

Proposed Amendments to the Patented Medicines Regulations: A Critical Appraisal of the Cost-Benefit Analysis

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This analysis, commissioned by Innovative Medicines Canada (IMC), was conducted and reported independently by PDCI Market Access.

1. INTRODUCTION

KEY MESSAGE: Health Canada significantly overstates the benefits of its proposed regulatory amendments and underestimates their likely negative impact—both to Canadians and to the pharmaceutical industry. PDCI’s reanalysis of Health Canada’s methodology raises significant questions about the rationale for the proposed amendments, and about their actual value to Canadians.

In December 2017, the Governor-in-Council published in Canada Gazette Part 1 the most comprehensive changes affecting patented medicines since Bill C-91¹ was passed by the Government of Canada more than 25 years ago. These proposed regulatory changes by Health Canada to the mandate of the Patented Medicines Prices Review Board (PMPRB) appear to suggest that events of the past 25 years have led to today’s scenario where patented drug prices are excessive and uncontrollable under existing price regulatory mechanisms. However, the evidence does not support this suggestion. On the contrary, available evidence confirms that current methods of drug cost management are generally working well across both public and private systems in Canada.

This analysis, conducted by PDCI Market Access, provides additional perspectives and evidence with the aim of helping policy-makers and all Canadians to critically assess the cost–benefit analysis (CBA) that Health Canada prepared, and which supports the proposed changes. The information herein investigates the extent to which the proposed changes will impact the balance among three key factors: the affordability of medicines, their availability in Canada, and the need to support a vibrant life-sciences sector.

This report details five key concerns:

1. Health Canada significantly underestimates the negative impact of its proposed regulatory changes and overstates the positive impact.
2. The proposed changes will result in longer delays for access to the most innovative medicines, and some may never be launched in Canada.
3. The proposal conveys an exaggerated sense of urgency for pricing regime change, which is not substantiated by available evidence.
4. The process for these regulatory changes has not been sufficiently transparent to date. At present, it is inconsistent with the government’s own framework for policy changes.
5. Health Canada has proposed changes that substantially duplicate existing strategies for assessing drug value, negotiating listings, and making reimbursement decisions.

Health Canada’s CBA provides an extensive and complicated assessment of how it believes the impact of the proposed amendments will affect the pharmaceutical industry. However, the document does not adequately explore those expected impacts. Rather its methods and assumptions skew Health Canada’s policy analysis towards overly optimistic perspectives and outcomes. The CBA also largely discounts or ignores the broad negative effects on the pharmaceutical industry—and, by extension, on the broader Canadian life-sciences sector, which benefits from a successful and robust pharmaceutical industry. Moreover, the changes effectively duplicate the current and effective cost management strategies of Canada’s public and private drug plans.

1.1. METHODS

This report critically analyzes Health Canada's proposed amendments, summarizing the key messages, observations and questions that arise. Documents reviewed for the purposes of this report include:

- Regulations Amending the Patented Medicines Regulations Regulatory Impact Assessment Statement (RIAS), December 2, 2017
- Amendments to the Patented Medicines Regulations, Patented Medicines Prices Review Board Modernization Cost-Benefit Analysis (CBA), September 8, 2017
- PMPRB Guidelines Scoping Paper, December 11, 2017

The reanalysis presented in this report is based on researched evidence and conventional economic assumptions accepted and used by health technology assessment organizations in Canada. These include Québec's Institut national d'excellence en santé et en services sociaux (INESSS), and the Canadian Agency for Drugs and Technologies in Health (CADTH).

Reanalyzing using these core assumptions, the reanalysis provides critical appraisals of the:

- Impact on patented medicines revenue
- The fiscal multiplier assumption and its impact on the CBA outcome
- Uncounted Indirect Effects on Canadians

2. DIRECT AND INDIRECT IMPACTS OF THE PROPOSED CHANGES

KEY MESSAGE: Health Canada's CBA uses unrealistically low financial assumptions, severely underestimating the direct and indirect negative impacts of its proposed regulatory changes to the innovative pharmaceutical industry in Canada and, by extension, the broader life-sciences economy.

KEY MESSAGE: The CBA significantly underestimates the direct costs of the proposed regulatory amendments to the innovative pharmaceutical industry in Canada.

2.1. DIRECT IMPACT ON CANADA'S INNOVATIVE PHARMACEUTICAL INDUSTRY AND LIFE-SCIENCES ECONOMY

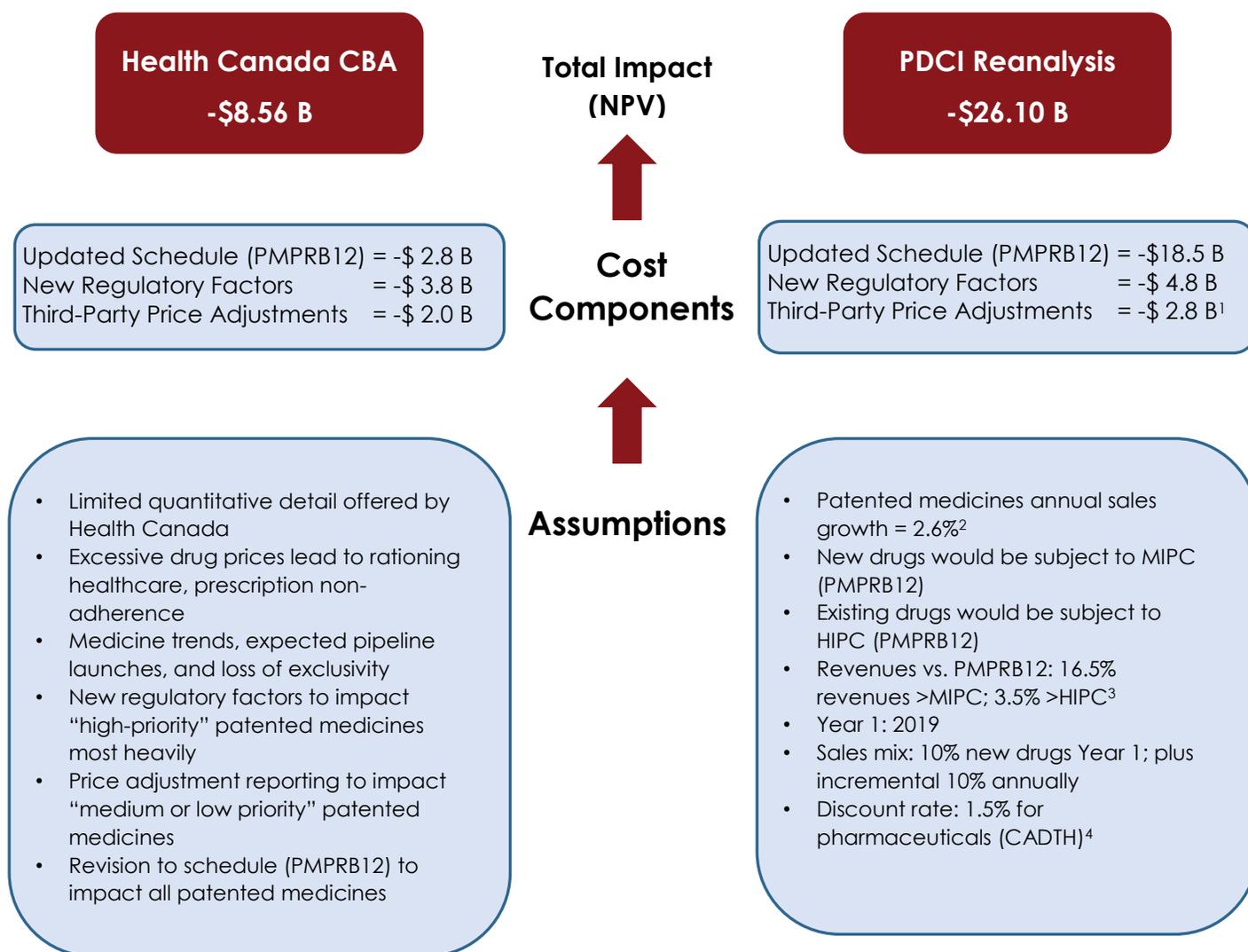
Health Canada's CBA suggests its regulatory changes will have a 10-year net present value (NPV) direct impact on the pharmaceutical industry of \$8.56B. However, as illustrated in Figure 1 PDCI's reanalysis estimates this impact is likely to be almost three times larger (**\$26.1B**) than Health Canada's CBA estimate. Moreover, neither estimate accounts for broader, indirect negative effects on Canada's life-sciences sector.

Prior to presenting PDCI's reanalysis, it is important to note that Health Canada's original assumptions are not always clearly and/or quantitatively defined in the CBA report, meaning the reanalysis may be based on different methods.² For example, in the January 10, 2018 CBA Information Session hosted by Health Canada, Government officials stated the CBA applied Economic Based Factors prior to New Price Regulatory Factors. The CBA method is

also inconsistent with the Scoping Paper issued by PMPRB, which illustrated the flow of evaluation to assess new PMPRB12 Price Regulatory Factors first, followed by New Economic Factors. PDCI based its reanalysis by applying the new factors independently, with emphasis on the new PMPRB12 Price Regulatory Factors. PDCI believes this approach is more consistent with the PMPRB Scoping Paper.

While grandfathering / transitioning for current patented medicines may reduce year 1 impact in the reanalysis, this is considered in neither the CBA nor the PDCI analyses.

Figure 1: Health Canada Significantly Underestimates the Negative Impact of its Proposed Regulatory Amendments on the Innovative Pharmaceutical Industry



1. Calculation = New Regulatory Factors + Third-Party Reporting at 1.5% discount rate
 2. PMPRB 2016 Annual Report
 3. PDCI Research on 110 Top-Selling Drugs in Canada
 4. CADTH: Reference-case rate for costs and outcomes is 1.5%. CADTH suggests this rate is “grounded in the principles of a social decision-making viewpoint on social choice.” https://www.cadth.ca/sites/default/files/pdf/CADTH_Economic_Guidelines-3rd_vs_4th_Editions.pdf

The PDCI reanalysis projects the impact on patented medicines revenue (at a 1.5% discount rate) to be \$26.1B for the ten-year period. This amount is within the upper range of potential impact projected in Health Canada's CBA.

The difference between Health Canada's and PDCI's estimates results from the fact that Health Canada uses an outdated discount rate of 7%.³ This is inappropriate in the context of the health system, and out of step with the economic forecasting rates used in the life-sciences sector. Even CADTH's previous discount rate (5%) was recognized as "substantially higher than the discount rates used by equivalent agencies in other economically developed economies."⁴ Therefore the 7% rate significantly understates the true 10-year impact on the pharmaceutical industry.

PDCI Reanalysis Key Assumptions

- PDCI's patented medicines revenue projections are adjusted to the observed 2016 annual growth rate, as per the PMPRB's 2016 Annual Report. Health Canada's projected 2019 patented medicines revenues (\$19.3 billion) exceed projections based on current growth. The values PDCI presents are in unadjusted dollars.⁵
- PDCI analyzed publicly available international price sources for current patented medicines from the new PMPRB12 reference countries. The analysis resulted in the following key assumptions:
 - 16.5% of existing patented medicines revenues exceeds the revised PMPRB12 Median International Price Comparison (MIPC). This percentage is applied as a negative revenue impact to products to be introduced to Canada over the ten-year period.
 - 3.5% of revenues from existing patented medicines revenues exceeds the revised PMPRB12 Highest International Price Comparison (HIPC). This percentage is applied as a negative revenue impact to products already available in Canada.⁶
 - The reductions are applied against the revised revenue projections.
- PDCI based its NPV calculations on CADTH's recognized discount rate for evaluating health technologies (1.5%), rather than on Health Canada's discount rate (7%).
- PDCI's assumptions about impacts of new factors (including the pharmacoeconomic factors) and third-party price adjustment reporting are unchanged from Health Canada's. The potential impact due to the inclusion of pharmacoeconomic factors will likely be significantly greater than what is projected in the CBA.
- Finally, PDCI assumes that each modified regulatory factor is independent, and not affected by application of other factors.

Table 1 compares key assumptions relied upon in PDCI's reanalysis to the assumptions that PDCI found to regenerate Health Canada's CBA results. The details of PDCI's revised analysis are presented in Table 2.

Table 1: PDCI Reanalysis Compared to Health Canada Assumptions

Factor	Health Canada Assumptions	PDCI Assumptions
Compound Annual Growth Rate*	4.2%	2.6%
Discount Rate**	7.0%	1.5%
Percent of Existing Drug Revenues Exceeding PMPRB Median International Price Comparison (MIPC)***	3.0%	16.5%
Percent of Existing Drugs Exceeding PMPRB Highest International Price Comparison (HIPC)***	0.7%	3.5%

*Compound annual growth rates are based on a projection period from 2015 base year to the end of 2028.

** PDCI based its NPV calculations on CADTH's approved discount rate for evaluating health technologies (1.5%).

***Based on PMPRB12 Reference Countries

Table 2: PDCI Reanalysis of Patented Medicines Revenue Impact

Canadian \$ Billion (Unadjusted)	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028
Baseline Industry Revenues*	\$16.7	\$17.2	\$17.6	\$18.1	\$18.5	\$19.0	\$19.5	\$20.0	\$20.5	\$21.0
Growth Rate	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%
PMPRB Regulatory Reforms Impacts (Canadian \$ Billion)										
Updated Schedule (PMPRB12)	(0.80)	(1.04)	(1.30)	(1.56)	(1.84)	(2.14)	(2.45)	(2.77)	(3.11)	(3.46)
New Regulatory Factors	(0.03)	(0.09)	(0.18)	(0.29)	(0.42)	(0.57)	(0.76)	(0.96)	(1.12)	(1.40)
Third-Party Price Adjustments	(0.05)	(0.10)	(0.15)	(0.21)	(0.27)	(0.33)	(0.40)	(0.46)	(0.51)	(0.61)
Subtotal: Patented Pharmaceutical Revenue Impact	(0.88)	(1.22)	(1.62)	(2.04)	(2.50)	(2.99)	(3.53)	(4.11)	(4.71)	(5.36)
Modified Patented Revenues	\$15.8	\$15.9	\$15.9	\$16.0	\$16.0	\$16.0	\$16.0	\$15.9	\$15.8	\$15.7
NPV (1.5%) of Updated Schedule (PMPRB12)					\$ 18.5 B					
NPV (1.5%) of New Factors					\$ 4.8 B					
NPV (1.5%) of 3rd-Party Price Adjustment Reporting					\$ 2.8 B					
Total NPV (1.5%) of Pharmaceutical Revenue Impact					\$ 26.1 B					

*Growth rate of 2.6% based on PMPRB 2016 Annual Report of 2016 patented medicines growth.

TAKEAWAY: Health Canada's base case estimate of the financial impact of the proposed amendments on patented medicine revenues is at the low end of its CBA's sensitivity analysis range. Potential negative impact of almost three times the presented base case is within Health Canada's sensitivity range.

2.2. FISCAL MULTIPLIER EFFECTS OF HEALTHCARE SPENDING

KEY MESSAGE: For its fiscal multiplier, Health Canada uses a figure based on a study of short-term health investment effects of multiple European nations. The chosen multiplier does not reflect Canadian context and overstates potential reinvestment benefits well beyond general Canadian government fiscal multipliers.

In its CBA, Health Canada's fiscal multiplier for health spending is based on a 2013 paper by Reeves et al., which examined experiences from 1995 to 2010 in 25 European Union countries.⁷ That study examined healthcare spending during periods of consistent economic activity—that is, before the 2008 economic crisis—and found that it was associated with a positive government investment multiplier of 4.3 (95% CI, 2.5–6.14). It concluded that there is a short-term benefit associated with healthcare investment that may aid recovery from a recession. During recession the health multiplier is attenuated (speculated to be due to the substitution of private health spending for public).

However, the use of the 4.3 multiplier for estimating the long-term impacts of changes in health spending is founded on a paper that is not exploring long-term fiscal effects; and more importantly, that multiplier is not based on Canadian experience or experience in an economy like Canada's. The EU countries have a wide variance of economic health, health policy, and Gross Domestic Product (GDP), and the economic effects may also be altered by their common currency and shared interest rates. A more appropriate multiplier for Canada might be that calculated by teams such as Owyang et al. (2013),⁸ and Ramey and Zubairy (2015).⁹ Their exploration of long-term economic data determined that Canadian government spending is associated with a 0.5 multiplier during periods of low unemployment, and a 1.5 multiplier during periods of high unemployment.

During normal (that is, non-recessionary) times, a more appropriate use for the savings associated with the drugs policy would be to return the excess government revenues to taxpayers. The primary source of the net benefit for Canadians rests on the assumed fiscal multiplier for reinvested public moneys. Applying a more modest multiplier of 2 (which still exceeds the general Canadian spending multiplier of 1.5 observed during periods of slack or recession periods) eliminates the positive benefits the CBA projects. Indeed, the CBA's potential benefits of Health Canada proposed changes depend significantly on the overly optimistic factor of 4.3 used in the CBA analysis.

TAKEAWAY: Health Canada presents an unrealistically low projection of the direct financial harm to the innovative pharmaceutical industry. The actual negative impact is likely to be at least three times greater.

2.3. INDIRECT IMPACTS

KEY MESSAGE: Health Canada fails to consider several critical factors that have important indirect economic effects for Canadians, such as the impact on related health industries, and the consequence of lost taxation revenues.

In its CBA, Health Canada does not seem to account for the significant revenue to governments (both federal and provincial) that would be lost because of the proposed amendments. For example, if all pharmaceutical industry revenues affected by amendments represent company profits, at a simple 39% corporate tax rate (effective tax rates for individual companies may vary), the NPV from loss of tax revenue would be between \$4.7 and \$10.4 billion.¹⁰

Health Canada also ignores the effects on the broader economic sectors, whose revenues are intertwined with or otherwise affected by the Canadian pharmaceutical industry. Some of these potential effects are outlined below.

- Distributors of medicines, including wholesalers and pharmacies, will see lower revenues. At present, the markup permitted by the Ontario Drug Benefit Program is approximately 8% of drug prices. If those drug prices are reduced, so too are the revenues for all stakeholders in the supply chain. However, no commensurate reduction in supply chain services will be possible to accommodate reduced revenues, as the same infrastructure is still required to get drugs to patients.
- If prices of patented medicines are reduced, there will be a trickle-down effect on the manufacturers of generic and biosimilar drugs, as the prices of their products are usually set at a fixed percentage of the corresponding innovative drugs' prices.
- Despite Health Canada's assumption that there will be "zero" economic impact to either the pharmaceutical or the life-sciences industry if \$8B is removed from the market, it seems unreasonable to believe that this would have no impact whatsoever on investments and other economic activity.
- Employment losses among Canadian pharmaceutical companies resulting from the proposed amendments will have residual effects on the economy.
- Two other factors missing from Health Canada's calculations are the loss of health and economic benefits Canadians would experience by continuing to access to new, innovative medicines. For instance, access to innovative medicines introduced over the last several decades has – in many disease areas – facilitated the healthcare system's transition from acute, reactive interventions in hospital beds, to more cases where patients can effectively manage diseases less invasively with medicines at home, and even allowing them to continue school and work. This creates a set of expenditure offsets for our healthcare system as well as residual economic benefits.

2.4. VALUING INNOVATION: RESEARCH & DEVELOPMENT

KEY MESSAGE: The current PMPRB definition of scientific research and development (R&D) significantly undervalues the important contributions of Canada's innovative pharmaceutical industry.

Health Canada's analysis relies on the PMPRB's definition of scientific R&D in Canada which is based on the 1987 Income Tax Act – an outdated definition from more than 30 years ago. This inappropriate definition suggests that R&D is only 4.4% of Canadian patentees' pharmaceutical sales. Relying on this number seriously understates the impact of contributions funded by innovative pharmaceutical companies.

Ernst & Young (EY), an internationally respected global accounting firm, reported that innovative pharmaceutical company ("patentee") R&D / investment in Canada represents 9.97% of innovative pharmaceutical sales in 2016. The EY research employs a more appropriate definition of R&D / investment which better reflects the modern innovation and investment landscape in Canada.¹¹ Health Canada has stated that one of its reasons for the proposed amendments is to modernize the PMPRB's regulatory framework, in order to be effective in today's environment. Retaining an outdated definition of R&D from decades ago is therefore both inappropriate and inconsistent with the stated policy objective.

The innovative pharmaceutical industry is also a significant employer: it supports more than 30,000 jobs across the country, including 12,800 directly employed by innovative pharmaceutical companies. The industry's footprint on our domestic economy was \$19.2B in 2016.¹¹

TAKEAWAY: Health Canada discounts the indirect economic value of the innovative pharmaceutical industry in Canada and ignores the potential harm that the proposed amendments will have on the life sciences economic ecosystem.

3. ACCESS TO INNOVATIVE MEDICINES

3.1. DRUG ACCESS DELAYS

KEY MESSAGE: Health Canada's CBA does not effectively measure the negative consequences that the proposed amendments would have on Canadians' access to drugs.

Compared to the current Canadian market access pathway for pharmaceuticals, significant additional delays could be anticipated as public payers and the pan-Canadian Pharmaceutical Alliance (pCPA) would struggle to manage greater negotiation workloads. There is a risk that already lengthy drug listing negotiations will become even more protracted, further delaying Canadians' public reimbursement of new innovative medicines.

- Payers and manufacturers will justifiably consider the regulatory changes to be significant "changes in market conditions". This in turn may trigger clauses in existing drug listing agreements which necessitate that agreements be renegotiated to accommodate new market conditions. Renegotiating these existing agreements could take extensive periods of time and create further backlogs at pCPA which will impede its ability to complete negotiations for new innovative drugs which Canadians cannot yet access. The impact of the proposed amendments on pCPA's ability to negotiate timely agreements is not addressed by Health Canada's CBA. Instead, it offers only qualitative views on the future of the pCPA.
- PDCI research confirms significant that there are already significant delays for new drugs to clear the pCPA and become reimbursed by federal, provincial and territorial (FPT) drug programs. The median time it took the pCPA to assume responsibility for a negotiation file was 104 days in 2016, an increase from 43 days in 2014. Once picked up by the pCPA, an estimated 50% of drugs remain under negotiations after six months – calling into question what further delays will result when pCPA is confronted with dozens of renegotiations for older drugs.

The additional backlog for pCPA negotiations is one of several growing disincentives for innovative drug launches in Canada. Additional access delays compound risks that Canada will be de-prioritized in the global launch sequences for new drugs.

It is worth recalling that the role of the PMPRB is to support a two-sided balance: protecting consumers from excessive patented medicines prices, while ensuring that incentive exists for patentees to introduce new innovative medicines to the country. Indeed, in 1993 when Bill C-91 came into law, the PMPRB mandate was to protect Canadians from excessive pricing of patent-protected medicines. In balance, intellectual property (IP) protection for patented medicines was more closely aligned to other Western economies. In other words, while there were reasonable controls on pricing, patent protections generally aligned with other global economies provided an incentive for innovative drug launch in Canada.

Since Bill C-91, and notwithstanding some periodic improvements, Canadian protection for pharmaceutical innovation has lagged behind the European Union (which includes many of the same countries that will comprise the new PMPRB12 schedule of comparator markets for Canadian patented drug prices). Figure 2 compares the pharmaceutical intellectual property regimes of Canada with other jurisdictions.

Figure 2: Comparison of Canadian and Non-Canadian Pharmaceutical IP Regimes

	JAPAN	CANADA	EUROPEAN UNION	UNITED STATES	
RIGHT OF APPEAL	Canada and US are the only major countries with "linkage" regimes	PM(NOC) regulations that link market approval to patent validity	No "linkage" regimes like in Canada or US	Linkage regime similar to Canada's (the "Hatch-Waxman" system)	
		CETA: Government commitment to ensure equivalent and effective rights of appeal (ROA) N.B. CETA implementation does not redress the ROA imbalance but, in fact, creates an entirely new pharmaceutical litigation regime and removes further rights of innovators in the process.	However, provisional measures (e.g. interlocutory relief) also available in EU to prevent patent infringement	Absence of problematic inequities: e.g. innovators have a right of appeal	
				Provisional measures available	
DATA EXCLUSIVITY	8 years re-examination period + generic approval time (1+ years)	8 years exclusivity	10 years exclusivity	Chemical Entities 5 years exclusivity + FDA approval time (1+ years)	Biologics 12 years exclusivity
	4 years re-examination period + generic approval time	No extension for new indications	1 year extension for new indications	3 year extension for new indications	
	(1+ years) for new indication	Restrictions on Scope of Products			
PATENT TERM RESTORATION	Maximum 5 years additional market exclusivity to one or more patents	CETA: Maximum 2 years additional market exclusivity	Maximum 5 years additional market exclusivity	Maximum 5 years additional market exclusivity	
			Maximum combined patent/Supplemental Protection Certificates (SPC) post-approval market exclusivity of 15 years	Maximum combined post-approval market exclusivity 14 years	
ORPHAN DRUGS IP INCENTIVES	Extension of re-examination period up to 10 years	None	10 years market exclusivity	7 years market exclusivity	

Source: Innovative Medicines Canada¹²

Moreover, since Bill C-91, public payers have continued to introduce policies for managing how and when innovative medicines are reimbursed. As these policies are established, the time to achieve public reimbursement has increased, as evidenced by the time it takes patented drugs to negotiate agreements with the pCPA, before they may proceed to reimbursement discussions with the provinces. These delays reduce the effective public reimbursed patent exclusivity period (i.e. the time a patented medicine is on the market and reimbursed by public payers without forced substitution to generic alternatives).

The increasing requirements for patentees to offer financial concessions to public payers in exchange for drug reimbursement, make the Canadian market increasingly difficult for innovative pharmaceutical manufacturers to achieve timely reimbursement for their products. With the new PMPRB pricing controls, innovative manufacturers are faced with yet another additional barrier to entry in the Canadian market.

3.2. ADMINISTRATIVE EFFECTS AND QUESTIONS

KEY MESSAGE: Implementing and administering proposed amendments represents an unnecessary regulatory burden and wasteful use of public finances.

Implementing new PMPRB regulatory factors will only duplicate the existing roles of drug review agencies and payers.

- Given their respective capacity, authority, and mandates, CADTH, INESSS and public and private payers are better positioned than PMPRB to effectively consider new proposed economics-based factors that inform decisions about drug access, affordability and appropriate use.
- To enforce and administer the new regulations, the budget for PMPRB would increase by 80% from its recent (2015-2016) operating budget of \$10.965M.¹³

New compliance reporting requirements represent an unnecessary regulatory burden on patentees.

- Costs to patentees to comply with new reporting requirements will be significantly more burdensome, and in the case of providing publicly available pharmacoeconomic (PE) studies, unnecessary given that PMPRB can source these studies independently.

The CBA has not effectively forecast new administrative and compliance costs on patentees.

- Remarkably, compliance costs are assessed at only \$10,000 per year for the entire industry. PDCI has projected a more accurate estimate considering costs on a per-Drug Identification Number (DIN) basis which estimates potential costs to be at least 100 times greater than the CBA estimate: an estimated range of \$1M-\$4M per year. Table 3, below, shows a summary of the projected administrative burden; a more detailed explanation of assumptions is given in Appendix 1.

Table 3 - Estimated Compliance and Administration Costs

Estimated Compliance and Administration Costs					
High Estimate	\$ / DIN / filing	DINs	Total Cost / Filing	Filings / Year	Annual Cost
International Price Filings (7 new countries)	\$500	1,250	\$625,000	2	\$1,250,000
Market Size Forecasts	\$500	1,250	\$625,000	4	\$2,500,000
Health Economic Studies	\$250	125	\$31,250	1	\$31,250
					\$3,781,250
Mid Estimate	\$ / DIN / filing	DINs	Total Cost / Filing	Filings / Year	Annual Cost
International Price Filings (7 new countries)	\$250	1,250	\$312,500	2	\$625,000
Market Size Forecasts	\$250	1,250	\$312,500	4	\$1,250,000
Health Economic Studies	\$125	125	\$15,625	1	\$15,625
					\$1,890,625
Low Estimate	\$ / DIN / filing	DINs	Total Cost / Filing	Filings / Year	Annual Cost
International Price Filings (7 new countries)	\$150	1,250	\$187,500	2	\$375,000
Market Size Forecasts	\$125	1,250	\$156,250	4	\$625,000
Health Economic Studies	\$125	125	\$15,625	1	\$15,625
					\$1,015,625

In the CBA's estimate of government costs, the projected incremental costs to administer and enforce the new regulations were projected to reach \$8.8 million per year. This estimate far exceeds the CBA estimates of the incremental costs to industry. It also represents an 80% increase to PMPRB's annual operating budget. Comparably, the revised PDCI estimates of industry costs more closely reflect the increased regulatory burden expected for industry and remain less than half (at the highest estimate) of acknowledged increases in government administrative burden. Further costs related to increased litigation costs comparable to PMPRB's projected Special Purposes Allotment should also be reflected for the industry.

KEY MESSAGE: Numerous questions remain about how PMPRB will implement and administer the proposed amendments, and how patentees will be able to comply.

What will be the time frames and schedule for PMPRB to review new information provided by patentees (e.g. PE studies)?

- Most reviews by CADTH and INESSS are typically not completed until a year or two after the product launches, which is generally after PMPRB has rendered its introductory pricing decisions. Accordingly, a new medicine would potentially be on the market for several years before PMPRB completes its analysis. Manufacturers need certainty before they invest in a product launch in Canada. A PMPRB PE review – in addition to those done by CADTH and INESSS is an additional regulatory burden that will create delays and uncertainty. The added time caused by a PMPRB review will contribute to the risks associated with drug launches in Canada. Some medicines may not be launched in Canada, or alternatively will be launched later, because of the proposed changes.

In addition, new reporting requirements for Market Size are not clear, and may also contravene principles against off-label marketing.

- The Regulatory Impact Assessment Statement (RIAS) discusses “the number of patients that can benefit from a medicine” whereas the proposed regulations require patentees to file forecasts of drug units (e.g. tablets) to be sold. It is unclear how such forecasts will be converted to patients given underlying variables such as multiple indications and dosing differences among patients (for example where dosing is based on weight, age, disease severity, or concomitant use of other medications that could potentiate or inhibit a medication).
- Additionally, since manufacturers are not permitted to market or promote off-label uses, estimating and forecasting this for purposes of PMPRB reporting may raise regulatory compliance concerns as these forecasts could reasonably fit within definitions of marketing activities.

TAKEAWAY: Numerous practical and administrative aspects have yet to be addressed.

4. CREATING A QUESTIONABLE SENSE OF URGENCY

4.1. JUSTIFYING SIGNIFICANT CHANGES WITH LIMITED EVIDENCE

The evidence does not support Health Canada’s and the PMPRB’s assertion that higher cost specialty drugs entering the market (such as drugs for rare diseases, other biologics and oncology drugs) are driving up drug budget expenditures.¹⁴

- It is inappropriate to look at and draw forecast conclusions upon one input into drug budget expenditures. Published data from PMPRB contradicts the presumption that high-cost drug products are driving up drug plan budgets. There are a combination of drivers and inhibitors that work together.
- While specialty drugs may account for 25% to 30% of drug plan expenditures¹⁵, the annual growth in drug budgets has been relatively modest.
 - i. PMPRB’s 2015-2016 CompassRx report, shows small year-over-year drug cost changes in public plans during the three previous fiscal years. These percentages of change were -0.8% in 2012-2013, +2.0% in 2013-2014, and +2.5% in 2014-2015.¹⁶

When it comes to private drug plans in Canada, it does not appear Health Canada’s CBA considered how plan design affects actual costs borne by insurers. Contrary to the narrative presented in the CBA and RIAS, private insurers usually do not pay full list prices for drugs, and they have the capacity to implement drug cost management tools of their own. The CBA’s assumption that private payers are paying list prices while the public market benefits from discounts and rebates is inaccurate.

- Private insurers benefit from lower drug costs through their plan designs. A common plan design is for private insurers to share drug costs with patients (it is generally accepted that private insurers pay in the range of 80% of drug costs).
 - i. According to TELUS Health published data its entire book of business paid for 78% of claimed drug costs.¹⁷
 - ii. When it comes to high-cost specialty drugs (often with retail costs upwards of \$10K per patient per year), it is standard practice for manufacturers to provide patients with direct financial co-pay

assistance. This practice helps ensure patients can afford to access these medicines; and it also supports private insurers to pay less than 100% of the drug cost.

TAKEAWAY: Health Canada has marketed both the need and urgency for this policy change in recent months by relying on incomplete or inappropriate data and assumptions to justify the PMPRB mandate changes.

5. A LACK OF TRANSPARENCY

5.1. A NON-TRANSPARENT POLICY DEVELOPMENT PROCESS

KEY MESSAGE: Lack of transparency in the consultation process and few changes resulting from it makes it appear that the policy outcome was pre-defined by Health Canada.

Health Canada did not disclose stakeholder feedback in response to its initial consultation. Subsequently the Canada Gazette Part 1 and the PMPRB Scoping Paper also provide no compelling indication that stakeholder feedback was meaningfully considered.

- The initial Spring 2017 consultation did not provide stakeholders with all the information needed to meaningfully assess the changes to provide informed input (e.g. the PMPRB Annual Report 2016 was not disclosed, nor were ideas about how amendments would be implemented made clear).
- The CBA (dated September 8, 2017) provides estimates of the impacts of the new excessive price factors. These estimates must have been based on information about how PMPRB intends to operationalize the proposed regulatory amendments, however these additional considerations used by Health Canada in the CBA that are not yet available to stakeholders.

The RIAS does not address key concerns of numerous stakeholders as expressed in consultation submissions:

- There is no mention in the RIAS of the expressed concern that lower prices may delay or prevent access to innovative medicines, (i.e. because the effect of lower revenues in Canada would make it a less desirable investment ecosystem into which pharmaceutical manufacturers will want to introduce their products).
- There is no accounting for the health outcomes costs resulting from delayed or reduced access to new medicines in the future.

TAKEAWAY: The non-transparent processes employed to develop and introduce the proposed amendments reinforces the concern that consultations processes were pro forma exercises designed to fulfill mandatory consultation requirements.

5.2. INCONSISTENCIES WITH THE FEDERAL POLICY FRAMEWORK FOR REGULATIONS

KEY MESSAGE: Several important inconsistencies with the Federal Policy Framework for Regulations undermine the legitimacy of the proposed amendments.

There are several conflicts to be concerned about between Health Canada's approach to its proposed regulatory changes, and the Privy Council Office's Guide to Making Federal Acts Policy Framework for Regulations.¹⁸

- **Canadians were not effectively consulted:** This was due to several limitations of the consultation process, most notably the absence of sufficient information to understand the proposed changes (i.e. the PMPRB

2016 Annual Report, the PMPRB Scoping Paper or similar understanding of how PMPRB would implement new regulations).

- ***That a problem or risk exists has not been confirmed:*** Given the effectiveness of organizations such as CADTH, INESSS, pCPA, and private payers and the initiatives of the manufacturers themselves, all of whom are contributing to reduced drug prices for Canadians, the changes seem to overlap with systems that are already in place to effectively manage drug prices in Canada.
- ***Regulation is not necessarily the best alternative:*** The PMPRB already has the authority to use new tools in determination of excessive drug prices under the *Patent Act*.
- ***Evidence that the benefits outweigh the costs to Canadians has not been established:*** PDCI's reanalysis of Health Canada's CBA exposes several serious limitations, faulty assumptions and missing cost and benefit variables, all of which make it a questionable evidentiary basis for Health Canada to conclude that benefits outweigh the costs to Canadians.
- ***Adverse impacts on the economy to generate wealth and employment are not minimized:*** Health Canada has presented insufficient evidence to assert that adverse impacts on the capacity of the economy to generate wealth and employment are minimized. The CBA does not effectively account for the broader negative impact on the Canadian economy from estimated financial losses to the pharmaceutical industry.
- ***Unnecessary regulatory burden is imposed:*** The amendments to compliance reporting for patentees are inconsistent with this concept. Patentees will be required to provide PMPRB with publicly available PE studies, which are – by definition – publicly available and therefore could be sourced by PMPRB in the public domain. Additionally, these studies are frequently conducted by third party organizations, meaning that manufacturers may not be able to attest to these studies being accurate or otherwise endorse them as the regulations require.

TAKEAWAY: Inconsistencies with the federal government's own framework to evaluate regulatory amendments are concerning. Health Canada falls short of demonstrating these amendments are desirable or, on balance, the right course of action for Canadians.

6. DUPLICATING EXISTING DRUG MANAGEMENT SYSTEMS

6.1. THE ECONOMICS OF VALUE ARE NOT UNIVERSAL AND ARE ALREADY ASSESSED IN CANADA

KEY MESSAGE: It is simplistic to presume that combining assessments of "PE value", with market size, and GDP or GDP/capita can address affordability question for Canada's drug plans. Such a presumption ignores Canadian public drug plans' preferences and priorities; private drug plans' abilities to control their costs through plan design; and the ability of all plans to negotiate drug reimbursement terms.

UNCERTAINTY: Measuring PE value can be subjective; methodological approaches are variable and contested; and the priorities for patients, drug plans, and governments may be inconsistent.

- Defining and measuring the value of a medicine in terms of cost per quality adjusted life year (\$/QALY) only captures the value the innovation provides to payers. If Health Canada is concerned about patient values, the appropriate measures to consider are clinical effectiveness and availability of technology to patients.

- Determining a single, reliable incremental cost-effectiveness ratio (ICER) is impractical due to the inherent uncertainty of PE evaluation inputs (e.g. clinical outcomes measures, quality of life measures). Additionally, there are several different methodological approaches and perspectives (e.g. societal, healthcare system) which may be used to prepare PE studies. These differing approaches often result in substantially different \$/QALY estimates, leaving the user with a potentially wide range of \$/QALY estimates to be expected by implementing the health technology. Instituting a \$/QALY threshold for the purposes of regulating prices seems both impractical and ineffective.
- Cost-utility analyses (CUA) for high-priority products – those that Health Canada and PMPRB appear to be most concerned about – are also the most likely to suffer from critical levels of uncertainty. This can be due to limited information on natural history (for a rare disease for example), a paucity of robust (e.g. large ‘N’) long-term clinical trial data, and either no or very limited Canadian trial data.
 - The PMPRB price ceiling should be established with reference to “abuse of patent monopoly” and must ensure that Canadians are protected from excessive prices that exceed all relevant price factors outlined in Section 85 of the Patent Act. However, there must be a flexible balance between price controls and patients’ access to new medicines, and a \$/QALY threshold contradicts this need. Consumer protection should not be limited to price controls: consumers also want access to new drugs.
- Additionally, it is inaccurate to suggest that CADTH and INESSS *develop* PE studies; rather, they critique those submitted by industry. These critiques often take a risk-averse approach, including ignoring or minimizing long-term value of new medicines for which the evidence may be immature. Considerable inconsistency with the manufacturer-submitted estimates is common, further contributing to the unintelligibility of PE studies for purposes of price regulation.

Drugs that treat rare diseases, cancer and other specialty product disease areas, provide our healthcare system and individuals with tremendous value – often treating small populations and conditions that may have few or no alternative treatments available.

- These products often exceed public payers’ willingness-to-pay thresholds (one notable exception are drugs used to cure hepatitis C) and are sometimes associated with previously unheard-of \$/QALY estimates. Due to the important patient benefits offered by these innovative medicines, these products continue to achieve public and private reimbursement today and currently provide substantial health value to Canadians.
- In general, \$/QALY thresholds have little relevance to willingness-to-pay, particularly for drugs in specialty or rare disease areas. This fact exposes the critical and paralyzing effect of imposing an inflexible \$/QALY threshold at the price regulation level.

7. CONCLUSIONS

Among the five key concerns identified in this report's introduction, perhaps the most notable is lack of a balanced and holistic assessment of the costs and benefits of the PMPRB changes for all interested stakeholders. It is also troubling that Health Canada has proposed the single largest change to Canada's patented pharmaceutical market in 25 years, absent proper collaboration with the Canadian life-sciences sector: the segment of our economy that will bear the brunt of the negative impact following from the proposals.

This report has demonstrated:

1. Health Canada significantly under-estimates the negative impact and over-states the positive impact of its proposed changes.
 - PDCI reanalysis indicates the actual impacts are expected to be at least three times worse than those projected by Health Canada.
2. The proposed regulatory changes will result in longer delays for access to the most innovative drugs in the world, and some innovative medicines may never be launched in Canada.
 - PMPRB's mandate, which has balanced patented medicines' price controls with maintaining incentives for innovative medicines to launch in Canada, is now poised to tip that balance away from access.
3. The proposal conveys an exaggerated sense of urgency to change the pricing regime, which is not substantiated by available evidence.
 - While it is true more specialty medicines are being introduced into markets (with relatively higher costs), the evidence confirms that overall drug budget growth remains modest.
4. The process for regulatory change to date has not been sufficiently transparent; and is inconsistent with the federal government's own framework for policy change.
 - It appears that Health Canada ignored input from dozens of stakeholders and questions remain about how much of its policy was determined before consultations even began.
5. Health Canada is proposing changes that substantially duplicate existing drug value assessments, listing negotiations, and reimbursement decisions.
 - With systems and processes already in place (INESSS, CADTH, pCPA and private plan designs) to review and negotiate reimbursement terms, PMPRB is not the right place in the Canadian market access pathway to impose PE factors for price control purposes.

8. APPENDIX 1: PATENTEE ADMINISTRATIVE AND FILING COSTS

Assumptions for Patentee Administrative Costs from Additional International Reference Countries

Assumptions:

- 7 new PMPRB reference countries, 1,250 DINs, average 2 pack sizes per DIN
- PMPRB will insist (as they do now) that patentees file price data from recognized sources only (internal corporate prices will not suffice)
- PMPRB will insist (as they do now) that VAT, upcharges and publicly available rebates be removed using appropriate formula posted on the PMPRB website
- PMPRB will insist (as they do now) that all reporting is on PMPRB excel spreadsheets sent to patentees and not automatically generated by patentees' computer systems
- Internal approvals – most patentees have formal internal approval process for all regulatory filings
- Acquiring (and translating) the PMPRB recognized price sources varies in cost by country (from free to several thousand dollars)
- Compiling and posting the data into the PMPRB Excel spread sheets is a manual exercise (most patentees do not the prices from PMPRB recognized sources in their internal systems)
- Verification and quality control requires bespoke programming or is adding calculation fields to the PMPRB excel sheets

Acquiring, translating, compiling, adjusting & backing out, posting to spreadsheet, verifying & QA, internal approvals, filing to PMPRB = \$150 - \$500/DIN * 2 semi-annual filings* 1,250 DINs = \$375K - \$1.25M

Assumptions for Patentee Administrative Cost for Reporting Market Size Forecasts

Assumptions

- 1250 Medicines, 2 DINS/Medicine, 4 filings per year per DIN/medicine
- Patentee forecasts are typically updated quarterly (therefore 4 filings / DIN / year)
- PMPRB will require use of a PMPRB approved form – patentees will have to manually restate their forecasts into PMPRB compliant format
- PMPRB will insist on explanations as to why forecasts have changed from one period to the next
- Extracting from internal systems
- Compiling and formatting to PMPRB forms
- Providing justifications to changes in forecasts, responding to PMPRB Staff queries

Extracting, compiling, formatting to PMPRB format, internal approvals, filing to PMPRB, preparing justifications, responding to PMPRB staff enquiries, \$125 - \$500/DIN * 4 quarterly filings * 1,250 DINs = \$625K - \$2.5M

Assumptions for Administrative Costs for Monitoring and Reporting of Canadian Health Economic Studies

Assumptions

- 125 (~10% of 1250) DINS will have Health Economic analyses each year
- Only CADTH and INESSS reports
- Monitoring and Filing CADTH, INESSS
- Filing with PMPRB

Monitoring, extracting, internal approvals and filing with PMPRB = \$125 - \$250 / DIN * 125 DINs = \$16K - \$31K

Total (International prices + Forecasts + Health Economic Studies) = \$1.0M - \$3.8M

9. ENDNOTES

¹ In 1993, Bill C-91 eliminated compulsory licencing under amendments to the Patent Act. In exchange, the industry made additional R&D commitments. The amendments also strengthened the price control powers of the PMPRB to address the hypothesis that improved intellectual property protection might lead to excessive pricing.

² PDCI's analysis methodology was applied to generate Health Canada results and led to assumptions of 3% of revenues above MIPC12 and 0.7% of revenues above HIPC12.

³ Although Treasury Board of Canada may allow the use of 7% discount rate in the CBA, this is not an appropriate rate in the Health System context.

⁴ Paulden, M., Galvanni, V., Chakroborty, S., Kudinga, B., McCabe, C., (2016), Discounting and the Evaluation of Health Care Programs. Available at: https://www.cadth.ca/sites/default/files/pdf/CP0008_Economic_Evaluation_Guidelines_Discount_Rate_Report.pdf

⁵ Health Canada's CBA inconsistently reports figures: sometimes they are in unadjusted dollars and sometimes constant 2017 dollars, while also calculating NPV to 2019, 2017 or 2012 dollars. Although NPV calculations in the CBA appear to discount to end of 2019 (not the beginning), at a January 10, 2018 information session a PMPRB analyst stated emphatically that NPVs and tables are presented in 2017 constant dollars. It should also be noted that according to Canada's CBA guidelines NPVs should not be calculated from constant dollars.

⁶ During its information session on January 10, 2018 Health Canada suggested some grandfathering may be considered for existing medicines falling outside revised guidelines. The specifics of and period of grandfathering were not specified and remained unclear at the time of publishing this report.

⁷ Reeves, A., Basu, S., McKee, M., Meissner, C., & Stuckler, D. (2013). Does investment in the health sector promote or inhibit economic growth? *Globalization and Health* 9:43. doi:10.1186/1744-8603-9-43

⁸ Owyang, M. T., Ramey, V. A., & Zubairy, S. (2013). Are government spending multipliers greater during periods of slack? Evidence from twentieth-century historical data. *American Economic Review: Papers & Proceedings* 103(3): 129–34. doi:http://dx.doi.org/10.1257/aer.103.3.129

⁹ Ramey, V. A., & Zubairy, S. (2015). Are government spending multipliers state dependent? Evidence from Canadian historical data. University of California San Diego, University TAM, editors, <https://www.aeaweb.org/conference/2016/retrieve.php?pdfid=435>

¹⁰ Based on Health Canada's discount rate (7.0%) NPV of 39% revenues = \$4.7B. However, using PDCI's reanalysis discount rate to calculate NPV (1.5%) produces NPV of \$10.4B. (This assumption may vary according to specific tax rates.)

¹¹ Innovative Medicines Canada: Data Analytics and Members' Economic Footprint and Impact in Canada, Ernst & Young, Oct 2017, p. 23. Available at: http://innovativemedicines.ca/wp-content/uploads/2017/10/20171030_EY-REPORT_IMC_FINAL.pdf

¹² Innovative Medicines Canada (2016). Comparison of Canadian and non-Canadian pharmaceutical IP regimes. Accessed Jan 15, 2018. Available at: <http://innovativemedicines.ca/resource/comparison-of-canadian-and-non-canadian-pharmaceutical-ip-regimes>

¹³ PMPRB 2016 Annual Report.

¹⁴ Health Canada's CBA states "expenditure for high-priority medicines (i.e. biologics, medicines for rare diseases, and oncology medicines) is expected to represent an increasing large share of total spending in the coming years," on page 15.

¹⁵ ESC Drug Trend Reports (2014, 2016); TELUS Health presentation to the Benefits Breakfast Club Meeting, June 2017.

¹⁶ Compass Rx, 3rd Edition: Annual Public Drug Plan Expenditure Report 2015/16, p. iii.

¹⁷ Ng, Vincent (2017). Presentation at TELUS Annual Conference 2017 (slide 14).

¹⁸ Privy Council Office. *Guide to Making Federal Acts and Regulations*. Accessed Dec 12, 2017. Available at: <http://www.pco-bcp.gc.ca/index.asp?lang=eng&page=information&sub=publications&doc=legislation/part3-eng.htm>