for regulatory approval. Notably, once a drug has been submitted to the regulatory agencies, all three are fairly comparable in their efficiency in approving the submissions. The differences in submission dates account for more than 95 percent of the differences in the dates of ultimate approval (Barua, Westcott, and Vo, 2021). [13]

Barua, Westcott, and Vo (2021) posit that a number of factors may be responsible for the innovative biopharmaceutical firms' reluctance to launch new drugs in Canada. These may include "differences in market-investment attractiveness because of prevalent intellectual-property protection regimes, the size and sophistication of the potential market of consumers, regulatory controls on drug pricing, and the reimbursement policies practiced by public and private insurers. Another reason, more directly related to regulatory activities, is the extra financial burden incurred through user fees and the costs associated with creating a submission for a particular agency." In this context, it is notable that approved COVID-19 vaccines were effectively exempt from regular PMPRB pricing oversight, suggesting that the federal government is aware of the discouraging effect such restrictions have on innovation in the pharmaceutical industry.

Launch delays have significant consequences for patients. The reality is that Canadian patients are denied the health benefits of many medicines for months, if not years. A 2013 study found that more than 5,000 patients may have been adversely impacted by delayed federal regulatory and provincial reimbursement for just five oncology drugs

[13] It is important to also recognize that delays exist in coverage as well, once a drug has been launched in Canada. From 2012 and 2018, this delay was 407 days longer in Canada than that of the median of 20 OECD countries (519 days) (Hoskyn, 2020)

Figure 4: Average Difference (Days) in Submission and Efficiency in the United States and the European Union Compared to Canada, 2012/13 to 2018-19



Source: Barua, Westcott, and Vo, 2021.

between 2003 and 2011 (Rawson, 2013). Multiplying this harm across the hundreds of drugs with launch delays is chilling. Between 2012 and 2018, 223 new pharmaceutical therapies were approved by either the US Food and Drug Administration or the European Medicines Agency before Health Canada, a median of 383 (average 742) days earlier (Barua, Westcott, and Vo, 2021).

For many, timely access to innovative therapies and cures is the greatest concern. However, based on its own unpublished analysis of international evidence, Health Canada claimed that the proposed regulations and price tests would not delay drug launches in Canada, stating that “list prices do not appear to be an important determinant of medicine launch sequencing.” This claim, however, contradicts the existing literature on drug launch timing though it is important to recognize that the majority of existing studies date from the 1990s. Given this, Spicer and Grootendorst (2020) examine recent data on drug launches and patented drug list process for a collection of OECD countries to establish the impact of the PMPRB regulatory changes on drug launch delays in Canada.

The econometric analysis of Spicer and Grootendorst demonstrates that “price is a particularly important covariate, and the impact of price on drug launch across this group of countries is greater in the short term than in the long term, indicating that drug price controls will lead to drug launch delays. Though [their] methods and data sources differed, [their] findings are in alignment with previous studies on this topic” (Spicer and Grootendorst, 2020: 13). Specifically, their study finds:

If our results are correct, the degree to which launches will decrease in Canada will be determined by the magnitude of price decreases after the new PMPRB regulations are implemented in January 2021 ... we predict that a 25% price decrease will lead to a 6-10% and 6% decrease in drugs launched over 1- and 8-year periods, respectively. Moreover, a 45% price decrease will lead to a 13-22% and 13% decrease in drugs launched over these respective periods. The estimates from the 8-year model also suggests that after a drug list price decrease, some drugs will likely not launch in Canada. (Spicer and Grootendorst, 2020: 13)

According to the results of the July 2020 study, the launch timing could delay access to therapeutically important new drugs for some Canadian patients, harming them. [14] This finding is echoed in the responses of industry executives. When surveyed on the federal government’s proposed patented drug pricing rules, more than one third of pharmaceutical executives in Canada reveal their companies had already delayed launches of new medicines in Canada due to the uncertainty caused by the changes. According to executives from 43 large and small firms, “[v]irtually all (98%) said the policy will negatively impact their business plans and 94% said product launches will be delayed, most by at least a year or more.” In addition, 90% also reported that the pricing reforms would negatively impact investments in research, clinical trials, and innovation. Further, the results of the survey confirm 2020 data that revealed that “Canada’s access to new globally available drugs had declined by 40% in the year the pricing rules were adopted” (Life Sciences Ontario, 2021). Finally, in a systematic review of the literature, Labrie (2020) found 44 peer-reviewed studies that confirmed a significant negative relationship between drug price controls and the availability of innovative drugs or industry investment in pharmaceutical research and development.

Beyond launch delays, lack of access is also a threat to patient health and there is evidence that Canadian patient access to potentially life-saving biologic medicines is already comparatively limited. According to a recent study by the Fraser Institute:

[A]s of December 2018, the latest month of comparable available data, Canada has approved only 10 biosimilars, which are the biologic drug equivalent of a generic ‘small molecule’ drug, compared to 15 in the United States, 20 in Australia and 62 in the European Union ... The ability of drug companies to protect their intellectual property—for example, by using data exclusivity to prevent competing firms from utilizing proprietary testing data to produce generic versions of the drugs—is essential for incentivizing the development of biologics. These protections are particularly critical because biopharmaceutical innovations are easily copied and sold by competitors, eliminating the financial incentives that drive innovation. Unfortunately, Canada’s current intellectual property laws are weak compared to laws in other jurisdictions including the U.S. and EU. For example, Canada has one of the shortest terms of data exclusivity for pre-clinical and clinical trials. (Acri, 2021)

Despite the concerns surrounding launch delays, the PMPRB has rejected them, stating that “prices do not appear to be an important determinant of medicine launching

[14] However, the authors do acknowledge that most drugs currently entering the Canadian market offer only moderate or slight improvements. “From the period of 2010-2018, the PMPRB reports that 5% of 811 drugs evaluated by its Human Drug Advisory Panel were categorized as either a breakthrough drug (2.3%) or a drug offering a substantial improvement over other medicines in Canada (2.7%)” (Spicer and Grootendorst, 2020: 14).

sequencing” (Canada Gazette, 2019). This claim ignores an extensive body of academic work that finds just the opposite.

- Spicer and Grootendorst (2020) studied drug launches and patented drug list prices for a collection of OECD countries, finding that the list prices exert an economically important effect on launch decisions, holding other factors constant.
- Rawson (2020) examined the pending introduction of the new PMPRB regulations and guidelines, finding that the share of new drugs approved in Canada decreased considerably in the years following the initiation of the legislative process for the new regulations. The findings suggest that drug launches in Canada are already being deprioritized.
- Kanavos et al. (2019) find that pharmaceutical innovators adopt launch sequencing strategies to mitigate downward price spirals, postponing the launch of new drugs in low-price countries or in countries with strictly regulated prices.
- Skinner (2018) analyzed 31 OECD countries to examine the correlation between the number of new drug launches and the market price level for patented drugs, GDP per capita, and population (market size) in each country. Market price level was the only one of the three independent variables that was a statistically significant predictor of new drug launches in regression analysis.
- Cockburn, Lanjouw, and Schankerman (2016) identify the adverse impact of price regulations on drug launches, studying the timing of 642 new drug launches in 76 countries between 1983 and 2002. The authors find that price regulations delay new product launches, while longer and more expansive patent rights accelerate product launches.
- Barua and Esmail (2013) examined new medicine delays in Canada relative to the United States and Europe, finding that delays in access in Canada stemmed from, not prices, but both a longer approval process as well as differences in dates on which manufacturers submitted drugs for regulatory approval.
- Danzon and Epstein (2012) analyzed drug launches in 15 countries between 1992 and 2003, across 12 therapeutic categories. The study established that the extent to which price regulations reduce price levels, such regulation directly translates into launch delays in the regulating country.

- Danzon et al. (2004) explored the impact of price on drug launches in 25 countries and the results show that firms delay or forego launching in markets where prices are visible to external price referencing and regulation reduces prices below levels predicted by local market characteristics.

Unfortunately, there is reason to believe that the launch delays have already begun. According to Innovative Medicines Canada, the industry's main lobby group, a minimum of seven drug launches have been delayed over the proposed regulations since August 2021. The group however declined to identify which drugs these were (Martell, 2021). "Indeed, over the previous year, more than a half-dozen innovative therapies have been delayed or withdrawn and an equal number of submissions for extended pediatric indications have been quietly cancelled" (Acri, 2021).

Historically, in terms of new medicine approvals and launches, Canada was just behind the United States, Germany, and the United Kingdom, ranking fourth (Stewart and Bradford, 2021). That is now changing. To put this in context consider that in 2018, biopharmaceutical companies developed 23 drugs (globally) and introduced 22 of them in Canada. Then, in 2019 that share fell to 13 out of 31. As of April 2021, fully 51 medicines approved in the US have not been submitted for consideration in Canada likely because of the proposed price regulations, initially announced in 2019. The impact is also reflected in the number of new clinical trials conducted in Canada. Specifically, a 52 percent decline in clinical trials since 2018 also indicates that many companies don't expect to market their drugs in Canada. Again, according to Labrie (2020), "[f]orty-four of the 49 studies reviewed showed a significant negative relationship between drug price controls and investment in pharmaceutical R&D or access to innovative drugs."

All of the evidence indicates that the federal government's proposed changes clearly disincentivized innovative drug launches in Canada and potentially deprioritized Canada in the global launch sequences for new drugs. As described by a pharmaceutical executive in a report by Life Sciences Ontario, 'A lot of companies have tiered launch waves. Canada was always considered a Tier 1 or 2 country, launched either with or just after US, Germany, UK, etc. ... Now it will be several years later since there will be access challenges before you even get to reimbursement. [Canada] will move down to Tier 3 or 4, or even worse, not launched at all' (Research etc., 2020). This is echoed in the findings of a study by Kanavos et al. (2019) which finds that pharmaceutical innovators adopt launch sequencing strategies to mitigate downward price spirals, postponing the launch of new drugs in low-price countries or in countries with strictly regulated prices.

In addition to access, one must also consider the impact of the proposed regulations on pharmaceutical prices. The impetus for this policy change was the government's claim that Canadian pharmaceutical prices are too high. As reported by the PMPRB (2021), "the median PMPRB11 to Canadian price ratio reported across all new medicines was 0.81, indicating that international prices in Q4-2019 were approximately 19% lower than in Canadian prices. In contrast, the median US price ratios show that the US pays about three times more than Canada for the same medicines."

The Canadian government’s proposed amendments to the PMPRB relied upon reference pricing to regulate pharmaceutical prices, as well as the use of cost-effectiveness analysis as criteria for public reimbursement decisions. Historically, pharmaceutical price comparisons have been based on a reasonable mix of reference countries with relatively high drug prices (the United States and Switzerland) and countries with relatively lower prices (such as Italy). In a bid to lower drug prices, the Trudeau government proposed changes in 2017 that would drop the US and Switzerland in favour of countries with relatively tighter price controls—Australia, Belgium, Japan, the Netherlands, Norway, and Spain. South Korea was also included in the earlier stages. Notably, fewer innovative drugs are generally approved and launched in the reference countries being added, than in those being removed. Accordingly, while the changes to the list of reference countries may result in lower prices for Canadians, they will also likely result in fewer new drugs being approved and launched in Canada (Barua, 2021).

Beyond this, the proposed regulations would have also required patentees to report to the PMPRB all indirect price reductions, promotions, rebates, discounts, refunds, free goods, free services, gifts, or any other benefit in Canada. [15] At first glance this seems to be a policy that would have lowered prices and benefited Canadian patients. However, this change would have run the risk of increasing costs to public drug plans rather than reducing them (Acri, 2018). The proposed amendment would have required biopharmaceutical manufacturers to report all confidential rebates and discounts provided to governments under their listing agreements. This essentially eliminates all incentives for manufacturers to offer such rebates. In addition, this would have been a downward spiral that would have reduced incentives to invest.

The proposed regulations did little to balance value and health outcomes. A 2019 study by Globerman and Barua describes the potential for conventional cost-effectiveness analysis to discourage technological change and delay access to new and effective therapies and cures. Examining the balance between social benefits and social costs at the margin, the study finds that such measures are likely to be biased in the direction of too little, rather than too much, spending on pharmaceutical therapies. [16] Specifically, the

[15] To place this in context, it is worth noting that there is some, albeit limited, public information on the size of the confidential discounts. In Canada, members of the pan-Canadian Pharmaceutical Alliance (pCPA)—provincial, territorial, and federal governments—obtain rebates that have been reported to be in the neighborhood of 25 percent of list prices. In Australia, there is evidence that rebates also are around 25 percent. A brief to the Commonwealth Fund (Rodwin, 2019) cites a study (Paris, 2009) that estimates rebates paid in France were in the order of 10 percent to 30 percent. A 2012 study by Vogler et al. indicates that confidential rebates are provided to the public drug plans in 21 of the European Union’s 27 member states. For further discussion of the importance and magnitude of the rebates, please see Blomqvist and Grootendorst (2021).

[16] Globerman and Barua focus their study on the role of the Quality Adjusted Life Year (QALY) in the evaluation of therapies and cures. “In principle, the value of a QALY in the calculation should represent the monetary value of an extra quality-adjusted life year to the insured users of the new technology. This is obviously difficult to measure, since insured users are typically not asked to pay the full cost of new drugs or other treatments at the point of care. (Cost sharing arrangements vary across countries and patient groups. For an overview, see Globerman (2016).) However, it is possible

study claims “public policy decision makers should be encouraging an efficient level of expenditures on pharmaceutical drugs, not simply containing expenditures on those drugs. Efficiency is achieved when the social benefits of drug expenditures, at the margin, equal their social costs. Effectively, this means that more, not less, should be spent on any drug as long as the social benefit from its increased usage exceeds the additional expenditure.”

While the would-have-been consequences of the proposed regulations are sobering for all Canadian patients, the potential implications for those with rare diseases could have been catastrophic. Put simply, under the new regulations, manufacturers would have been forced to lower their prices to an extent that launching new treatments in Canada would be unsustainable. These concerns are not illusory and are confirmed by evidence compiled in several independent studies. Rawson (2021) cites a study in which the maximum allowable price for a new medicine for a rare disorder under the new regulations was estimated to require a price reduction of up to 84 percent, while another estimated price reductions of up to 68 percent. As described by Rawson, “[i]t’s also possible that drugs for rare diseases or very expensive drugs won’t be available here at all, because if they have a price reduction demand of say 70 percent it’s a big deterrent, especially with all the bureaucracy these companies have to go through to get approvals. Whether drug access is delayed or denied, it will be impacted” (Harvatin, 2021). A recent study by Balijepalli et al. (2020) explore the subtleties more fully.

Orphan drugs have high acquisition costs and when standard health technology assessment (HTA) approaches are used to assess their cost-effectiveness, they often appear not cost-effective. The Canadian Patented Medicine Review Board (PMPRB), through new regulations, will apply HTA assessment results from the Canadian Agency for Drugs and Technologies in Health (CADTH) and Institut national d’excellence en santé et en services sociaux (INESSS) when setting the maximum price that can be charged for Category I patented medicines (treatments with an annual cost exceeding 150% of GDP per capita of Canada or with expected annual market size >\$50M). Through these regulations, PMPRB has also established a willingness-to-pay threshold of CAD\$200,000 or CAD\$150,000 per quality adjusted life year (QALY) [17] for medications with a prevalence of no more than 1 in 2000 across all approved indications. [18] We reviewed the orphan drug submissions made to

that there are systematic biases in evaluating the cost-effectiveness of new therapies, and that the net effect of the biases is to understate the benefits of new therapies or, equivalently, to underestimate the cost-effectiveness of those therapies” (Globerman and Barua, 2019).

[17] See Balijepalli et al. (2020) for discussion of QALY limits.

[18] Importantly, a dollar threshold will be applied to CADTH’s cost-effectiveness assessment. Drugs above the threshold risk not being insured. According to Rawson (2018b), “[t]hresholds of this type have been abandoned by every developed country that has adopted or considered them because they fail to reflect considerations, such as patient and insurer willingness to pay and health trade-offs, that should guide insurance coverage decisions.” Given that the PMPRB is not a payer, justifying this as the right point in the drug review process for incorporating the proposed pharmacoeconomic factors is tremendously difficult. Moreover, it is the public drug plans and private insurers that already fill this role (Acri, 2018).

CADTH's Common Drug Review (CDR) January 2015–May 2020 to understand how the methodology of assessing cost-effectiveness of orphan drugs has guided pricing in Canada. A total of 35 orphan drug submissions were assessed by CDR in this period, none of which met the willingness-to-pay threshold of CAD\$50,000 per QALY. Only one drug met the CAD\$200,000 per QALY for Therapeutic Criteria Level I, and two drugs met CAD\$150,000 per QALY for other Therapeutic Criteria Levels proposed by PMPRB. Price reductions of 32–99% were recommended for treatments that were approved in order to be listed for reimbursement. This review showed that the new PMPRB regulations could be creating challenges for manufacturers of rare disease treatments to meet Canadian pricing regulations. These regulations may jeopardize the launch of new medicines and limit opportunities to add to the development of real-world evidence of orphan drugs, which can be used in reimbursement approaches such as pay-for-performance.

This review showed that no rare disease drugs submitted to CADTH over the past five years have met the arbitrary ICUR thresholds and using such thresholds make it challenging for rare disease drugs to appear cost-effective. Considering the difficulties for HTA agencies to interpret the results of an economic evaluation associated with a level of uncertainty inherent to orphan drugs, the proposed PMPRB guidelines and federal regulations will potentially lead to obstacles for manufacturers of rare disease treatments to meet Canadian pricing regulations. Manufacturers having to reduce the prices substantially (e.g., up to 90% or more) to meet the new requirements might find the business model to be unsustainable and this may jeopardize the launch of some new medicines in Canada. (Balijepalli et al., 2020)

This possibility would exacerbate the current situation which is already quite grim for patients with rare diseases. Prior to 2018, Canada received faster and more extensive access to new medicines and therapies relative to other countries. However, 2019 showed a sharp decline in the number of new drug launches in Canada: from 22 in 2018 to just 13 in 2019, despite the overall number of global launches actually increasing during the year. Moreover, in the last quarter of 2019, Canadian patients saw just one new drug launch. According to a report commissioned by Life Sciences Ontario, “among 37 new therapies launched globally in 2018, over half of them (21) were not launched in Canada. The majority of the medicines not commercialized in Canada were for rare diseases and cancer” (Life Sciences Ontario, 2020).

Viewed from the perspective of patient access, the proposed regulations failed to deliver. Viewed from the perspective of patient affordability, again, the new regulations failed to deliver. Systematic analysis of the consequences of these proposed changes indicate that Canadian patients would not have been made better off, and those suffering from rare diseases might have been hit the hardest. Given the potential consequences, one must question whether patient well-being truly motivated these policy changes or whether patient well-being was even considered when the policy changes were instigated.

6. Global Consequences

Canada’s proposed regulatory amendments were presented by the PMPRB as being justified by high Canadian drug prices, a claim presumably bolstered by evidence of Canada’s rank in international comparisons. The PMPRB argues that the changes are needed to fulfill its mandate to prevent “excessive” prices for patented medicines. The narrative presented by the agency relies on its own internal analysis to support this claim, however these conclusions were not independently audited. Canadian prices were compared to seven other countries (the PMPRB 7), which include France, Germany, Italy, Sweden, Switzerland, the United Kingdom, and the United States. According to PMPRB, Canada ranked fourth among the PMPRB 7, behind the higher-priced countries of the United States, Switzerland, and Germany. Relative to the 31 OCED countries, Canada also ranked fourth.

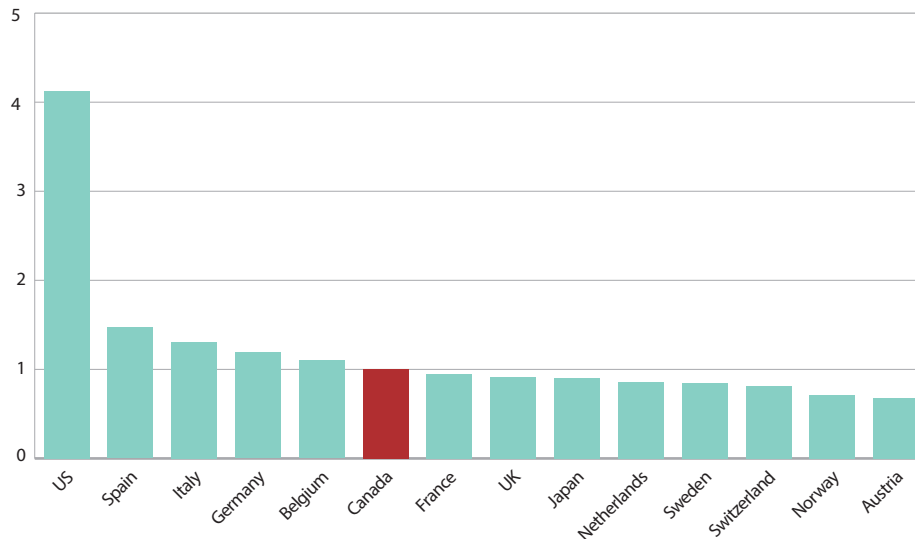
Upon examination this justification falls apart and the amendment appears to be both unwarranted and risky. The estimate presented by Health Canada indicates that the new policies would result in a decrease of 52 percent in the maximum price allowed for some patented medicines. Independent studies place this reduction at 61 percent to 84 percent. Skinner (2021) tested the validity of the PMPRB’s justification and their estimates by comparing the prices for Canada’s top 100 selling patented medicines to symmetrical products in the 11 new reference countries specified by the new regulations—the new reference country basket—in addition to the former reference countries of the United States and Switzerland. [19]

The study by Skinner (2021) showed that bilateral price ratios for Canada consistently ranked in the middle of the 14 countries included in the analysis (figure 5). These results are robust, no matter whether prices were measured as averages or as medians, whether prices were denominated at market exchange rates or purchasing power parities, and when compared to GDP per capita. Fundamentally, the PMPRB’s narrative is not supported by the evidence given that Canada’s prices (and rank) are modest relative to the full list of reference countries, past and present.

The primary finding of the Skinner (2021) study is that the PMPRB’s “excessive” pricing justification for amending the regulations and guidelines is not supported by the evidence. Canada’s position, in the middle of the 14 countries, remained consistent across the three calendar years studied, across every one of the methods used for measuring prices. There is nothing that suggests that Canadian prices for patented medicines are “excessive”. Given this, Skinner determines that the amendments are unnecessary, and the previous regulations and guidelines are adequate to achieve the government’s explicit policy goal and for the PMPRB to fulfil its mandate. The study also claims that

[19] Data were obtained for the calendar years 2018, 2019 and 2020 from the IQVIA® MIDAS® database, which is the same source used by the PMPRB. (Skinner, 2021).

Figure 5: Average Foreign-to-Canadian Price Ratios, Manufacturers' List Price, US \$ PPP, Average 2018 to 2020



Source: Skinner, 2021.

the selection of the new reference countries is “purposely overrepresented by lower priced markets”. Skinner writes:

The exclusion of higher priced markets and the inclusion of additional lower priced markets artificially causes Canada’s price rank to be higher relative to the remaining countries used for comparison. The biased result might suit the PMPRB’s narrative, but it is not the basis for sound regulation. One underappreciated aspect of the new regulations is that the exclusion of Switzerland and the United States from the PMPRB reference countries deprives policymakers of vital information about the effect of price regulations on the availability of new medicines, industry investment in clinical research, and the development of an innovative domestic pharmaceuticals industry in Canada. The United States has the highest drug prices in the world, but Americans enjoy the earliest access to new medicines and the country attracts the highest levels of industry investment in research and development of innovative pharmaceuticals. It serves the public interest for policymakers to be informed of this reality and the trade-offs associated with alternative policy approaches. (Skinner, 2021)

Not only were the full set of amendments unwarranted, but the consequences could have inflicted real harm. These changes had the potential to impact the trajectory and scale of biopharmaceutical research and development, global drug prices, international trade agreements, and the public good that is biomedical technology. The juxtaposition of the federal government’s objectives is striking: on the one hand, aiming to introduce new PMPRB regulations that will deter R&D and, on the other, the Minister for Innovation, Science and Industry seeking to increase innovation, research, and development in Canada.

Consequences for Global Drug Prices

The proposed amendment establishes a new set of reference countries, the PMPRB11, which will significantly impact both the highest international price and the median international price comparison metrics. Fundamentally, the change will lower the maximum allowable price, requiring pharmaceutical innovators to lower their prices in Canada to be in compliance (Acri, 2018). The result will be a ratcheting downward of global pharmaceutical prices.

Given that Canada is a frequent reference country for other nations who utilize international price comparisons (including Taiwan, Brazil, Colombia, Egypt, South Africa, and New Zealand among others), this change has the potential to impact pricing in other countries. [20] When a country mandates lower average prices for drugs, either directly or indirectly, that jurisdiction becomes attractive for other countries to include in their “country baskets” for their own reference pricing. If the proposed changes have the anticipated effect of lowering the maximum allowable price in Canada, it can be expected that the impact will ripple across other reference-price based regimes, potentially lowering drug prices across numerous markets. In addition, given that Canada is an important reference country in other nations’ reference pricing formulas, a lower drug price in Canada may encourage innovative pharmaceutical companies to forego sales in Canada. Canada would become less attractive for pharmaceutical companies marketing new drugs because the price reductions extracted by Canada may lead to lower allowable prices in other countries that include Canada in their reference baskets. “Canada is a reference country in other markets and prices in Canada have an impact elsewhere in the world. Most of these markets are much larger than Canada and innovators will sacrifice the Canadian market to be able to retain value in other markets. Canada is 2% of the global market. The US is 50%. We are not going to risk the rest of the world for the sake of Canada” (Research etc., 2020). Ultimately, the proposed changes to the PMPRB’s reference pricing procedure have the potential to limit or delay Canadians’ access to new and highly beneficial drugs (Acri, 2018; Globerman and Barua, 2019).

Consequences for International Trade Agreements

“Technology and knowledge have global benefits, and the question how large a portion of the world’s economic resources should be devoted to R&D, and who should pay for it, can be settled in an efficient and equitable manner only through negotiations among the major countries that are part of the international economic system. (Blomqvist and Grootendorst, 2021)

[20] It is important to recognize this potential is debated in the literature. According to Spicer and Grootendorst (2020), “[i]t is unlikely a company would delay a launch in Canada to attain a higher list price in these countries [Egypt, Taiwan, Colombia, Brazil, and South Africa]. However, there is a risk that relatively large countries will begin to reference Canadian drug prices should Canada markedly lower its prices.”

Over the past several decades, biopharmaceutical advances have assumed an increasingly larger and larger role in the healthcare ecosystem. Specifically, new medicines have increased longevity, accounting for 40 percent of the two-year increase in life expectancy achieved in 52 countries between 1986 and 2000 (Lichtenberg, 2003). Consider too the treatment of HIV/AIDS and cancer. Following the development of a new wave of medicines to treat HIV/AIDS in the mid-1990s, the death rate in the US from AIDS dropped approximately 70 percent (CASCADE Collaboration, 2003). In addition, in the years since 1971, our arsenal of cancer medicines has tripled, accounting for 50–60 percent of the increase in six-year cancer survival rates since 1975 (Lichtenberg, 2004). In particular, data shows that in 2003 the total number of people who died of cancer went down for the first time in more than 70 years (Hoyert et al., 2006).

Combined with the rising costs of biopharmaceutical research and development, it is not surprising that intellectual property rights, specifically biopharmaceutical patents, have emerged as an increasingly important—and contentious—component in international trade agreements. Central to the debate is the role of US patent rules and pharmaceutical pricing policies which have led to much higher drug prices in the United States than anywhere else in the world. In parallel with this is the criticism that Canada and other countries have sometimes acted as “free riders”. In the 2020 Special Report 301, the United States Trade Representative included Canada on the list of countries with alleged sub-standard levels of intellectual property protection (which includes patents). In the context of the pharmaceutical sector specifically, the report reads, “[t]he United States urges Canada to appropriately recognize the value of innovative medicines in both the private and public markets, to ensure its decisions are made transparently, and to contribute fairly to research and development for innovative treatments and cures.”

Given this, it is not surprising that the rules for pharmaceutical patent protection have figured prominently in US-Canada trade negotiations. Most recently this has played out with the US putting pressure on Canada to provide additional patent protection for biologics. [21] As a high-income industrialized nation, Canada is expected to contribute proportionately to global R&D financing. Policies that can be construed as free ridership are damaging to Canadian relations with other countries and its standing in the international community.

[21] A thorough review of biologic medicines may be found in Lybecker (2016) and Acri (2020). “Biologics are defined as “a large molecule typically derived from living cells and used in the treatment, diagnosis, or prevention of disease. Biologic medicines include therapeutic proteins, DNA vaccines, monoclonal antibodies, and fusion proteins.” Specifically, most biologic medicines are developed using recombinant DNA (rDNA) technology. They are produced by genetically engineering living cells to create the required proteins rather than through traditional chemical synthesis.” ... Biopharmaceutical firms specialize in the manufacture of a social good characterized by high fixed costs, substantial informational and regulatory costs, and a comparatively low marginal cost of production. Biopharmaceutical innovations are easily copied and sold by their competitors—the knowledge is non-rival (that is, available to all and undiminished by use), and non-excludable (the innovator cannot prevent the knowledge from being used). Given the inherent challenges in delineating and enforcing property rights to new technologies, it is difficult for innovative firms to appropriate the returns accruing from their investments.” (Lybecker, 2016)

As described by Blomqvist and Grootendorst (2021):

To avoid this, Canadian policy must produce a pricing structure that would make other countries agree that Canada is abiding by the spirit of the international patent system and that its consumers are contributing their fair share to the global revenues that incentivize most of the sector's R&D. [Earlier in the study], we referred to the tension between the conflicting objectives of lower drug prices as a tool for controlling overall healthcare costs and that of more R&D to discover and develop new and more effective drug therapies. For a small country like Canada, a hypothetical strategy of trying to sidestep this conflict through more aggressive price controls and weak patent laws may seem tempting, but it will backfire if it makes other countries see us as free riders and they become less willing to make concessions as we negotiate with them about other global issues. (Blomqvist and Grootendorst, 2021)

Intellectual property rights and pharmaceutical pricing policies will almost certainly be central to future trade negotiations. Getting these policies right now is critical to how those negotiations will play out going forward.

Consequences for Biomedical Public Goods

Innovation in global and biomedical advances are a public good: once discovered this knowledge has the potential to benefit everyone, regardless of where it was developed. Importantly, research and development spending is driven by world returns. Accordingly, Canada should contribute proportionally to global research and development financing. As described by Owens (2021), this currently is not the case:

The US naturally would like to regain the consumer surplus Canada steals from its citizens. The moral high ground belongs to them. And maybe price controls that make our domestic supply fragile are not such a good idea, after all. If countries like Canada paid fairly for patented drugs, everyone everywhere would be much better off. We'd have more of the vaccines, antibiotics and drug therapies that extend life, make us happier and productive, generate wealth and save healthcare costs—a great improvement over our current mendacious, pusillanimous, immoral scrimping. (Owens, 2021)

At present, the global pharmaceutical economy is based on massively unfair exploitation of the American consumer, who pays an average of approximately 3.5 times the prices paid in Europe and three times the price paid in Canada. The market in the United States accounts for 64 to 78 percent of biopharmaceutical company profit, that which funds the drug development from which everyone in the world benefits (Owens, 2020). The appropriate point of comparison, however, is value not price. It is essential to note that criticism of increases in drug spending fail to account for the value delivered

by innovative treatments and cures, especially in comparison to the costs and benefits of hospitalization and other interventions available through the healthcare system. Drug interventions are an undeniably cost-effective means of treating illness and disease. One of the earliest studies (Lichtenberg, 1996) found that a \$1 increase in spending on pharmaceuticals resulted in \$3.65 reduction in hospital care expenditures. More generally, under reference pricing, individual governments have incentives to spend less on drugs with the expectation that their individual efforts to economize will not reduce global R&D spending on drugs. The truth, however, is that these policies do reduce global spending on biopharmaceutical research and development, to the detriment of all.

Rejecting Free Riding

In order to avoid the negative consequences outlined here, Canada must reject the temptation of free riding and commit to contributing proportionally to the financing of global research and development. As stated above, research and development spending is driven by world returns, and failure to equitably contribute amounts to free riding. When a significant number of countries behave in this way, global research and development spending declines to the detriment of biomedical innovation. By altering its reference pricing countries in order to rein-in expenditures on biopharmaceuticals, Canada will be indirectly exacerbating this “free-rider” problem. Adopting a longer-run policy perspective for drug reimbursement and pricing policies is essential. The health of future generations both in Canada and internationally depends on it (Globerman and Barua, 2019).

While the appeal to “free-ride” on the research and development activities carried out in other countries is understandable, national health care authorities should resist. As described by Philipson (2016), biopharmaceutical R&D is driven by world returns to R&D, not by the returns from individual domestic markets. Given this, taxation to fund the reimbursements and profits of innovative firms involves a private (country-specific) cost with the global benefit of stimulating innovation. Under these conditions, “if medical innovation benefits all countries, any individual country has an incentive to reimburse manufacturers at less than the socially efficient rate from a multi-country perspective. As a result, there will be too little medical innovation from a global perspective given the public goods characteristic of pharmaceutical R&D” (Globerman and Barua, 2019).

Potential Benefits

The benefits of new technology are potentially available everywhere in the world, regardless of where it was developed. Accordingly, virtually all countries embrace intellectual property laws that provide patent protection to both domestic and foreign innovators. Through this system, the buyers of patented products all over the world contribute at least a portion of the monopoly profits that help recoup the R&D expenditures in whatever country (or countries) the product was developed. However, in the biopharmaceutical industry, patent owners’ pricing power may be restricted through price controls, or by policies that create countervailing market power on the buyers’ side. These differences affect the expected profits from sales of patented products and must

be counterbalanced to preserve the system's incentives to develop new knowledge (Blomqvist and Grootendorst, 2021).

In designing policies and institutions to reduce the prices of medicines, it is essential to keep in the mind the obligations that Canada has as a member of the international community that shares the financing of pharmaceutical research and development under the existing global patent system (Blomqvist and Grootendorst, 2021). The benefits of a vibrant innovative biopharmaceutical industry translate into treatments that enhance and extend life. Fundamentally, more modest biopharmaceutical pricing policies in Canada would add to pharmaceutical R&D at the margin. While we cannot know which drugs in recent years were not approved or sold in Canada because of PMPRB pricing strategies, it is clear that more stringent regulations would reduce the potential for R&D investment in the pharmaceutical industry. That sacrifice comes at too high a cost.

7. Conclusions

The 1987 amendments that created the PMPRB reflected a thoughtful balance across several policy objectives, protecting consumers from excessive patented medicines prices, while ensuring sufficient incentives for patentees to introduce new medicines to Canada. However, for many years, successive federal governments have created a pharmaceutical policy environment that discourages investment in innovations, pharmaceutical research, development, and manufacturing within Canada. This is only amplified in the now-abandoned Amendments which were limited to solely lowering patented drug prices. As a result, the aforementioned policy balance was put at risk. The proposed amendments would have clearly reduced investment in the Canadian biopharmaceutical industry and disincentivize innovative drug launches in Canada, potentially de-prioritizing Canada in the global launch sequences for new drugs. In addition, the proposed reporting requirements would have represented an unnecessary regulatory burden, and increased the time to achieve public reimbursement.

As documented here, the proposed PMPRB amendments had the potential for inflicting numerous harms on Canadian patients and the biopharmaceutical industry, principle among them, delaying the availability of new treatments for Canadians. Canadian patients are already denied the health benefits of many medicines for months, if not years, and the stage is set for this to only get worse through the adoption of the new PMPRB 11 set of countries. As noted above, Rawson (2013) found that more than 5,000 patients may have been adversely impacted by delayed federal regulatory and provincial reimbursement for just five oncology drugs between 2003 and 2011. Multiplying this harm across the hundreds of drugs with launch delays is alarming. While Health Canada claims, based on its own unpublished analysis, that the proposed regulations and price tests would not have delayed drug launches in Canada, the evidence in the existing literature on drug launch timing contradicts this, suggesting that the impacts would have been chilling.

The proposed changes could have also been expected to reduce biopharmaceutical research and development, as well as reducing employment in the Canadian health care sector. While this reasoning alone presents a compelling case for abandoning the proposed policy changes, it also seems that the crisis claimed by the PMPRB appears to be nonexistent and the alarm unwarranted. As reported by Rawson (2021), “despite the PMPRB’s claims to the contrary, patented medicine prices are not causing a sustainability crisis for the health care system. Using the PMPRB’s own data, the gross national sales of patented drugs at manufacturers’ list prices in Canada in 2019 were \$17.2 billion, which accounts for only 6.5 percent of the \$265.5 billion reported by the Canadian Institute for Health Information for national health spending—virtually the same as in 2009. This percentage would be even lower after confidential manufacturers’ rebates were applied.” Rawson goes on to point out that the prices paid by government drug programs are lower

than the maximums allowed by the PMPRB, noting that the Ontario public drug plan receives rebated prices averaging 36 percent lower than PMPRB ceiling prices.

The proposed amendments failed to incorporate the experiences of other jurisdictions and draw from their practices in order to better balance innovation and health-care costs. As described by Glennie (2018), “Many of the proposed regulatory changes appear to take the PMPRB away from its core mandate, create duplication of effort, and potentially encourage decision-making based on flawed data. It is important to seriously consider stakeholder input to generate more coherent reforms that do not undermine innovation in the Canadian and/or global pharmaceutical system.”

The concern for undermining innovation in the Canadian biopharmaceutical industry is real and justified. While the modification in reference pricing comparator countries is a simple, albeit short-sighted, change, the now-abandoned regulations would have been undeniably burdensome, adding greater complexity to a pharmaceutical policy environment that’s already burdened with barriers that manufacturers must overcome to make their medicines accessible to a majority of Canadian patients. These changes would have also exacted a real economic price. As reported in a recent study by Ernst & Young (2017), the activities of the Innovative Medicines Canada members contributed more than \$19.2 billion in gross value to the Canadian economy in 2016. Specifically, for every \$1.00 attributed directly to participating member firms, another \$0.59 is generated indirectly through activities in the supply chain, and an additional \$0.44 of induced impact is “supported by the employment income and associated spending across the Canadian economy”. These contributions would have been put at significant risk. With this in mind, it is unsurprising that the majority of the proposed Amendments were abandoned on April 14. This study considers both the national impact and the global effect of the totality of the original amendments. With this perspective, it is clear that the revision of the PMPRB Amendments is a step in the right direction.

This evaluation of the full set of initially proposed PMPRB amendments and the potential consequences makes clear that the narrative that justified the changes was unfounded and the proposed regulatory changes would have fundamentally altered the role and responsibilities of the PMPRB, in ways that would have been harmful to Canadian patients, the industry and innovation. The proposed policies would have likely reduced Canadian patients’ access to medicine, stymied the biopharmaceutical industry’s incentive to innovate and decreased the jobs and income generated in the life sciences sector. As is, the new basket of comparator countries will serve to exacerbate the free riding problem that characterizes global research and development in the biopharmaceutical industry. Rather than bolstering the Canadian healthcare system, the proposed changes only serve to undermine it.

The COVID-19 pandemic demonstrated that a thriving biopharmaceutical industry is more important than ever. Again, it is worth noting that Canadians had relatively rapid access to COVID vaccines and drugs because they were exempted from PMPRB scrutiny. For Canada to support and embrace the biopharmaceutical sector and establish Canada as a frontrunner in drug development and vaccine production, it must embrace

an environment that encourages and incentivizes biomedical innovation. The proposed PMPRB Amendments and Guidelines sought to do exactly the opposite. Rather than benefiting from avoiding PMPRB scrutiny, innovative drugs should get to Canadian patients faster and at lower cost through PMPRB channels. They don't. While the revision of the PMPRB Amendments and the abandonment of the most drastic changes are encouraging, the Amendments taking effect on July 1st do not bode well for the future of Canadian healthcare or patients. Fundamentally, significant uncertainty remains surrounding how the PMPRB will implement the "status quo" as they call it, or what the eventual guidelines will be. The PMPRB has not yet published new guidelines to operationalize the amendments, and PMPRB won't even consult on the revised guidelines until September 2022. Implementation is even further off. The PMPRB and the government are still intent on reducing drug prices and the PMPRB maintains a lot of leeway to interpret its role as it and the federal government see fit. The lack of certitude in the Canadian market reduces its attractiveness as a place to invest, create jobs and launch new medicines in a timely way, which should worry us all.

References

- Acri née Lybecker, Kristina M. L. (2018). *Implications of the Proposed Changes to Canada's Pharmaceutical Pricing Regulations*. Fraser Institute. <<https://www.fraserinstitute.org/sites/default/files/implications-of-changes-to-pharmaceutical-pricing-regulations.pdf>>
- Acri née Lybecker, Kristina M. L. (2020a). *Biologics and Biosimilars: A Primer*. Fraser Institute. <<https://www.fraserinstitute.org/sites/default/files/biologics-and-biosimilars-a-primer.pdf>>
- Acri née Lybecker, Kristina M. L. (2020b). *Trudeau Government Move Undermines COVID-19 Response*. Fraser Institute. <<https://www.fraserinstitute.org/article/trudeau-government-move-undermines-covid-19-response>>
- Acri née Lybecker, Kristina M. L. (2021). *Proposed 'Drug Price' Changes Threaten Access for Canadian Patients*. Fraser Institute. <<https://www.fraserinstitute.org/blogs/proposed-drug-price-changes-threaten-access-for-canadian-patients>>
- Bach, Peter (2015). New Math on Drug Cost-Effectiveness. *The New England Journal of Medicine* 373, 19: 1791–99.
- Balijepalli, Chakrapani, Lakshmi Gullapalli, Eric Druyts, Kevin Yan, Kamal Desai, Stephane Barakat, and Jason Locklin (2020). Can Standard Health Technology Assessment Approaches Help Guide the Price of Orphan Drugs in Canada? A Review of Submissions to the Canadian Agency for Drugs and Technologies in Health Common Drug Review. *ClinicoEconomics and Outcomes Research* 12: 445–57. <<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7455764/>>
- Barua, Bacchus (2021a). *Canada Should Improve Access to Pharmaceuticals in Post-COVID World*. Fraser Institute. <<https://www.fraserinstitute.org/blogs/canada-should-improve-access-to-pharmaceuticals-in-post-covid-world>>
- Barua, Bacchus (2021b). *Ottawa Postpones Short-Sighted Drug-Pricing Regulations*. Fraser Institute. <<https://www.fraserinstitute.org/blogs/ottawa-postpones-short-sighted-drug-pricing-regulations>>

Barua, Bacchus, and Nadeem Esmail (2013). *The Case for Mutual Recognition of Drug Approvals*. Fraser Institute. <<https://www.fraserinstitute.org/sites/default/files/case-for-mutual-recognition-of-drug-approvals.pdf>>

Barua, Bacchus, Will Westcott, and Van Nghiem Vo (2021). *Timely Access to New Pharmaceuticals in Canada, the United States, and the European Union*. Fraser Institute. <<https://www.fraserinstitute.org/sites/default/files/timely-access-to-new-pharmaceuticals-in-canada-US-and-EU.pdf>>

Benefits Canada (2019). *Draft PMPRB Guidelines Include Changes to Reference Countries, Drug Price Factors*. Benefits Canada. <<https://www.benefitscanada.com/news/bencan/draft-pmprb-guidelines-include-changes-to-reference-countries-drug-price-factors/>>

Blomqvist, Åke, and Paul Grootendorst (2021). *Cutting Square Deals: Drug Prices, Regulation, and Patent Protection*. Commentary no. 605. C. D. Howe Institute. <https://www.cdhowe.org/sites/default/files/attachments/research_papers/mixed/Commentary_605_0.pdf>

Boothe, Katherine (2018, 23 July). *Debunking the Myths about a Canadian Pharmacare Program*. The Conversation. <<https://theconversation.com/debunking-the-myths-about-a-canadian-pharmacare-program-100299>>

Brennan, Zachary (2017). *Canada Proposes to Amend Drug Pricing Regulations*. RAPS: Regulatory Affairs Professionals Society. <<https://www.raps.org/regulatory-focus%E2%84%A2/news-articles/2017/5/canada-proposes-toamend-drug-pricing-regulations>>

Canada Gazette (2019). *Regulations Amending the Patented Medicines Regulations (Additional Factors and Information Reporting Requirements): SOR/2019-298*. Canada Gazette, Part II, Volume 153, Number 17. Registration: SOR/2019-298, August 8, 2019. PATENT ACT: P.C. 2019-1197 August 7, 2019.

Cockburn, Iain, Jean Lanjouw, and Mark Schankerman (2016). Patents and the Global Diffusion of New Drugs. *American Economic Review* 106, 1: 136–64.

Craig, Brian (2020). *New Federal Drug Pricing Rules are Already Delaying Medicine Launching and Costing Jobs in Canada, Survey Reveals*. Life Sciences Ontario. <<https://lifesciencesontario.ca/new-federal-drug-pricing-rules-are-already-delaying-medicine-launches-and-costing-jobs-in-canada-survey-reveals/>>

Critchley, Wayne, and Richard C. Owens (2018). *The Unkindest Cut*. Macdonald-Laurier Institute Series. <<https://www.macdonaldlaurier.ca/economic-health-consequences-patented-medicine-price-review-boards-new-reforms-new-mli-study/>>

Danzon, P. M., and A. J. Epstein (2012). Effects of Regulation on Drug Launch and Pricing in Interdependent Markets. *Advances in Health Economics and Health Services Research* 23: 35–71.

Danzon, P. M., R. Wang, and L. Wang (2004). The Impact of Price Regulation on the Launch Delay of New Drugs—Evidence from Twenty-Five Major Markets in the 1990s. *Health Economics* 14, 3: 269–92.

DiMasi, J. A., H. G. Grabowski, and R. W. Hansen (2016). Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs. *Journal of Health Economics* 47: 20–33.

Ernst & Young (2017). *Innovative Medicines Canada: Data Analytics and Members' Economic Footprint and Impact in Canada*. Ernst & Young. <http://innovativemedicines.ca/wp-content/uploads/2017/10/20171030_EY-REPORT_IMC_FINAL.pdf>

Field, Jason (2021, March 4). *Canadians Paying the Price for Failed Drug-Pricing Policy*. Healthy Debate. <<https://healthydebate.ca/2021/03/topic/failed-drug-pricing-policy/>>

Frank, Richard, and Paul B. Ginsburg (2017). *Pharmaceutical Industry Profits and Research and Development*. Brookings. <<https://www.brookings.edu/blog/up-front/2017/11/17/pharmaceutical-industry-profits-and-research-and-development/>>

Garrison, Louis, and Adrian Towse (2017). Value-Based Pricing and Reimbursement in Personalised Healthcare: Introduction to Basic Health Economics. *Journal of Personalized Medicine* 7, 10: 1–10.

Gastrointestinal Society (2020). Patented Medicine Prices Review Board Changes and Their Impact on Canadians: Impact Report. Gastrointestinal Society. <<https://badgut.org/wp-content/uploads/PMPRB-Impact-Report-2021.pdf>>

Giacotto, Carmelo, Rexford Santerra, and John Vernon (2005). Drug Prices and Research and Development Investment Behavior in the Pharmaceutical Industry. *Journal of Law and Economics* 48, 1: 195–214. <<https://www.journals.uchicago.edu/doi/pdf/10.1086/426882>>

Glennie, Judith (2018). *Significant Change Coming to Patented Medicine Pricing in Canada*. Global Forum. <<https://globalforum.diaglobal.org/issue/february-2018/significant-change-coming-to-patented-medicine-pricing-in-canada/>>

Globerman, Steven (2016). *Select Cost Sharing in Universal Health Care Countries*. Fraser Institute. <<https://www.fraserinstitute.org/sites/default/files/select-cost-sharing-in-universal-health-care-countries.pdf>>

Globerman, Steven, and Bacchus Barua (2019). *Pharmaceutical Regulation, Innovation, and Access to New Drugs: An International Perspective*. Fraser Institute. <<https://www.fraserinstitute.org/sites/default/files/pharma-regulation-innovation-access-to-new-drugs.pdf>>

Graham, John (2014, July 25). Politicizing Gilead's Research and Development Costs for Sovaldi is a Reckless and Dangerous Misadventure. *Forbes*. <<https://www.forbes.com/sites/theapothecary/2014/07/25/politicizinggileads-research-and-development-costs-for-sovaldi-is-a-reckless-and-dangerousmisadventure/#s5ac45471865>>

Harvatin, Vanessa (2021). *PMPRB: Why Lower Drug Prices May Mean Less Access*. Healthing. <<https://www.healthing.ca/policy/pmprb-why-lower-drug-prices-may-mean-less-access/>>

Health Canada (2022). *Statement from Minister of Health on the Coming-into-Force of the Regulations Amending the Patented Medicines Regulations*. Government of Canada. <<https://www.canada.ca/en/health-canada/news/2022/04/statement-from-minister-of-health-on-the-coming-into-force-of-the-regulations-amending-the-patented-medicines-regulations.html>>

Hoskyn, Sarah Lussier (2020). *Explaining Public Reimbursement Delays for New Medicines for Canadian Patients*. Innovative Medicines Canada. <<http://innovativemedicines.ca/wp-content/uploads/2020/07/CADTH-TTL-8.5x11-EN-Final.pdf>>

Hoyert, Donna L., Melonie Heron, Sherry L. Murphy, and Hsiang-Ching Kung (2006). *Deaths: Final Data for 2003—Health E-Stats*. Centers for Disease Control and Prevention. <<https://www.cdc.gov/nchs/data/hestat/finaldeaths03/finaldeaths03.htm>>

Humphries, Brittany, and Feng Xie (2019). Canada's Amendment to Patented Drug Price Regulation: A Prescription for Global Drug Cost Control? *Journal of the American Medical Association* 321, 16: 1565–66. <<https://jamanetwork.com/journals/jama/article-abstract/2730014>>

Innovative Medicines Canada (2018). *Submission: Canada Gazette, Part I – Regulations Amending The Patented Medicines Regulations*. Innovative Medicines Canada. <http://innovativemedicines.ca/wp-content/uploads/2018/02/20180212_IMC_CG1_Submission_Regulations_Amending_the_Patented_Medicines_Regulations_Final.pdf>

Janssen Inc. (2021). *Health Canada's Review of the Patented Medicines Prices Review Board (PMPRB)*. Janssen Inc. <<https://www.janssen.com/canada/pm-prb>>

Kanavos, Panos, Alessandra Ferrario, Sotiris Vandoros, and Gerald F. Anderson (2013). Higher US Branded Drug Prices and Spending Compared to Other Countries May Stem Partly from Quick Uptake of New Drugs. *Health Affairs* 32, 4. <<https://www.healthaffairs.org/doi/10.1377/hlthaff.2012.0920>>

Kanavos, Panos, Anna-Maria Fontrier, Jennifer Gill, and Olina Efthymiadou (2019). Does External Reference Pricing Deliver What it Promises? Evidence on its Impact at National Level. *European Journal of Health Economics*.

Labban, Margaret (2021). Canada's PMPRB Reform Delays Add Uncertainty. *Pharmaceutical Technology*. <<https://www.pharmaceutical-technology.com/pricing-and-market-access/canadas-pmprb-reform-delays-add-uncertainty-html/>>

Labrie, Yanick (2020). *Evidence that Regulating Pharmaceutical Prices Negatively Affects R&D and Access to New Medicines*. Canadian Health Policy. <<https://www.canadianhealthpolicy.com/products/evidence-that-regulating-pharmaceutical-prices-negatively-affects-r-d-andaccess-to-new-medicines.html>>

Lakdawalla, Darius N. (2018). Economics of the Pharmaceutical Industry. *Journal of Economic Literature* 56, 2:397–449. <<https://www.jstor.org/stable/26494193>>

Lexchin, Joel (2018, 14 March). *Pharmacare and the Chaotic World of Canadian Drug Prices*. The Conversation. <<https://theconversation.com/pharmacare-and-the-chaotic-world-of-canadian-drug-prices-93343>>

Lichtenberg, Frank R. (1996). *The Effect of Pharmaceutical Utilization and Innovation on Hospitalization and Mortality*. NBER Working Paper #5418. National Bureau of Economic Research.

Lichtenberg, Frank R. (2011). Pharmaceutical Companies' Variation of Drug Prices Within and Among Countries Can Improve Long-Term Social Well-Being. *Health Affairs* 30, 8. <<https://www.healthaffairs.org/doi/10.1377/hlthaff.2010.0891>>

Life Sciences Ontario (2020). *Canada May be Losing its Status as a Top Global Destination for New Medicine Launches*. Life Sciences Ontario. <<https://www.newswire.ca/news-releases/canada-may-be-losing-its-status-as-a-top-global-destination-for-new-medicine-launches-855431139.html>>

Life Sciences Ontario (2021). *Federal PMPRB Drug Pricing Rules Already Stopping What Canadians Want: Access to New Cancer Medicines and Other Treatments as Soon as Possible*. Life Sciences Ontario. <<https://www.businesswire.com/news/home/20210121005102/en/Federal-PMPRB-Drug-Pricing-Rules-Already-Stopping-What-Canadians-Want-Access-to-New-Cancer-Medicines-and-Other-Treatments-as-Soon-as-Possible>>

Lucas, Paul (2020). *Canada's Vaccine Development Capacity and the Federal Government's Management of COVID-19*. Canadian Health Policy. <<https://www.canadianhealthpolicy.com/products/canada---s-vaccine-development-capacity-and-the-federal-government---smanagement-of-covid-19.html>>

Lybecker, Kristina M. (2017). *Intellectual Property Rights Protection and the Biopharmaceutical Industry: How Canada Measures Up*. Fraser Institute. <<https://www.fraserinstitute.org/sites/default/files/intellectual-property-rights-protection-and-the%20biopharmaceutical-industry.pdf>>

Lybecker, Kristina M. (2016). *The Biologics Revolution in the Production of Drugs*. Fraser Institute. <<https://www.fraserinstitute.org/sites/default/files/biologics-revolution-in-the-production-of-drugs.pdf>>

Martell, Allison (2020, 20 February). *Exclusive: Canadian Regulator Considers Changes to New Drug Pricing Plan*. Reuters. <<https://news.yahoo.com/exclusive-canadian-regulator-considers-changes-184639667.html>>

McMahon, Eileen, and Denise Ramsden (2021). *Orphan Drugs in Canada: A 'One Size Fits All' Regulatory Regime*. Food and Drug Law Institute. <<https://www.fdli.org/2021/05/orphan-drugs-in-canada-a-one-size-fits-all-regulatory-regime/>>

Oakes, Kari (2020). *Canada's Drug Price Reforms Delayed to 2021*. Regulatory Affairs Professionals Society. <<https://www.raps.org/news-and-articles/news-articles/2020/6/canadas-drug-price-reforms-delayed-to-2021>>

Organisation for Economic Co-operation and Development [OECD] (2017). *New Health Technologies: Managing Access, Value and Sustainability*. OECD.

Owens, Richard C. (2021, 11 February). *The U.S. Outsources Control of Drug Prices to Canada: Weird!* Financial Post. <<https://financialpost.com/opinion/richard-c-owens-the-u-s-outsources-control-of-drug-prices-to-canada-weird>>

Owens, Richard C. (2017). *Defending our Rights Series: An Intellectual Property Strategy for Canada*. Macdonald-Laurier Institute. <<https://www.macdonaldlaurier.ca/defending-rights-series-intellectual-property-strategy-canada/>>

Owens, Richard C. (2021, 3 June). Quebec Gets the Constitution Right (On Drug Price Control). *Financial Post*. <<https://financialpost.com/opinion/richard-c-owens-quebec-gets-the-constitution-right-on-drug-price-control>>

Owens, Richard C. (2020, 31 July). Drug Prices Can Go Too Low. *Financial Post*. <<https://financialpost.com/opinion/drug-prices-can-go-too-low>>

Paris, Valérie (2009). La regulation du prix de médicament en France. *Régards croisés sur l'économie* 1, 5: 215–25. <<https://www.cairn.info/revue-regards-croises-sur-l-economie-2009-1page-215.htm#>>

Patented Medicine Prices Review Board [PMPRB] (2021). *Meds Entry Watch*. 5th Edition. PMPRB. <<https://www.canada.ca/content/dam/pmprb-cepmb/documents/npduis/analytical-studies/meds-entry-watch/MedsEntryWatch-5th-en.pdf>>

Patented Medicine Prices Review Board [PMPRB] (2016). *PMPRB Guidelines Modernization: Discussion Paper*. PMPRB. <http://www.pmprb-cepmb.gc.ca/CMFiles/Consultations/DiscussionPaper/PMPRB_DiscussionPaper_June2016_E.pdf>

Paterson, Jennifer (2020). *PMPRB Publishes New Draft Guidelines, Launches 30-day Consultation*. Benefits Canada. <<https://www.benefitscanada.com/news/bencan/pmprb-publishes-new-draft-guidelines-launches-30-day-consultation/>>

Philipson, Tomas (2016). Unique Aspects of Patents for Medical Innovation: Recent Research Developments. In Steven Globberman (ed.), *Intellectual Property Rights and the Promotion of Biologics, Medical Devices and Trade in Pharmaceuticals* (Fraser Institute). <<https://www.fraserinstitute.org/sites/default/files/intellectual-property-rights-and-promotion-of-biologics-medical-devices-and-trade-in-pharmaceuticals-post.pdf>>

Philipson, Tomas (2017). Paying for Cost-Effective Health Care: Does it Violate Both Static and Dynamic Efficiency? *Nordic Journal of Health Economics* 5, 1: 58–61. <<https://journals.uio.no/NJHE/article/view/1289/1178>>

Rabson, Mia (2021, 29 June). Canada Delays New Drug-Pricing Regulations until January 2022. *Toronto Star*. <<https://www.thestar.com/politics/2021/06/29/canada-delays-new-drug-pricing-regulations-until-january-2022.html>>

Raffoul, Natalie (2021, 10 May). Caught in the Geopolitical Innovation Warfare Over COVID-19 Patent Waivers, Canada Needs a More Strategic IP Policy. *Globe and Mail*. <<https://www.theglobeandmail.com/business/commentary/article-caught-in-the-geopolitical-innovation-warfare-over-covid-19-patent/>>

Rawson, Nigel S. B. (2013). *Potential Impact of Delayed Access to Five Oncology Drugs in Canada*. Fraser Institute. <<https://www.fraserinstitute.org/studies/potential-impact-delayed-access-five-oncology-drugs-canada>>

Rawson, Nigel S. B. (2020a). *Clinical Trials in Canada Decrease: A Sign of Uncertainty Regarding Changes to the PMPRB?* Canadian Health Policy. <<https://www.canadianhealthpolicy.com/products/clinical-trials-in-canada-decrease--a-sign-ofuncertainty-regarding-changes-to-the-pmprb-.html>>

Rawson, Nigel S. B. (2020b). *Fewer New Drug Approvals in Canada: Early Indications of Unintended Consequences From New Patented Medicines Regulations*. Canadian Health Policy. <<https://www.canadianhealthpolicy.com/products/fewer-new-drug-approvals-in-canada--earlyindication-of-unintended-consequences-from-new-pmprb-regs-.html>>

Rawson, Nigel S. B. (2021a). *Clinical Trials in Canada: Worrying Signs that Uncertainty Regarding PMPRB Changes will Impact Research Investment*. Canadian Health Policy. <<https://www.canadianhealthpolicy.com/products/clinical-trials-in-canada--worrying-signs-that-pmprbchanges-will-impact-research-investment.html>>

Rawson, Nigel S. B. (2021b). *Clinical Trials in Canada: Worrying Signs Remain Despite PMPRB's Superficial Response*. Canadian Health Policy. <<https://www.canadianhealthpolicy.com/products/clinical-trials-in-canada--worrying-signs-remain-despite-pmprb---s-superficialresponse.html>>

Rawson, Nigel (2021). *New Review Rules—The Impact on Drug Access in Canada*. Fraser Institute. <<https://www.fraserinstitute.org/blogs/new-review-rules-the-impact-on-drug-access-in-canada>>

Rawson, Nigel S. B., and John Adams (2021). *More than a Dose of Collaboration: What Ottawa Should Do if it Wants Drugs and Vaccines to be Made in Canada and Benefit Patients*. Macdonald-Laurier Institute. <<http://gtipa.org/publications/2021/06/03/more-dose-collaboration-what-ottawa-should-do-if-it-wants-drugs-and-vaccines>>

Rawson, Nigel, Olaf Koester, and John Adams (2020, 30 November). *Our Vaccine Gap Reflects Years of Policy Self-harm*. *Financial Post*. <<https://financialpost.com/opinion/opinion-our-vaccine-gap-reflects-years-of-policyself-harm>>

Rawson, Nigel S. B., and Richard C. Owens (2022, 9 March). *Opinion: Time to Decide: Do We Want Foreign R&D or Not?* *Financial Post*. <<https://financialpost.com/opinion/opinion-time-to-decide-do-we-want-foreign-rd-or-not>>

Research etc. (2020). *Impact of PMPRB Pricing Changes: Final Research Report*. Life Sciences Ontario. <<https://lifesciencesontario.ca/wp-content/uploads/2020/02/Research-Etc.-PMPRB-Survey-02-03-20.pdf>>

Rodwin, Marc A. (2019). *What Can the United States Learn from Pharmaceutical Spending Controls in France?* The Commonwealth Fund. <<https://www.commonwealthfund.org/publications/issue-briefs/2019/nov/what-can-united-stateslearn-drug-spending-controls-france>>

Rolfe, Kelsey (2019). *What Will PMPRB Drug Pricing Changes Mean for Plan Sponsors?* Benefits Canada. <<https://www.benefitscanada.com/news/bencan/what-will-pmprb-drug-pricing-changes-mean-for-plan-sponsors/>>

Skinner, Brett J. (2018). *Consequences of Over-Regulating the Prices of New Drugs in Canada*. Canadian Health Policy. <<https://www.canadianhealthpolicy.com/products/consequences-of-over-regulating-the-prices-of-new-drugs-in-canada.html>>

Skinner, Brett J. (2019). *Patented Drug Prices and Clinical Trials in 31 OECD Countries 2017: Implications for Canada's PMPRB*. Canadian Health Policy. <<https://www.canadianhealthpolicy.com/products/patented-drug-prices-and-clinical-trials-in-31-oecd-countries-2017--implicationsfor-canada---s-pmprb-.html>>

Skinner, Brett J. (2021). *Prices for Patented Medicines in Canada and 13 Other Countries: Testing the PMPRB's Narrative Justification for Amending the Regulations*. Canadian Health Policy. <<https://www.canadianhealthpolicy.com/products/prices-for-patented-medicines-in-canada-and-13-other-countries.html>>

Spicer, Oliver, and Paul Grootendorst (2020). *An Empirical Examination of the Patented Medicine Prices Review Board Price Control Amendments on Drug Launches in Canada*. Working Paper no. 200003, Canadian Center for Health Economics. <<https://www.canadiancentreforhealtheconomics.ca/wp-content/uploads/2020/08/Spicer-Grootendorst-2020.pdf>>

Stewart, David J., and John-Peter Bradford (2021). *Opinion: Stiff Price Controls will hurt Access to Ground-Breaking Drugs*. Healthing. <<https://www.healthing.ca/wellness/opinion/opinion-stiff-price-controls-will-hurt-access-to-ground-breaking-drugs/>>

US Chamber of Commerce (2021). *International IP Index*. US Chamber of Commerce. <https://www.valueingenuity.com/wp-content/uploads/2021/03/GIPC_IPIndex2021_FullReport.pdf>

US Congressional Budget Office (2021). *Research and Development in the Pharmaceutical Industry*. Government of the United States. <<https://www.cbo.gov/publication/57126>>

About the Author

Kristina M. L. Acri, née Lybecker

Kristina M.L. Acri, née Lybecker, Senior Fellow at the Fraser Institute, is an Associate Professor of Economics and Chair of the Department of Economics and Business at Colorado College in Colorado Springs. Her research focuses largely on issues related to intellectual property (IP) rights protection with a particular focus on pharmaceutical-related IP. Prof. Lybecker's recent publications include an evaluation of Canada's IP protection for pharmaceutical products based on international best practices, as well as examinations of alternatives to the existing patent system and the balance between pharmaceutical patent protection and access to essential medicines. She has testified in more than a dozen US states on the economics of pharmaceutical counterfeiting and at the recent Trans-Pacific Partnership trade negotiations on the economics of access to medicine. Prof. Lybecker has also worked with the US Food and Drug Administration, the OECD, and the World Bank on issues of innovation and international trade. She earned a B.A. from Macalester College and received her Ph.D. in Economics from the University of California, Berkeley.



Acknowledgments

The author wishes to thank the anonymous reviewers for their comments, suggestions, and insights. Any remaining errors or oversights are the sole responsibility of the author. As the researcher has worked independently, the views and conclusions expressed in this study do not necessarily reflect those of the Board of Directors of the Fraser Institute, the staff, or supporters.

Publishing Information

Distribution

These publications are available from <<http://www.fraserinstitute.org>> in Portable Document Format (PDF) and can be read with Adobe Acrobat® or Adobe Reader®, versions 7 or later. Adobe Acrobat Reader® DC, the most recent version, is available free of charge from Adobe Systems Inc. at <get.adobe.com/reader/>. Readers having trouble viewing or printing our PDF files using applications from other manufacturers (e.g., Apple's Preview) should use Reader® or Acrobat®.

Ordering publications

To order printed publications from the Fraser Institute, please contact us via e-mail: sales@fraserinstitute.org; telephone: 604.688.0221, ext. 580 or, toll free, 1.800.665.3558, ext. 580; or fax: 604.688.8539.

Media

For media enquiries, please contact our communications department via e-mail: communications@fraserinstitute.org; telephone: 604.714.4582.

Copyright

Copyright © 2022 by the Fraser Institute. All rights reserved. No part of this publication may be reproduced in any manner whatsoever without written permission except in the case of brief passages quoted in critical articles and reviews.

ISBN

978-0-88975-704-2

Citation

Acri (née Lybecker), Kristina M. L. (2022). *An Evaluation of the Proposed PMPRB Amendments*. Fraser Institute. <<http://www.fraserinstitute.org>>.

Supporting the Fraser Institute

To learn how to support the Fraser Institute, please contact us via post: Development Department, Fraser Institute, Fourth Floor, 1770 Burrard Street, Vancouver, British Columbia, V6J 3G7, Canada; telephone: toll-free to 1.800.665.3558, ext. 548; e-mail: development@fraserinstitute.org; or visit our webpage: www.fraserinstitute.org/support-us/overview.aspx.

Purpose, Funding, and Independence

The Fraser Institute provides a useful public service. We report objective information about the economic and social effects of current public policies, and we offer evidence-based research and education about policy options that can improve the quality of life.

The Institute is a non-profit organization. Our activities are funded by charitable donations, unrestricted grants, ticket sales, and sponsorships from events, the licensing of products for public distribution, and the sale of publications.

All research is subject to rigorous review by external experts, and is conducted and published separately from the Institute's Board of Directors and its donors.

The opinions expressed by authors are their own, and do not necessarily reflect those of the Institute, its Board of Directors, its donors and supporters, or its staff. This publication in no way implies that the Fraser Institute, its directors, or staff are in favour of, or oppose the passage of, any bill; or that they support or oppose any particular political party or candidate.

As a healthy part of public discussion among fellow citizens who desire to improve the lives of people through better public policy, the Institute welcomes evidence-focused scrutiny of the research we publish, including verification of data sources, replication of analytical methods, and intelligent debate about the practical effects of policy recommendations.

About the Fraser Institute

Our mission is to improve the quality of life for Canadians, their families and future generations by studying, measuring and broadly communicating the effects of government policies, entrepreneurship and choice on their well-being.

Notre mission consiste à améliorer la qualité de vie des Canadiens et des générations à venir en étudiant, en mesurant et en diffusant les effets des politiques gouvernementales, de l'entrepreneuriat et des choix sur leur bien-être.

Peer review—validating the accuracy of our research

The Fraser Institute maintains a rigorous peer review process for its research. New research, major research projects, and substantively modified research conducted by the Fraser Institute are reviewed by experts with a recognized expertise in the topic area being addressed. Whenever possible, external review is a blind process. Updates to previously reviewed research or new editions of previously reviewed research are not reviewed unless the update includes substantive or material changes in the methodology.

The review process is overseen by the directors of the Institute's research departments who are responsible for ensuring all research published by the Institute passes through the appropriate peer review. If a dispute about the recommendations of the reviewers should arise during the Institute's peer review process, the Institute has an Editorial Advisory Board, a panel of scholars from Canada, the United States, and Europe to whom it can turn for help in resolving the dispute.

Editorial Advisory Board

Members

Prof. Terry L. Anderson

Prof. Herbert G. Grubel

Prof. Robert Barro

Prof. James Gwartney

Prof. Jean-Pierre Centi

Prof. Ronald W. Jones

Prof. John Chant

Dr. Jerry Jordan

Prof. Bev Dahlby

Prof. Ross McKittrick

Prof. Erwin Diewert

Prof. Michael Parkin

Prof. Stephen Easton

Prof. Friedrich Schneider

Prof. J.C. Herbert Emery

Prof. Lawrence B. Smith

Prof. Jack L. Granatstein

Dr. Vito Tanzi

Past members

Prof. Armen Alchian*

Prof. F.G. Pennance*

Prof. Michael Bliss*

Prof. George Stigler*†

Prof. James M. Buchanan*†

Sir Alan Walters*

Prof. Friedrich A. Hayek*†

Prof. Edwin G. West*

Prof. H.G. Johnson*

* deceased; † Nobel Laureate