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SUBMISSION

CANADA GAZETTE, PART I

REGULATIONS AMENDING THE PATENTED MEDICINES REGULATIONS

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EXECUTIVE SUMMARY

The draft regulatory changes published in Canada Gazette Part 1, December 2, 2017 ("CG1") fundamentally alter the role and responsibilities of the PMPRB. Collectively, they would change the PMPRB's original purpose as a safeguard against the potential for excessive pricing of patented medicines in Canada, and transform the PMPRB into a national patented medicines price control regulator.

This new and expanded role will have serious and negative consequences for patients' access to medicines in Canada and the Canadian life sciences sector. Based on launch and reimbursement data from other countries,[1] 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.

In light of the significant consequences of the proposed regulatory changes, IMC would welcome an urgent dialogue with the federal government regarding alternative options that would allow the Health Minister to successfully address her mandate objectives[2] while respecting current timelines to enact new regulations. IMC believes that these objectives can be achieved through the implementation of more pragmatic and predictable measures that will yield significant savings for Canadian payers, while preserving access to medicines and a viable innovative pharmaceutical sector in Canada.

IMC's alternative proposal to significantly lower patented drug prices for all Canadians is reflected in ANNEX A to this submission. We present this proposal as one possible option, but wish to emphasize that our industry is open to exploring alternative options with the Government of Canada. We hope to move forward with a reasonable policy alternative in partnership with the government.

The need for an alternative arises from serious flaws and legal questions arising from the CG1 regulatory proposals. To further explore our concerns with the proposals and why an alternative solution is required, IMC has prepared an analysis and commentary on several major issues posed by the proposed regulations, the accompanying Regulatory Impact Assessment Statement (RIAS) and Health Canada's Cost Benefit Analysis (CBA) document.[3] These documents are characterized by what we believe to be numerous deficiencies, unsubstantiated assertions, and unrealistic assumptions. The following summarizes our major concerns with the CG1 proposals:

1. **UNSUBSTANTIATED POLICY RATIONALE: The policy rationale for changes of this magnitude is flawed.** The scope and magnitude of the proposed regulatory changes have not been justified. The analysis provided in CG1 does not support the nature of the changes proposed nor the magnitude of the impacts to the life sciences sector and to patients in Canada. These significant changes may lead to avoidable litigation as well as costs for government including an "increased number of compliance and

enforcement activities" that will cost taxpayers some $82.5 million according to Health Canada.[4] The proposals will also result in additional costs for all parties in excess of those estimated in the CBA.

2. **FLAWED COST-BENEFIT ANALYSIS: The CBA understates the negative impact of the proposed changes to industry and patient access, while overstating the potential benefits to Canada.** The CBA[5] underestimates the magnitude of impacts and does not account for several important associated impacts to manufacturers, patients, and governments. The CBA's range of the potential impacts is so large that the estimates are of very limited value, and also lack clarity with respect to assumptions and impact variables.[6] The CBA analysis does not account for impacts to new product launches, industry employment, R&D, or tax revenue loss to government. Furthermore, the CBA was apparently compiled without input from the Ministry of Innovation, Science and Economic Development[7] or other government agencies that could offer expertise and insight on the overall impact on the Canadian pharmaceutical industry and life sciences sector.

3. **NEGATIVE IMPACT: The proposed changes would have a significant negative impact on the number of new drugs available to Canadian patients and life sciences research and investment in Canada.** The proposals would have the effect of downgrading Canada as at top-tier jurisdiction for new product launches and will negatively impact Canada as a destination for clinical trials and investment. The primary beneficiary of the proposed changes would appear to be the private insurance market. Canada's Premiers have acknowledged "[a]s of March 31, 2017, the pCPA's efforts have led to a $1.28 billion a year in estimated combined jurisdictional savings."[8] A net transfer of value to private drug plans risks making it more difficult for government-funded drug plans to secure best value for the vulnerable populations they cover.

4. **LACK OF MEANINGFUL CONSULTATION: To date, the consultation process has been deficient and has not meaningfully addressed critical stakeholder feedback.** Insufficient information has been provided to satisfy federal consultation guidelines. Despite the issuance of the proposed Regulations and RIAS, preceded by the Health Canada May 2017 consultation document, there is still inadequate information for patentees to understand and comment on the full effect of the proposed changes. This confusion is only exacerbated when reading the regulatory proposals in conjunction with a Scoping Paper subsequently released by the PMPRB.[9] The proposals lack clarity and empower the PMPRB with inappropriately wide discretion with respect to implementation. Most pre-CG1 input from the regulated patentees and thoughtful perspectives from patients appears to have been ignored, given that the CG1 proposals are essentially identical to the original regulatory proposals set out in the May 2017 consultation document.

5. **NEW COUNTRY SCHEDULE UNREFLECTIVE OF CANADIAN ECONOMIC POSITION: The International Schedule proposals are not reflective of Canada's economic standing or aspirations regarding access to medicines.** Health Canada's stated objective for selecting new comparator countries was to target alignment with "OECD median prices."[10] However, Canada's advanced economic status is well above the OECD median in terms of GDP-per-capita and many other economic criteria. Canada should seek to benchmark internationally against other leading global economies and health systems. The proposed Schedule adds countries that have poorer access (i.e. fewer product launches) or significant launch delays compared to Canada (ANNEX C).

6. **INAPPROPRIATE USE OF PHARMACOECONOMICS: Pharmacoeconomic analysis as expressed "pharmacoeconomic value" is inappropriate within the federal price ceiling regulation context.** Pharmacoeconomic analyses cannot be validly used to regulate excessive price ceilings and would extend the role of the PMPRB well beyond its mandate under the *Patent Act*. Cost-effectiveness evaluation conducted by Health Technology Assessment (HTA) bodies such as CADTH and INESSS (Quebec), are used downstream in reimbursement decision-making and are meant to inform payers regarding value-based negotiations. The PMPRB is not a payer: this role is already being filled by the public drug plans or private insurers in the Canadian context. With the changes proposed by Health Canada, Canada will be out of step with many comparator countries (e.g. Germany, Spain) regarding applicability of cost-effectiveness thresholds in price regulation. Moreover, CADTH conducts re-analyses and issues non-binding recommendations from a public drug plan perspective, and not from a societal perspective. It is inappropriate to use CADTH evaluations for any purpose other than the intended objective of supporting reimbursement decision making at the public drug plan level.

7. **UNECESSARY NEW MARKET SIZE and GDP FACTORS: These proposed additional factors add complexity and regulatory burden with no clear purpose, and should not be incorporated into regulation.** Market size factors are outside the jurisdiction of the PMPRB. Market size reporting would require additional regulatory filing burden for *prospective* market size forecasts that by their very nature are uncertain and unreliable, and are best left as a factor to be included in risk-based negotiations between manufacturers and provinces. Unlike market forecasts used by payers and submitted by manufacturers on a voluntary basis, the incorporation of prospective market forecasts into mandatory federal regulations designed to monitor excessive pricing of patented medicines would appear to be unique internationally, and discriminatory to the pharmaceutical sector. In addition, and given the outstanding questions related to how GDP and GDP-per-capita may be applied by the PMPRB, IMC recommends against their adoption as new mandatory factors.

8. **CONFIDENTIAL INFORMATION REPORTING IS INAPPROPRIATE AND RAISES LEGAL ISSUES.** IMC is opposed to the mandatory submission of confidential price adjustment information to the PMPRB. Without limitation, this opposition arises from the questionable purpose and use of the information to be collected by the PMPRB, potential legal concerns, the risk of significant and negative consequences for public payers and other market participants. There are also numerous practical challenges regarding access to and use of such information while protecting its confidentiality.

9. **INCREASED REGULATORY BURDEN: The proposals would introduce significant incremental regulatory burdens that are unnecessary to regulate excessive prices.** The complexity and red tape that arise from the proposals is not necessary to effectively regulate potential excessive pricing of patented drugs. The proposed accountabilities and surveillance requirements regarding "every cost-utility analysis prepared by a publicly funded Canadian organization" are concerning.[11] Similarly, proposed new reporting requirements for "maximum use" forecasts would be onerous and impose ongoing business forecasting requirements for patented products.[12] Market forecasts and other new regulatory burdens are not necessary to regulate excessive pricing of patented medicines and should be avoided. Canadian public and private drug markets already have an abundance of cost-containment tools administered through a highly complex system of agencies and practices. If lowering patented medicine prices at the federal level is the policy objective, this can be achieved in a simpler manner than that set out in the proposed regulations.

10. **PROSPECTIVE APPROACH: In the interest of fairness and to reflect investment decisions already made in Canada, the grandfathering of existing products from the proposed amendments is necessary.** The PMPRB has already deemed current products to be non-excessive. Potential future transition measures in the PMPRB's Guidelines are an insufficient substitute for *regulating* the grandfathering (i.e., exemption) for all existing products. The prospective application of the Regulations is essential to avoid undermining vested patentee economic interests in currently marketed medicines, and to do otherwise will create chaos with respect to the status of existing product listing agreements with Canadian public and private payers.

11. **TRADE IMPACTS: The proposals may impact Canada's relations with the United States and undermine trade commitments including those to the EU under CETA**. The proposed regulations are inadvisable at a particularly sensitive time in the important Canada-U.S. relationship. The practical impact of CG1 is also likely to result in delayed access to medicines in Canada which will, in turn, undermine a practical benefit for patentees stemming from Canada's intellectual property commitments under the Comprehensive Economic and Trade Agreement (CETA).

1. **UNSUBSTANTIATED POLICY RATIONALE**: THE POLICY RATIONALE FOR CHANGES OF THIS MAGNITUDE IS FLAWED.

Policy rationale not supported by evidence

Health Canada has not demonstrated or sufficiently supported its fundamental policy rationale for regulatory changes that would completely alter the role of the PMPRB beyond its statutory and excessive pricing mandate. The proposals would increase regulatory uncertainty and attempt to address issues that are beyond the PMPRB's legislative mandate with respect excessive patented medicine prices.

The regulatory changes have been advanced on the premise that current policy tools are incapable of regulating excessive price ceilings.[13] This assertion has not been substantiated. CG1 notes Canada's ranking in aggregate per-capita consumption (expenditure) patterns of all medicines (prescription, non-prescriptions, patented, non-patented).[14] Data such as per-capita expenditure of all medicines and changes in the composition of drug expenditure relative to other healthcare spending are employed as a key part of the justification for proposed changes to the regulatory mechanism for patented ex-factory prices. This reflects a disconnect between policy objectives and actual regulatory powers granted through legislation.

The PMPRB's 2016 Annual report indicates that patented medicine prices have been remarkably stable over time. The annual rates of change of the Medicines Price Index (PMPI) has not exceeded 0.9% since 1992.[15] Prices have also declined relative to Canada's regulatory comparators: in 2016, the average international median price was 25% higher than Canadian prices (versus 18% in 2015, and 11% in 2001).[16] This metric is more relevant to the PMPRB's legislative mandate in that it addresses *patented drug prices* rather than comparative *expenditures for all medicines* (including non-patented), as described in the policy justification for these proposals..

CG1 also states that Canadian patented drug prices are the 3rd highest in the OECD, and provides a calculation of Canadian prices in relation to OECD median prices, but provides no citation for this information for the purposes of validation. The same assertions were made in Health Canada's May 2017 consultation document,[17] which cites the PMPRB Annual Report 2015, which in turn cites IMS AG MIDAS™ database, but provides insufficient methodological notes for validation. IMC members have previously raised concerns[18] with respect to the use and interpretation of these data sources with Health Canada. Furthermore, this assertion conflicts with other data from the PMPRB from actual regulatory filings suggesting that Canadian prices are essentially tied for forth highest,[19] notwithstanding sizable product listing agreement (PLA) discounts that are not included in this assessment.

Another important component of Health Canada's policy rationale relates to industry research and development (R&D). CG1 cites a metric of R&D-to-sales ratios that is well known to be flawed and incomplete.[20] Health Canada has been made aware of these deficiencies on many occasions, and most recently in IMC's June 28, 2017 submission.[21] Furthermore, in October 2017, new analysis was published by the international accounting firm EY and presented by IMC to Health Canada in advance of CG1. The analysis concludes that IMC members reinvested an estimated total of 9.97% of gross patented product revenue into R&D in 2016.[22] While there can be ongoing debate on methodological approaches, we would encourage the Government of Canada to adopt a more balanced perspective on the industry's R&D contribution and not predicate policy on flawed R&D data collected in compliance with an outdated 1987 *Income Tax Act* definition.

Significant mandate departure

Taken together, the CG1 proposals would change the PMPRB's original purpose as a safeguard against the potential for excessive pricing of patented medicines in Canada, and transform the PMPRB into a national patented medicines price control regulator, in support of public policy objectives that are unrelated to patents and are therefore beyond the jurisdiction of the PMPRB under the *Patent Act*.[23]

As illustrated by the RIAS, and particularly relevant for the "new factors" discussed below, several elements of the CG1 proposals are unrelated to the PMPRB's mandate to regulate patent "abuse" in the form of excessive prices. Rather, they seek to extend the PMPRB's authority beyond the limits of its mandate into matters of pure price control such as affordability, value, and market access. Statements made in the RIAS also indicate that the government is looking to expand the PMPRB's role to one that is similar to the role already being performed by CADTH and the Institut National d'Excellence en Santé et en Services Sociaux (INESSS) for the public market. Consideration of "whether a medicine's price is commensurate with the benefits it provides to patients within the context of the Canadian health care system" and "market impact tests for medicines that are likely to pose affordability challenges for insurers due to the market size for the medicine"[24] are already being made by Canadian HTA organizations and are not appropriate for the PMPRB to consider when completing their excessive pricing assessment. These are matters outside the jurisdiction of the PMPRB and authority to consider this type of information cannot validly be granted by amendments to regulations under the *Patent Act.*

Recognizing the significance of these changes and the likelihood of challenges flowing from the changes, Health Canada has signaled that the PMPRB will require $82.5 million in additional resources to administer and defend the new regime. This is a fundamentally flawed approach to public policy. It is more advisable to create rules that are clearly within the legislative mandate regarding an excessive price standard, and that encourage predictability and industry compliance. While the need for such a significant regulatory departure from current practices has not been demonstrated, it is a certainty that the CG1 proposals will increase both government and patentee expenditures related to administration and compliance with the new regime.

2. **FLAWED COST-BENEFIT ANALYSIS:** THE CBA UNDERSTATES THE NEGATIVE IMPACT OF THE PROPOSED CHANGES TO INDUSTRY AND PATIENT ACCESS, WHILE OVERSTATING THE POTENTIAL BENEFITS TO CANADA.

The cost-benefit analysis provided by Health Canada to support the CG1 changes is inaccurate and based on questionable assumptions. It underestimates the financial impact to the innovative pharmaceutical industry and the downstream impacts on the healthcare system. A recent critique of the CBA produced by PDCI Market Access Inc. highlights the following key concerns:

- *"Health Canada significantly underestimates the negative impact of its proposed regulatory changes and overstates the positive impact.*
- *The proposed changes will result in longer delays for access to the most innovative medicines, and some may never be launched in Canada.*
- *The proposal conveys an exaggerated sense of urgency for pricing regime change, which is not substantiated by available evidence.*

- *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.*
- *Health Canada has proposed changes that substantially duplicate existing strategies for assessing drug value, negotiating listings, and making reimbursement decisions*."[25]

Without limitation, several issues with the CBA are reflected in Table 1.

Table 1: Critical Issues and Omissions Regarding the CBA

	CBA	Issue
1.	No negative impact on product availability, international launch sequence, and/or access to drugs	Not reflected in CBA assessment of "other costs" or elsewhere in the CBA document. This assumption is flawed. See ANNEX C and the section below.
2.	Use of 7% discount rate drastically underestimates the actual financial impact to industry when expressed as Net-Present Value (NPV): $8.6 billion over 10 years[26]	Health Canada uses 7% discount rate and notes a 2007 Treasury Board Guidelines that is significantly out of date and irrelevant for the pharmaceutical sector.[27] There is no strict requirement that this discount rate be used. For example, several recent Health Canada and Environment Canada CBAs and have used 3% discount rate.[28] Further, for the pharmaceutical sector, the accepted discount rate is 1.5%. For example, CADTH's Economic Guideline (2017) recommends this 1.5% discount rate grounded in the principles of a social decision-making viewpoint on social choice in the health sector.[29] PDCI estimates put total NPV cost to industry much higher: $26.1 billion over 10 years (closer to the upper range of Health Canada CBA estimate) based on a more appropriate discount rate and other factors.[30] For various methodological reasons, even this impact assessment is likely a significant underestimate.
3.	Lack of clarity on impacts and assumptions that influence sensitivity analysis Range: $6.4 - $24.9 billion; Health Canada current estimate is $8.6 billion[31]	Sensitivity analysis provides an unacceptable range and a lack of predictability on actual impacts. Regardless of any methodological discrepancies due to discount rates, Health Canada has not provided clarity regarding full impacts to regulated parties and the assumptions regarding future regulatory scenarios that influence impact ranges.
4.	No estimate of tax revenue impact to Canadian governments included in CBA	To assume that $8.6 billion in revenue loss to industry, (and potentially as much as $24.9 billion) will have no impact to government tax revenues is a highly questionable assumption. Tax impacts would arise both directly from reduced manufacturer revenue as well elsewhere in the supply chain (wholesalers, pharmacies, insurance companies etc.).

	CBA	Issue
5.	Significant underestimate of compliance cost to industry: $100,000 over 10 years[32] This compares to $82.5 million over 10 years for increased government program costs including PMPRB compliance and enforcement activities[33]	CBA estimate of compliance costs to industry reflects a fundamental lack of understanding about the regulatory burden for the pharmaceutical industry that will be caused by the regulatory changes. PDCI has estimated increased regulatory burden and compliance costs to be $1 to 4 million per year ($10 -$40 million over 10 years).[34] If PMPRB faces new costs in the range of $82.5 million, it is reasonably foreseeable that the industry would face comparable costs.
6.	Impact assessment on employment: explicitly rejected	This is a mistaken assumption in light of impacts to industry of this magnitude. Also, this neglects likely impacts associated with significant erosion of pricing and market predictability.
7.	Impact assessment on R&D and investment: explicitly rejected	This is a questionable assumption in given the reasonably foreseeable impacts to the industry. This also neglects likely impacts associated with significant erosion of pricing and market predictability. In support, CBA document references "studies by various experts" without identification or citation.
8.	No impact on the present and future value of investments already expended in Canada	Given that the proposals will have an immediate impact on January 1, 2019, the regulatory changes will impact the value of investments already made in the Canadian market. For example, separate from future investment flows (see 6 above) the regulations would impact the real-world value of foreign direct investment *stock*. Without limitation, this is relevant in the context of a lack of appropriate grandfathering for existing products, impacts to the asset value of intellectual property, and the value of related investments previously made in Canada.
9.	Value of payer discounts assumption: "Medium/low-impact drugs are discounted by 10% below what is currently reported to the PMPRB"[35]	The 10% rebate discount average (public and private market) would appear to be exceedingly low. Information in the public domain and readily available to Health Canada suggests that rebating in the public system is closer to 30%: In Ontario, for example, "for 2016/17, the total rebate received is close to 30% of the total expenditures for brand-name drugs."[36] The CBA estimate of rebates assumes private payers are not currently obtaining listing agreement discounts, which is inaccurate. Health Canada has not indicated if it consulted with private payers to obtain an estimate of the extent of discounting in the private market prior to making the 10% average discount assumption.

	CBA	Issue
10.	"Literature review" is not a legitimate reference	CBA document (September 8, 2017) contains a three-paragraph "Literature review" with no citations. It references data without sources. It contains no search methodology or information on actual sources consulted. It provides no literature to support assertions made elsewhere in the document, without limitation: • "It is unlikely that this proposal would generate an adverse impact on employment or overall R&D spending." • High prices can "threaten the financial sustainability of public health systems." • "lower prices should result in greater quantities of medicines demanded and higher domestic production."
11.	Overstates benefits of policy through flawed fiscal multiplier for Canada	A 4.3% fiscal multiplier[37] is inconsistent with the Canadian experience and overestimates benefits of the policy.[38] Literature provided in support of 4.3% multiplier is not rooted in the Canadian context.

In addition, during a stakeholder briefing on the CBA on January 10, 2018, officials acknowledged that they had not consulted with the Department of Innovation, Science and Economic Development (ISED) with respect to the CBA. Given ISED's role as the lead federal government department with respect to promoting innovation and economic development, and particularly given that the CBA assesses no impact whatsoever on industry employment, investment, or R&D, this lack of consultation with ISED or other relevant federal departments further calls into question the validity of the CBA analysis that has been provided to justify the changes proposed in CG1. Given the aforementioned issues, IMC recommends that the CBA be thoroughly reviewed, and this review process should include consultation with ISED, International Trade, and other relevant government departments.

3. **NEGATIVE IMPACT:** THE PROPOSED CHANGES WOULD HAVE A SIGNIFICANT NEGATIVE IMPACT ON THE NUMBER OF NEW DRUGS AVAILABLE TO CANADIAN PATIENTS, AND ON LIFE SCIENCES RESEARCH AND INVESTMENT IN CANADA.

Based on launch and reimbursement data from other countries (see ANNEX C) the proposed changes would restrict access to new innovative medicines for Canadian patients. The changes would also reduce patentee financial capacity to invest in the Canadian life sciences sector. IMC has obtained 3rd party analysis from EY[39] suggesting that potential price reduction on a per-product basis could range from 15% to 90% if the proposed cost-effectiveness thresholds[40] were implemented to determine ceiling prices. This analysis will be soon be published in the public domain. The pharmacoeconomic value factor alone will prevent many new products from being launched in Canada.

While there are many issues with the CBA, the lack of any consideration of the potential impact on new product launches and the timing of those launches in Canada, stands out. Despite the clearly negative impact of the CG1 changes on patentees, Health Canada noted during a January 10, 2018 stakeholder session on the CBA that: "*Canada is an appealing market for new drug launches and will remain so after the PMR Proposal and estimated price reductions*." This statement is not reflected in the CBA section on "other potential costs" or supported by the CBA literature review. Furthermore, this position ignores the business uncertainty associated with the changes: patentees may not be able to determine the maximum allowable price in Canada at launch, and may not be able to determine the impact of the new proposed PMPRB factors (other than being generally negative) post-launch. This uncertainty can only delay or discourage the introduction of new medicines in Canada.

Contrary to the statement above, there is a considerable literature base on the links between low prices, cost-containment, and impacts on product availability and launch sequence. Research has established that price controls and other cost containment mechanisms significantly slow the sequence of launch as well as the number of countries in which a drug is launched. Moreover, countries with lower expected prices or smaller expected market size due to cost-containment measures and other reasons have fewer launches.[41] [42] [43] [44] [45]

The primary beneficiary of the proposed changes would appear to be the private insurance market. A net transfer of value to private drug plans risks making it more difficult for government-funded drug plans to secure best value for the vulnerable populations they cover.

The changes also introduce an unacceptable level of uncertainty and instability for manufacturers doing business in Canada (See ANNEX B). The proposals do not provide a predictable price ceiling or "bright line" rules, and would use subjective pharmacoeconomic data and market forecasts for a "ceiling" that may be perpetually under review. Unless amended, the CG1 proposals will negatively impact new product introductions in Canada, to the detriment of Canadian patients and our healthcare system.

4. LACK OF MEANINGFUL CONSULTATION: TO DATE, THE CONSULTATION PROCESS HAS BEEN DEFICIENT AND HAS NOT MEANINGFULLY ADDRESSED CRITICAL STAKEHOLDER FEEDBACK.

Critical Stakeholder feedback ignored or not meaningfully addressed

IMC and many other stakeholders made submissions in response to the May 2017 consultation document for consideration when drafting regulations. While the receipt of these submissions is acknowledged in the RIAS, the concerns identified have not been substantively addressed. The RIAS provides no explanation on how stakeholder submissions were considered or why input was rejected. Rather, the proposed regulations are nearly identical to the proposals in the consultation document apart from minor changes regarding international filing requirements and other modest modifications. Stakeholders are hindered in their ability to provide responsive comments on the draft Regulations without understanding the government's reasons for rejecting the comments it has already received on substantially the same policies.

Table 2 provides a summary of key industry recommendations made in response to the June 2017 consultation and how each was addressed within the CG1 proposals. We also note that the government should confirm if, and how, the thoughtful input from patients was reflected in the regulatory proposals. [46]

Table 2: Prior Industry Recommendations Against Proposals in Current Draft Regulations

Key Industry Recommendation	Current Proposals	Changes to Draft Regulations?
Benchmark against leading global economies and health systems based on transparent criteria	Range of comparators which generate the result of OECD median, based on vague criteria	No change
Pharmacoeconomics should not be incorporated in regulation as an additional factor	Pharmacoeconomic value added as a factor in regulation which must be considered	No change
Market size should not be incorporated in regulation, but if is, not as a primary factor	Market size added as a factor in regulation which must be considered	No change
GDP should not be incorporated in regulation, but if is, not as a primary factor	GDP must be taken into consideration	No change
Complaint-based process should be extended beyond ANDS generic drugs to patented medicines without exclusivity, vaccines, blood	Reduced reporting for patented generic, veterinary and over-the-counter medicines, but no change with respect to multi-source	Partial

Key Industry Recommendation	Current Proposals	Changes to Draft Regulations?
products, and products within a competitive class with similar mechanisms of action	products within a competitive class, despite need for risk prioritization	
Information related to proposed new factors should not be required for submission to PMPRB	Additional information related to proposed new factors must be submitted to PMPRB	No change
No mandatory submission of indirect price reduction information	Indirect price reduction information must be submitted	No change

Insufficient information provided to satisfy consultation obligations

It is a very difficult exercise for patentees to consider the CG1 in isolation, as stakeholders are being asked to do in this CG1 consultation. Although Health Canada and the PMPRB maintain an arm's-length relationship with divided control over the *Regulations* and the PMPRB's Guidelines, respectively, these instruments form a single system in practice that defines the compliance obligations of patentees.

The full impact of the regulatory changes cannot be ascertained by regulated parties at this time on the basis of the information provided by the government to date. This is acknowledged in Health Canada's CBA document: "How the PMPRB decides to translate the proposed regulatory changes to its guideline reforms can have a significant impact on lowering projected medicine expenditure in Canada."[47] Indeed, the CBA reflects a vast 10-year impact range of $6.4 billion - $24.9 billion (present value), and would reflect considerably more, under a discount rate appropriate to the health sector.[48] In estimating this range, Health Canada notes that "extensive consultation with the PMPRB produced various guideline reform scenarios." While this may be the case, stakeholders have no access to these scenarios and the associated assumptions.

Treasury Board's *Canadian Cost-Benefit Analysis Guide: Regulatory Proposals* notes:

> [I]n order to minimize the negative impacts of regulations, and enhance their effectiveness, it is important that ***all relevant information about how they will affect Canadians is obtained before they are implemented (emphasis added)***. This will require extensive consultation with all Canadian stakeholders that will be impacted by the proposed regulation. It is primarily through these consultations that the impacts will be best understood [emphasis added]. [49]

IMC members, who constitute the majority of patentees under the PMPRB's jurisdiction, currently have insufficient relevant information about the operation and impacts of the regulatory proposals. While Health Canada and PMPRB have hosted information sessions, to date patentees have not been provided with enough information to provide fully informed responses to the CG1 regulatory proposals.

Effective consultation is required not only under the government's own *Cabinet Directive on Regulatory Management* and *Guidelines for Effective Regulatory Management*, but also as a condition precedent to making regulations under paragraphs 101(*d*), (*f*), (*h*), or (*i*) of the *Patent Act*. Given the sweeping changes being proposed and the jurisdictional concerns they may present, the current consultation process not only jeopardises the legitimacy of the eventual changes to the regulations, it also risks implementing an unworkable system that does not benefit patentees or the Canadian public.

IMC also respectfully disagrees that the current proposals reflect a "risk-based" approach. IMC could support a genuinely risk-based system which balances the need for consumer protection against excessive patented medicine pricing, predictability for patentees, and ensures that Canada is maintained as a leading destination for pharmaceutical innovation, clinical trials, and timely access to innovative medicines for all Canadian patients. IMC discussed this issue in greater detail in its June 2017 submission at pp. 15 – 18. However, when read in conjunction with the PMPRB's Scoping Paper (December 2017), the CG1 proposals seem to reflect an "actively interventionist" rather than a "risk-based" approach to regulation..

5. NEW COUNTRY SCHEDULE UNREFLECTIVE OF CANADIAN ECONOMIC POSITION: THE INTERNATIONAL SCHEDULE PROPOSALS ARE NOT REFLECTIVE OF CANADA'S ECONOMIC STANDING OR ASPIRATIONS REGARDING ACCESS TO MEDICINES.

As noted in its June 2017 submission at pp. 19-22, IMC cannot support the proposed "PMPRB12" Schedule of International Reference countries. The proposed schedule is not reflective of Canada's economic standing and stated aspirations regarding access to innovative medicines. The regulations remove the United States and Switzerland, and add Australia, Belgium, Japan, Netherlands, Norway, South Korea and Spain. From the current schedule of seven (PMPRB7) countries, the proposed list would include twelve (PMPRB12) countries. We have provided extensive commentary on the schedule issue in our June 2017 submission and would encourage a review of our previous submission on this topic.[50]

The proposed Schedule includes countries that have poorer access (i.e. fewer new product launches) and significant launch delays compared to Canada. Based on the PMPRB's own analysis, ANNEX C illustrates that all of the new proposed comparator countries have worse access than Canada to new drugs as measured by products launched.

Patentees still do not have sufficient clarity on the application of the stated criteria. CG1 cites the following selection criteria:

- "medicine pricing policies that are well aligned with the consumer protection mandate of the PMPRB;"
- "reasonably comparable economic wealth as Canada, such as a country having a similar economic standing to Canada, as measured by GDP per capita;" and

- "similar medicine market size characteristics as Canada"[51]

The method of application for these factors is inconsistent. For example, "pricing policies" is used to exclude the United States on the basis of criterion satisfaction. Whereas for other selections, it is noted that a criterion must be satisfied, yet countries are not excluded on this basis. For example, there are compelling arguments to be made for the exclusion of South Korea, The Netherlands, and Australia on the basis of significant differences in the "market entry of new products."[52] According to the PMPRB's April 2017 "Meds Entry Watch" Report, these countries have much lower market entry characteristics than Canada which enjoys 61% share of new active substances launched, the fourth highest among the OECD countries. This compares favorably to the low levels of access to new medicines recorded in South Korea (33%), Netherlands (36%), Japan (38%), and Australia (40%) (See illustration in ANNEX C).[53] Furthermore, we would note that Health Canada is referencing countries due to "medicine pricing policies" where there is a guarantee of public access that comes along with a successful price negotiation. Many of these comparators are not based only on pricing policies, but rather, *pricing and reimbursement* policies, which are already addressed at a different level of government in Canada.

The criteria-based country exclusion process noted in CG1 (p 4510) would also seem *inconsistent* with other CG1 statements noting that the purpose is to align with "median OECD prices."[54] By any objective measurement, the OCED median does not reflect Canada's international economic standing.

This selection process, which presents a conflict between a criteria-based approach and an OECD median target, leads to the selection of comparators with radically different pharmaceutical markets than Canada. For example, South Korea is an inappropriate comparator for Canada due to its low per-capita spending on healthcare,[55] low reimbursement rates, and prices for newly listed medicines that are 45% of the average across the OECD countries, lower than many other countries in Asia.[56]

Similarly, the selection of some countries appears arbitrary and unrelated to broader Government of Canada innovation objectives. For example, current comparator country Switzerland is excluded despite recent government efforts to promote *alignment* of innovation policy such as the recent Canada-Switzerland joint cooperative initiative on Science, Technology and Innovation. [57]

6. INAPPROPRIATE USE OF PHARMACOECONOMICS: PHARMACOECONOMIC ANALYSIS AS EXPRESSED "PHARMACOECONOMIC VALUE" IS INAPPROPRIATE WITHIN THE FEDERAL PRICE CEILING REGULATION CONTEXT.

PMPRB is not the right point in the drug review process for incorporating the proposed pharmacoeconomic factors because it is not a payer.

As noted in our June 2017 submission, Innovative Medicines Canada (IMC) does not support the proposal to use pharmacoeconomic factors such as cost-effectiveness analyses to regulate prices of patented medicines in Canada.

The *Patent Act* bases the mandate of the PMPRB on the concept of monitoring non-excessive pricing. Cost-effectiveness evaluation conducted by Health Technology Assessment (HTA) bodies such as CADTH and INESSS (Quebec) are used downstream in reimbursement decision-making and meant to inform payers regarding value-based negotiations. The PMPRB is not a payer: this role is already being filled by the public

drug plans or private insurers in the Canadian context. With the changes proposed by Health Canada, Canada will be out of step with many comparator countries (e.g. Germany, Spain)[58] regarding applicability of cost-effectiveness thresholds in price regulation.

CADTH reviews and recommendations do not represent a societal perspective

Health Canada has indicated that "[i]n recognition of the significant expertise that can be necessary to prepare and validate cost-utility analyses, reporting would be limited to those that have been prepared by a publicly funded Canadian organization, such as the Canadian Agency for Drugs and Technologies in Health (CADTH) or the Institut national d'excellence en santé et services sociaux (INESSS)."[59] During an outreach session on January 29, 2018, PMPRB staff confirmed that they plan to use CADTH re-analyses of the cost-effectiveness information submitted by manufacturers if the regulatory changes proposed by Health Canada are approved. CADTH's mandate for cost-effectiveness reviews is limited in scope to only reflect the public drug plan perspective. Cost-effectiveness analyses appraised by Common Drug Review (CDR) and pan-Canadian Oncology Drug Review (pCODR) are developed by the manufacturers based on CADTH economic guidance. CADTH conducts re-analyses and issues non-binding recommendations from a public drug plan perspective, and not from a societal perspective. In contrast, INESSS considers a broader societal perspective in its pharmacoeconomic evaluations.

The assessment of value by CADTH does not reflect value assessments within the private market because patients, families, and employers have different tolerance levels for uncertainty, and willingness-to-pay. For example, employers are interested in indirect costs (i.e. promoting a healthy and productive workforce and reducing absenteeism). Public payers are more focused on direct cost (i.e. hospitalizations, doctor visits, etc.). Given that the population covered by public plans and private plans differ, their value assessments will also differ. It is inappropriate to use CADTH evaluation for any purpose other than the intended objective of supporting reimbursement decision making at the public drug plan level.

A single equitable or fixed ICER threshold for all Canadian payers (public, private, individuals) is unattainable

Two key concepts or measures used in pharmacoeconomics analyses include quality adjusted life year (QALY)[1] and incremental cost-effectiveness ratio (ICER).[60] There are several inherent limitations that make the use of QALYs and fixed ICER thresholds inappropriate tools for determining ceiling price of patented medicines. QALYs and ICERs have traditionally been used to compare an intervention against a payer's willingness-to-pay, and should take payer preferences into account. Payers' willingness to pay for a medicine depends on several factors including unmet need, budget or funding available, value offered compared to available treatment options, etc.

However, QALYs or ICERs do not fully represent an individual's preferences[61] and excludes other important factors related to patient and societal values. ICERs undervalue society's willingness to pay for drugs for palliative care and rare diseases because they underestimate an almost universal acknowledgment by societies of the need to provide extraordinary help to those with desperate medical need (i.e., the rule of rescue). Furthermore, QALYs are criticized for discrimination against the elderly, the disabled, and pediatric patients because their use may underestimate the clinical benefit of interventions in these

[1] *QALYs have been used as a measure of the health benefit effect offered by a treatment option. ICER represents the average incremental cost associated with 1 additional unit of the measure of effect (i.e. QALY).*

populations and result in artificially high ICERs, adversely impacting the number of treatment options being made available.[62]

ICERs are also impacted by the methods used, such as the time horizon and clinical *comparators* selected. Although there are guidelines on conducting economic analyses, there can be high variability in assumptions between individuals and this may have serious consequences to the final analysis. There are usually significant differences between manufacturer-submitted ICERs and CADTH-generated ICERs (the latter are almost invariably higher), and there is a need to fully understand the subjectivity of pharmacoeconomic analysis in order to properly apply these estimates to a decision-making process.

It is important to note that the results of a cost-effectiveness analysis (e.g. the ICER) are dependent on the perspective of the analysis (e.g., public payer, societal perspective, private payer). The use of fixed ICERs would be prohibitively complicated to operationalize it across public *and* private markets, with vastly different willingness to pay.

A price referenced to a fixed ICER threshold will be a step backwards, ignoring the significant work payers and industry have done in Canada to identify many factors that they consider adding value over-and-above what the QALYs and ICERs measure. It is important to note that most of the orphan drugs (i.e. drugs used to treat rare diseases) appraised by CADTH's CDR process to date have ICERs well above the generally 'accepted' thresholds and would not be reimbursed according to any conventional criteria.[63] Manufacturers and payers have been able to reach agreements in some cases and provide access to patients, which would be almost impossible to reach agreements if fixed ICERs were used. This is especially true for serious conditions, where breakthrough medications may be costly but the burden of illness is high and there are limited treatment alternatives.

Very few countries use fixed ICER thresholds. Even where they are used, there is no universal agreement as to what constitutes an appropriate ICER threshold. This is not surprising, given that different jurisdictions and payers will have different willingness to pay. The limitations described above have led CADTH, INESSS, and other HTA agencies across the globe to incorporate additional measures of value. Beyond the QALY and ICER, the pCODR Expert Review Committee Deliberative Framework explicitly considers "burden of illness", "unmet need", "patient values", "economic feasibility" and "organizational feasibility." Because these deliberations measure additive or incremental value, the ICER serves more appropriately as a base for these deliberations than a ceiling. Several comparable jurisdictions including Germany and Spain have banned the use of ICERs for price regulation.

Potentially significant negative impacts on patient access and the life sciences ecosystem in Canada

The use of fixed ICER thresholds for determination of ceiling prices of patented medicines will likely result in significantly negative impacts on the availability of innovative medicines. ICERs are poorly suited to evaluate treatment options for rare disease where there are often evidence gaps due to small patient populations. Patients in countries where fixed ICER thresholds are used have faced significant access issues, particularly those with cancer and/or rare diseases. The UK, where the ICER threshold is most rigidly applied based in guidance issued by National Institute of Clinical Excellence (NICE), has come under intense criticism for refusing to fund life-extending drugs for patients with cancer due to price. Patients in the UK have more restricted access to oncology medications than in other EU counties, which is an important factor contributing to poorer patient outcomes.[64] [65]

The current PMPRB regime relies on verifiable facts in its price tests, namely Canadian and international drug prices. As a result, patentees can reasonably predict the allowable price ceiling prior to drug launch. Considering cost-effectiveness analyses to regulate ceiling price would introduce significant uncertainty and unpredictability with regards to the ceiling price. That uncertainty would be due to the fact that manufacturers could not use their models, as submitted to CADTH, to predict the launch price. Industrial economics demonstrates that uncertainty and unpredictability leads to underinvestment.[66] By introducing uncertainty with respect to achievable ceiling price, it may cause manufacturers to rethink their launch sequencing for new products. This could significantly delay the launch of innovative medicines for Canadian patients, or lead to no launch or access in several cases.

Establishing regulatory price ceilings based on ICER thresholds would significantly alter the pharmaceutical market in Canada and lead to considerable uncertainty for not only patients' access to medicines but also risk serious business sustainability issues for manufacturers. This could significantly diminish incentives for innovation and lead to fewer innovative products being launched in Canada. In particular, this would severely impact the future viability of many drugs for rare diseases and oncology treatments in Canada.

IMC recommends that the function of conducting and using cost-effectiveness analyses to inform public payers should remain with CADTH and INESSS, which make recommendations to public payers based on a variety of factors. If both the PMPRB and the pCPA use HTA evaluations for pricing decisions, this would result in clear and unnecessary duplication.

We have noted above the various reasons why cost-effectiveness analyses are inappropriate and unacceptable for use by the PMPRB in setting ceiling prices of innovative medicines. A more appropriate way to manage the diversity across payers is through payer negotiations with manufacturers. Both public payers and private payers currently engage in negotiating price discounts. IMC strongly encourages Health Canada to remove the use of pharmacoeconomic factors or cost-effectiveness as one of the future considerations for PMPRB in determining the ceiling prices of patented medicines.

7. **UNECESSARY NEW MARKET SIZE AND GDP FACTORS:** THESE PROPOSED ADDITIONAL FACTORS ADD COMPLEXITY AND REGULATORY BURDEN WITH NO CLEAR PURPOSE, AND SHOULD NOT BE INCORPORATED INTO REGULATION.

Size of the Market

As explained in IMC's June 2017 submission at pp. 27, market size should not be a mandatory factor within the regulations given the inherent challenges with the widespread application of market size factors for assessing whether a given price may or may not be excessive. Market size is more appropriately used in payer evaluations rather than excessive pricing determinations. Only payers can identify their system needs and priorities, and only payers can assess the value of, for example, new indications of a currently reimbursed product and whether that should trigger a renewed conversation about reimbursement criteria.

Market size is typically estimated based on modelling but may evolve differently over time as the product is used and integrated into the healthcare system. There are multiple explanations and variables, such as market mix dynamics, which may influence why estimated and actual markets differ. Operationally, the tool would introduce inappropriate bias, since it would be used uniquely to lower price. If, for example,

public access was not achieved, resulting in lower than expected market size, it would be impossible from a practical standpoint to raise a price that had already been established in the market.

As a result, various forms of risk-sharing occur at the level of payers managing expenditures and system requirements. For example, the use of overall limits or caps may render overall market size or growth irrelevant from a payer expenditure perspective. There are many situations, such as the market withdrawal of a competitor or a temporary drug shortage of a competitor, that would make market size assessments untenable.

Health Canada notes it would require information on "Estimated maximum use of the medicine, by quantity of the medicine in final dosage form, for each dosage form and strength that are expected to be sold" and this information is "to be kept current."[67] This would result in a significant burden as internal forecasts change many times throughout a given year and may or may not be completed using the required unit of measure, or to the degree of granularity and detail, that may be expected by the government.

Based on the nature of contracting in the pharmaceutical industry, the idea that a price ceiling could potentially change upwards based on a change of market size would have no real-world advantages to patentees who would not be able to leverage this ceiling. Furthermore, the reporting requirement could essentially mandate the production of any internal estimate of market size. It is questionable whether it is within PMPRB's jurisdiction to compel the production of internal commercial forecast information or, where none exists, to require the compilation of detailed forecasts regarding the anticipated future market for patented products

Size of Market reporting would reflect unsound additional regulatory filing requirements for *prospective* market size forecasts. Unlike market forecasts used by payers and submitted by manufacturers on a voluntary basis, the incorporation of prospective market forecasts into mandatory federal regulations concerning patented medicines would appear to be unique and discriminatory with respect to the pharmaceutical sector.

GDP and GDP/capita

As noted in IMC's June 2017 submission at pp. 27, and given the outstanding questions related to how this factor may be applied, IMC recommends against its adoption as mandatory within regulation. If this factor is adopted nonetheless, IMC recommends that it should be used only in a secondary capacity, for example for the purposes of hearings or specific investigations, for products with no comparators and a high cost burden, and where the existing factors are insufficient to make a determination with respect to a specific product.

Above we have noted the various technical reasons why market size and GDP are inappropriate for review by the PMPRB. Moreover, IMC questions whether such information can be considered 'Pricing Information' appropriate for inclusion under Section 80 of the *Patent Act*. In IMC's view, the current practice of negotiated product listing agreements is a more effective tool for ensuring that budget spending matches expectations, and for enabling specific agreements based on payer preference.

8. CONFIDENTIAL INFORMATION REPORTING IS INAPPROPRIATE AND RAISES LEGAL ISSUES.

Consistent with the previous sections, IMC's ability to provide additional comments on this proposed regulatory change is limited given that we have received no feedback on the previous comments submitted in June 2017, nor has additional material information been provided to stakeholders since that provides insights beyond the original May 2017 consultation document.

Accordingly, IMC again refers to its June 2017 submission at pp. 30 for further detailed discussion on the issue of mandatory disclosure of confidential price adjustment information. Given the lack of information on purpose and use of the information, legal concerns and the risk of significant and negative consequences for public payers and other market participants—not to mention the practical barriers of accessing and using such information—IMC remains strongly opposed to mandatory reporting of confidential information per subsection 4(4) of the draft regulations.[68] This information does not relate to excessive pricing as, by definition, it is related to marketplace activities which occur below those thresholds.

It has long been recognized that rebates and discounts delivering value to patients should be encouraged as part of the Canadian pharmaceutical marketplace However, by requiring the mandatory disclosure of such information with no clear policy purpose, the PMPRB would be interfering in contractual relations between manufacturers and payers. This in turn risks undermining an effective system which has evolved for public plans to manage their drug expenditures.

Manufacturers may currently enter into PLAs with private and public payers as a condition of product reimbursement.[69] These agreements address affordability, among other factors, such as eligible population and utilization criteria. Comparing a new drug with an established drug that may have a variety of unique product listing agreement (PLA) mechanisms such as pay-for-performance, utilization caps, or market-share based rebates makes little sense and would cause market disruptions. IMC also notes that the proposed reporting of confidential price adjustments would reflect a fundamental change to the bargaining assumptions and confidentiality provisions that gave rise to existing PLAs and their specific terms.

In IMC's view, the jurisdiction of the PMPRB is limited to pricing information between a patentee and its customer (i.e., factory gate or ex-factory sale). This practice has been long established by the PMPRB. Attempts to access information regarding "any adjustment" within the supply chain, including specific reference to entities that reimburse for such medicines, is beyond the jurisdiction of the PMPRB under the *Patent Act*.

9. INCREASED REGULATORY BURDEN: THE PROPOSALS WOULD INTRODUCE SIGNIFICANT INCREMENTAL REGULATORY BURDENS THAT ARE UNNECESSARY TO REGULATE EXCESSIVE PRICES.

Taken together, the proposals would create a significant incremental regulatory burden. The complexity and red tape that arise from the proposals is also unnecessary to effectively regulate potential excessive pricing of patented drugs in Canada. Many of the proposals appear to be solutions in search of a problem. The Canadian drug pricing system already has an abundance of costs-containment tools. If lowering

patented prices at the federal level is the policy objective, this can be achieved in a much simpler manner without the need for:

- Significant outlays of time and resources for patentees and government (discussed above);
- Frequent negotiations between the PMPRB and manufacturers regarding the minutia of cost-effectiveness assumptions and modeling for which another agency has responsibility;
- Successive price decreases that will reflect considerable administrative burden and uncertainty for patentees, wholesalers, pharmacies, and patients as patentees attempt to determine the net price of comparator drugs. The use and protection of confidential information would entail major administrative burdens and uncertainty for all parties;
- Mediation between conflicting HTA reports and QALYs (these estimates frequently conflict among HTA agencies, and differ from manufacturer submissions); and
- The inevitable increase in hearings before the Board and subsequent proceedings before the Federal Court.

Of the many incremental regulatory burdens, two are particularly onerous and unnecessary:

1. Measures that would require manufacturer surveillance and reporting of "every cost-utility analysis prepared by a publicly funded Canadian organization, if published, for which the outcomes are expressed as the cost per quality-adjusted life year for each indication that is the subject of the analysis."[70] This creates unnecessary and onerous surveillance obligations. It also raises numerous definitional issues, without limitation:
    - "publicly funded organization" - this could include all universities, hospitals, NGOs and any number of other organizations;
    - "cost-utility analysis" and "cost per quality-adjusted life year;" and
    - "Published" -this could be interpreted broadly as any disclosure that makes draft or final analyses available to the public, in any country.

    Given that any failure to comply with the reporting requirements in this section could engage the PMPRB's "failure-to-file" process, including disclosure of failure-to-file status and an order under section 81 of the *Patent Act*, the ambiguities noted above are concerning. Further, it is unrealistic to presume that patentees will be able to discover, obtain, and report all such information to the PMPRB within 30 days of publication.

2. Proposed new reporting requirements for "maximum use" forecasts would be onerous and require ongoing business forecasting for patented products.[71] As currently drafted, this information requirement is not limited to information that might already be generated in the ordinary course of business. Patentees should not be obligated to conduct any further or additional forecasting analysis for the sole purpose of reporting to the PMPRB.

10. **PROSPECTIVE APPROACH:** IN THE INTEREST OF FAIRNESS AND TO REFLECT INVESTMENT DECISIONS ALREADY MADE IN CANADA, THE GRANDFATHERING OF EXISTING PRODUCTS FROM THE PROPOSED AMENDMENTS IS NECESSARY.

The prospective application of any Regulatory changes to new products is essential to avoid undermining patentee economic interests in currently marketed medicines. To do so otherwise would create uncertainty with respect to the status of existing negotiated product listing agreements. Lack of appropriate regulatory transition (as opposed to transition only in Guidelines) would also put employment and investments at risk. Accordingly, the amended regulations should provide specific provisions that grandfather all existing products. Any new regulations should apply only to medicines with a date of first sale in Canada after any amendments come into force, and that existing products will continue to be governed under the current price regulations, Guidelines, and all associated reporting requirements.

Investment decisions in Canada related to current products have already been made. As currently proposed, the immediate implementation of the regulations to new sales of existing patented medicines would significantly undermine the value of those investments. Canada can only avoid diminishing the real-world value of past investments and intellectual property assets by grandfathering existing products. IMC does not believe any potential future transition measure in PMPRB's Guidelines would be a sufficient substitute for the regulatory grandfathering for all existing products.

11. **TRADE IMPACTS:** THE PROPOSALS MAY IMPACT CANADA'S RELATIONS WITH THE UNITED STATES AND UNDERMINE TRADE COMMITMENTS INCLUDING THOSE TO THE EU UNDER CETA.

The CG1 document notes "[r]egulating the prices for patented medicines to be non-excessive is not subject to trade provisions."[72] No rationale is provided for statement and we believe it to be inaccurate. To the contrary, the effect of price regulation on the benefits conferred by the patent monopoly is subject to treaty obligations under the North American Free Trade Agreement (NAFTA) and the Trade Related Aspects of Intellectual Property Protection (TRIPS) Agreement of the World Trade Organization ("WTO") at a minimum. The 75-day regulatory consultation period chosen for these proposals implicitly acknowledges that there could be impacts to Canada's trading partners. However, nowhere in the CBA or elsewhere are impacts to trading partners and trading relations discussed or considered.

The proposed regulatory changes would have significant impacts for some of Canada's major trading partners, notably with respect to the United States, the European Union, and Japan. They would also complicate future progress of the Canada-U.S. Regulatory Cooperation Council. Regarding trade with the United States, the decision to impose uncertain regulation in the Canadian market is inadvisable at a particularly sensitive time in the Canada-U.S. trading relationship and given the importance of NAFTA. The policy proposals could trigger international trade issues for Canada. Significantly lowering the ceiling price for the entire Canadian market through regulatory amendments constitutes a deliberate government policy that effectively devalues the intellectual property of non-Canadian patentees.

The proposals also undermine a practical benefit to patentees of Canada's intellectual property commitments under the Comprehensive Economic and Trade Agreement (CETA). Canada's implementation of Certificates of Supplementary Protection (CSPs) under CETA includes a "timely filing requirement", which was ostensibly included in the CSP Regulations to incent earlier filing of new medicines in Canada. Patentees have only 12 months from first filing for product approval with certain other designated national health regulators within which they must file for product approval with Health Canada, otherwise they will be ineligible to apply for a CSP.[73]

Due to the time-limited nature of the CSP "timely filing requirement" eligibility provision, CSP eligibility will be unattainable for many future products due to potential launch delays attributable to the proposed PMPRB changes. Canada will lose its first-tier status as a preferred jurisdiction in which new medicines are launched. As identified above and in ANNEX C, this launch delay is reasonably foreseeable. The government's ostensible rationale for the CSP timely filing requirement was "[t]o incentivize the early introduction of innovative drugs into the Canadian market". However, it is reasonable to assume that one effect of the proposed PMPRB Regulations will be to delay or prevent the introduction of new medicines into the Canadian market, which both contradicts and undermines the policy intent set out in the CSP Regulations.

ANNEX A - IMC POTENTIAL ALTERNATIVE – COMMON GROUND SOLUTION

IMC proposes the following alternative option for further discussion with the Government of Canada.

To ensure the affordability of new medicines for Canadians, we are open to explore and collaborate on:

1. Utilization of the G10 Countries[74] minus the United States as new basket, applying the Highest International Price Cap rule;
2. Price freezes on existing patented medicines (which would constitute an exception to the principle of grandfathering for existing medicines, articulated below);
3. Co-creation of a new approach to price regulation for medicines that have no comparators (owing to substantial therapeutic improvement or breakthrough status) and potential high cost burden, provided such changes do not require additional price regulatory factors or mandatory disclosure of confidential pricing information.

The alternatives above are conditional on the following:

1. Full grandfathering of existing products. New PMPRB pricing measure would apply only to products with a **first** date of sale after any new regulations come into force. This is absolutely required to protect the value of investments (both human resources and financial investments) that have already been made in the Canadian market.
2. No use of "pharmacoeconomic value" or incorporation into regulation. Cost-effectiveness should not be used in setting price ceilings. Public and private payers currently have solid processes in place to ensure affordability.
3. No mandatory disclosure of confidential price adjustment information. Without limitation, we firmly reject mandatory PLA disclosure in regulation on the basis this would have significant legal ramifications and create uncertainty for all stakeholders.

This alternative can be supplemented external to the PMPRB with strengthened value-based agreements with Federal, Provincial, and Territorial government payers and the pan-Canadian Pharmaceutical Alliance, where these issues appropriately reside. It should be noted that, in contrast to the IMC proposal, the CG1 changes would not address what public drug plans have identified as their most pressing problem: managing drugs with no comparators that present a potential high cost burden.

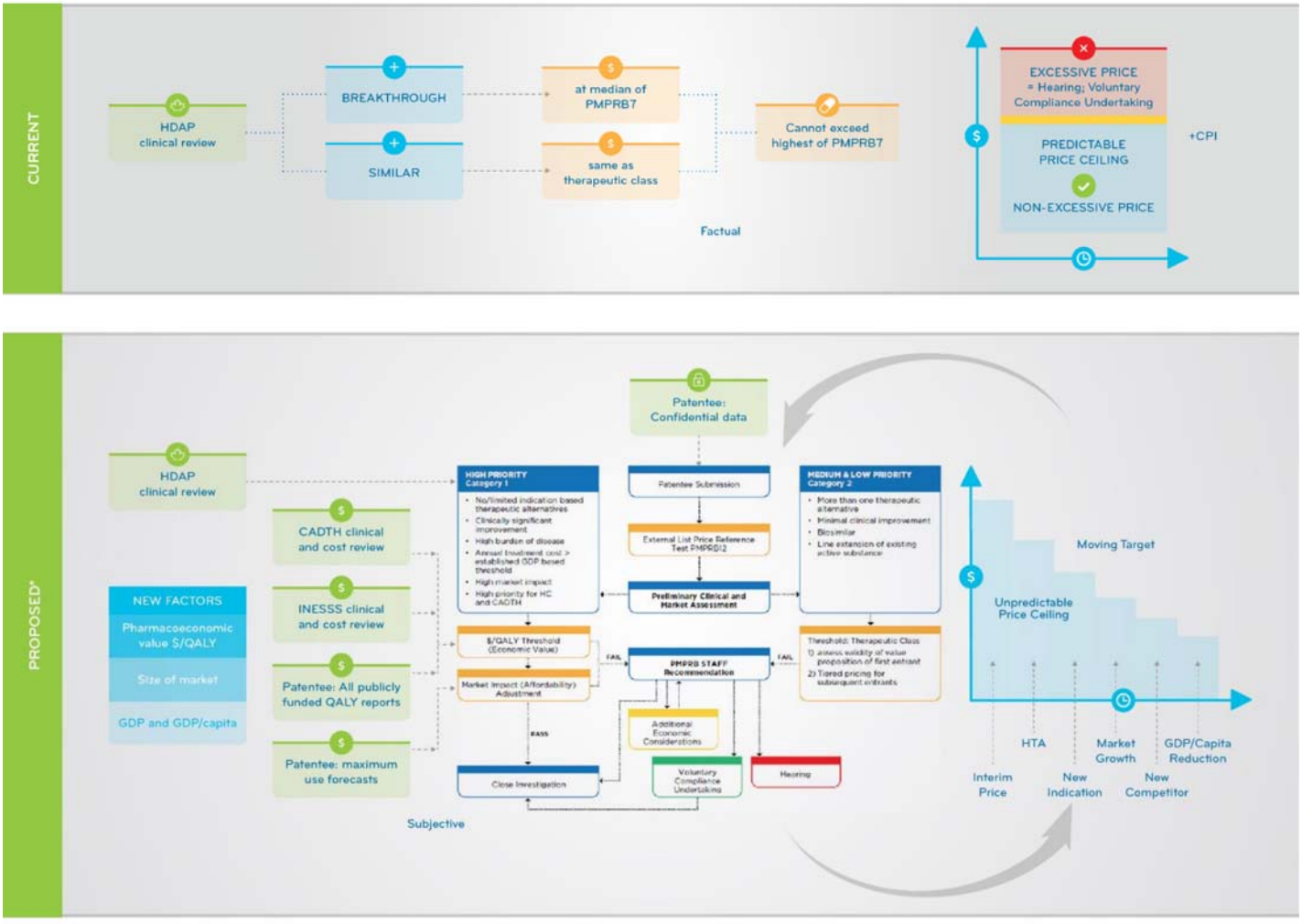
We would welcome a collaborative approach to a thorough re-review of the cost-benefit analysis and development of a common understanding of the assumptions through data sharing and model testing to ensure an evidence-based policy approach.

Current Schedule and Alternative Schedule (contingent on conditions described above)

Current Schedule (PMPRB7)	**Alternative Schedule: G10 Minus U.S. (PMPRB9)**
France, Germany, Italy, Sweden, Switzerland, the United Kingdom, and the United States	Belgium, France, Germany, Italy, Japan, the Netherlands, Sweden, Switzerland, the United Kingdom ~~the United States~~

ANNEX B – SELECT EXAMPLES EXPLAINING WHY THE PROPOSALS CANNOT BE OPERATIONALIZED

Health Canada has advanced changes that would significantly alter the operations and complexity of the PMPRB's regulatory function and these changes will not provide a basic level of regulatory predictability for patentees. The diagram below shows the predictable, fact-based and "bright line" rules associated with the current regulatory model. This is set in contrast to the highly complex model proposed that does not provide a predictable price ceiling nor "bright line" rules, and would use subjective pharmacoeconomic data and market forecasts for a "ceiling" that is perpetually under review.

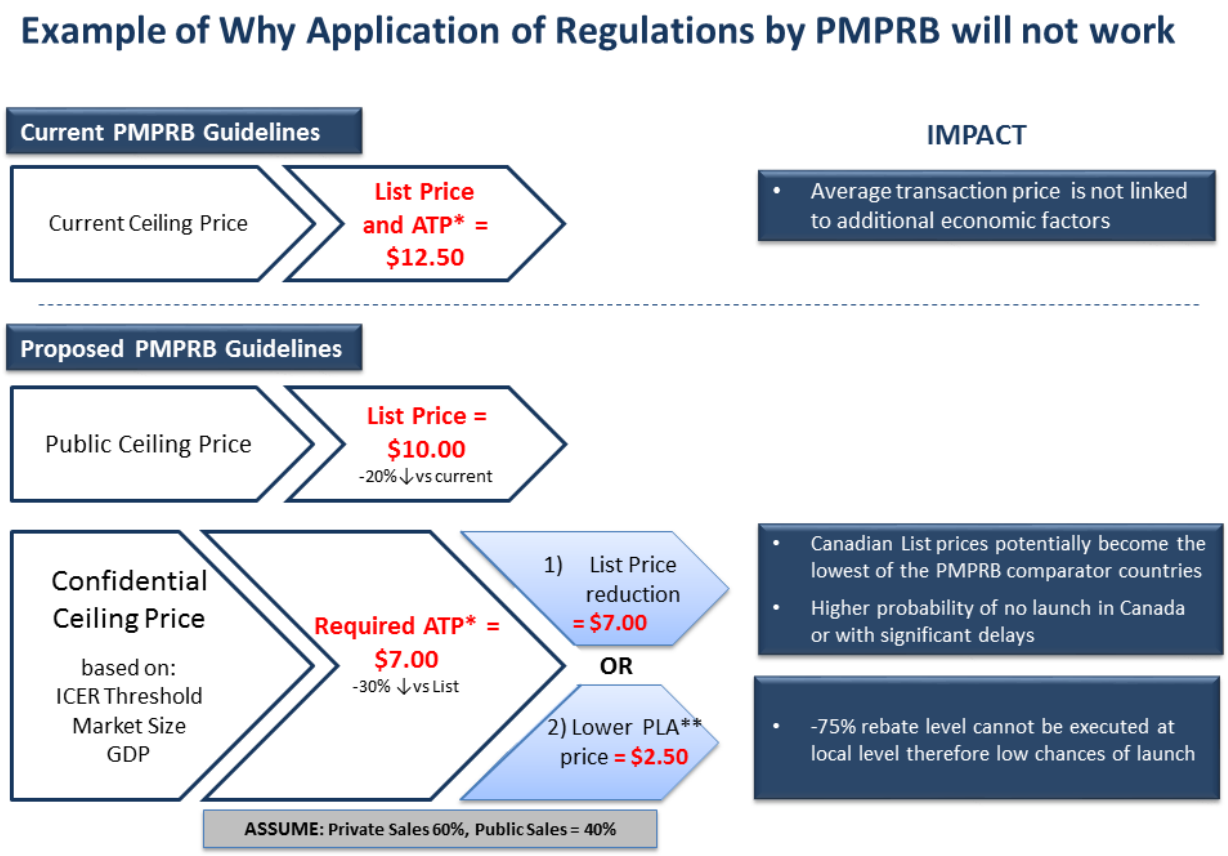


*Source: "Proposed Price Review Schematic," PMPRB Guidelines Scoping Paper, December 2017;
"Regulations Amending the Patented Medicines Regulations," Canada Gazette, Part I, Vol. 151, No. 48 – December 2, 2017

Furthermore, some proposals would be impossible to operationalize by the PMPRB. Even with revisions, the Proposed Price Review Schematic, as highlighted in the PMPRB Guidelines Scoping Paper, cannot be implemented in a real-world setting. We feel there would be significant timing issues related to confidential

contracts that would make benchmarking of net prices by the PMPRB impossible for the relevant reporting years (contract invoices are often only available 9 -24 months after sales accrue).

Strictly for the purposes of illustration, we use a numerical example illustrated in the diagram below. We assume that the current ceiling list price for a new medicine under the current PMPRB guidelines would be $12.50 per unit. Under the proposed regulatory changes and based on the proposed price review schematic in the PMPRB Guidelines Scoping paper, the interim price test using the suggested PMPRB basket could reduce the list price to $10.00 per unit representing a 20% reduction. Assuming the new medicine is assessed as a high priority drug, then PMPRB would apply the economic factors to determine the confidential ceiling price, which would also represent the targeted confidential average transaction price (ATP); for this example, the ATP is calculated as $7.00 per unit.



*ATP = Average Transaction Price, **Confidential product listing agreements

Assuming public sales to be 40% and private sales to be 60% of total sales, a patentee would have one of the following two options to comply with the PMPRB Guidelines; i.e. an ATP not exceeding $7.00 per unit.

- Reduce the transparent list price of $10.00 per unit to $7.00 per unit (i.e. a 30% reduction)
    - Canadian list prices could potentially become the lowest within the PMPRB comparator countries; which extend beyond the scope of the *Patent Act* and the PMPRB Board
    - Due to the unpredictable nature of determining a transparent list price of a new medicine, there would be severe delays in launching such medicines in Canada, or a decision not to

launch could be made due to the depressed transparent list prices for such a high GDP country as Canada.

- It is important to note that there is no country in the world that asks manufacturers to turn confidential prices, which were negotiated using ICER thresholds and market size, into transparent list prices.

OR

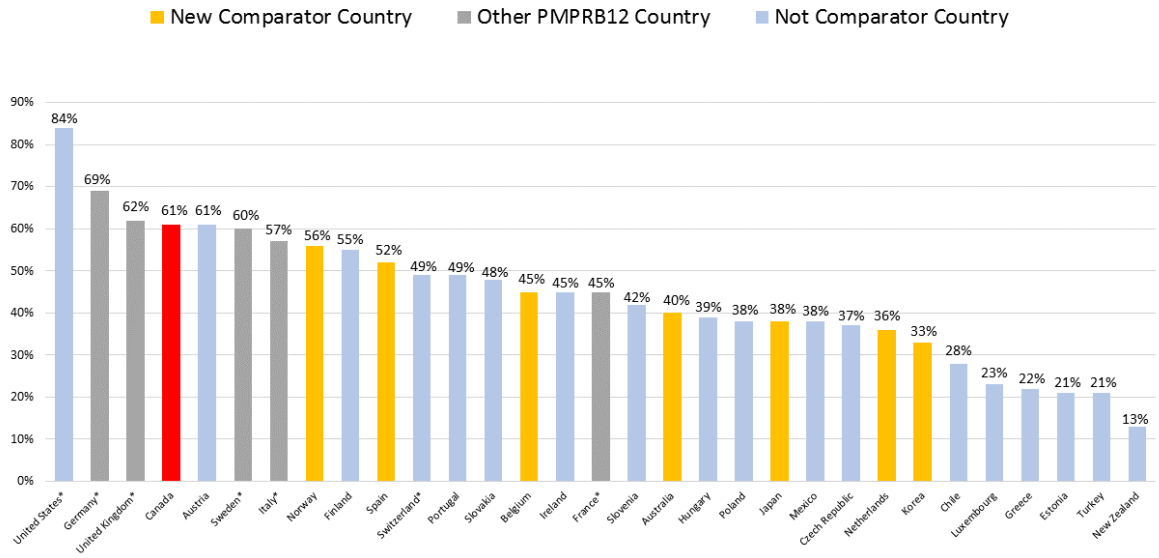
- Provide increased confidential rebates to payers. With the assumed public/private sales split, the PLA price would need to be $2.50 per unit in order to be at or below the $7.00 average transaction price;
  - This would represent a -75% rebate level, which would not be possible for manufacturers.
  - In addition, if the product has a sales split of 30% public and 70% private, then the PLA price would need to be $0 to be in compliance; which is impossible to execute.

Manufacturers cannot operate under such an unpredictable and unstable pricing environment. No subsequent Guideline development can address the fundamental flaws regarding the core CG1 policy proposals.

ANNEX C – IMPACTS TO PATIENT ACCESS ARE FORESEEABLE

Canada proposes to amend the Schedule of international comparators. According to data from the PMPRB, all of the new comparator countries proposed (in yellow below) have worse access than Canada to new drugs as measured by products launched. Innovative Medicines Canada has serious concerns that Canada would become a low-access, late-launch jurisdiction under the proposed regulations.

New Drugs Launched: Share of New Active Substances Launched by OECD Country, 2009-2014, Status at Q4 2015 in OECD Countries



* Current PMPRB7 countries

Source: Adapted from PMPRB, Meds Entry Watch 2015, Appendix 1, Figure 1.1

Potential impacts are demonstrated in the following two examples from jurisdictions where significant changes occurred in price regulation:

Germany's Pharmaceutical Market Restructuring Act (AMNOG) came into law in 2011 subjecting new medicines to a rigid early benefits assessment, either forcing medicines with perceived additional benefits to enter into price negotiations with the government – or forcing medicines with no perceived additional benefits to accept reimbursement limited to the therapeutic reference price that often includes generics. In addition, an element of price transparency was implemented. The impact on access to medicines in Germany has been significant:

- 23% of medicines (40 drugs) that have received centralized approval by the European Medicines Agency were not launched in Germany between 2010-2015, compared to just 5% (or 8 drugs) before AMNOG, between 2006-2010.
- Additional assessment hurdles post-launch, with a potential for pricing rollbacks at the end of the first year on the market have led to the withdrawal of 29 products during the evaluation and negotiation process.

Prior to 2010, the Japanese market was regarded as challenging by multinationals and was low on new drug launch plan lists, as a result.[75] In addition to a highly selective review process to qualify for reimbursement, Japan also employed a drug reimbursement system that lowered the prices of all products across-the-board biennially.[76]

In the context of this environment it took an average of 3.8 years for a new drug to be launched – 2.5 years longer than it took in the US.[77] Only 1/3 of new drugs are launched in Japan, including just 23% of new cancer drugs.[78]

In April 2010, changes were made to Japan's drug pricing system, allowing certain drugs still under patent protection to be exempt from the mandated biennial drug price reduction.[79] This change, along with other efforts to improve the environment, meant that, by 2015, the launch lag in Japan versus the US had been cut to 1.1 years.[80]

ENDNOTES

[1] See ANNEX C.

[2] Minister of Health Mandate Letter (October 4, 2017), https://pm.gc.ca/eng/minister-health-mandate-letter "Work with improve access to necessary prescription medications. This will include joining with provincial and territorial governments to negotiate common drug prices, reducing the cost Canadian governments pay for these drugs, making them more affordable for Canadians, and exploring the need for a national formulary".

[3] Health Canada, Strategic Policy Branch, "Amendments to the Patented Medicines Regulations: Patented Medicine Prices Review Board Modernization, Cost-Benefit Analysis" September 8th, 2017.

[4] Health Canada, "Proposed Amendments to the Patented Medicines Regulations: Cost-Benefit Analysis (CBA)," Presentation January 10, 2018, slide 15.

[5] Health Canada, Strategic Policy Branch, "Amendments to the Patented Medicines Regulations: Patented Medicine Prices Review Board Modernization, Cost-Benefit Analysis" September 8th, 2017.

[6] Ibid. CBA document (September 8, 2017) provides a heavily discounted (7%) present value (PV), 10-year range ($6.4- $24.9 billion) with a government estimate of $8.6 billion PV.

[7] Verbal Communication, Health Canada stakeholder session on the Cost-Benefit Analysis, January 10, 2018.

[8] Canada's Premiers, "The pan-Canadian Pharmaceutical Alliance," http://www.canadaspremiers.ca/pan-canadian-pharmaceutical-alliance/

[9] PMPRB Guidelines Scoping Paper: High Level Overview of Potential New Framework - CGI Consultation Phase, December 2017, http://www.pmprb-cepmb.gc.ca/CMFiles/Consultations/scoping_paper/pmprb_scoping_paper_e.pdf

[10] Canada Gazette Part I, Vol. 151, No. 48, pp 4528, http://www.gazette.gc.ca/rp-pr/p1/2017/2017-12-02/pdf/g1-15148.pdf

[11] Canada Gazette Part I, Vol. 151, No. 48, pp 4532, http://www.gazette.gc.ca/rp-pr/p1/2017/2017-12-02/pdf/g1-15148.pdf

[12] Ibid.

[13] Ibid, pp 4497. CG1 states a need for "more relevant and effective regulatory tools."

[14] Ibid, pp 4450. CG1 states "Canadians are spending more per capita on medicines than any other country in the world, with the exception of the United States."

[15] PMPRB Annual Report 2016, Figure 6, http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1334#a5.

[16] PMPRB Annual Report 2016, Figure 14, http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1334.

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[18] Merck Canada Submission to Health Canada, June 2017, pp 6, http://www.pdci.ca/wp-content/uploads/2017/08/Merck-Canada-Inc..pdf

[19] PMPRB Annual Report 2016, Figure 12, http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1334.

[20] In the past, the Government of Canada has "agreed on the need to gain a better understanding of the full spectrum of Canadian pharmaceutical R&D spending and other investments" and even chaired a steering committee which included the PMPRB to explore "investments not normally captured by PMPRB or Statistics

Canada." CIHR, "Summary of Pharmaceutical Survey Findings on R&D Spending and Investments by Rx&D Members – 2010," http://www.cihr-irsc.gc.ca/e/45304.html

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[23] *Patent Act* (R.S.C., 1985, c. P-4) http://laws-lois.justice.gc.ca/eng/acts/P-4/FullText.html

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[26] Health Canada, Strategic Policy Branch, "Amendments to the Patented Medicines Regulations: Patented Medicine Prices Review Board Modernization, Cost-Benefit Analysis" September 8th, 2017, pp 10.

[27] Ibid.

[28] For example, Health Canada and Environment Canada - Regulations Respecting Reduction in the Release of Volatile Organic Compounds (Petroleum Sector) – employs 3% discount rate: http://gazette.gc.ca/rp-pr/p1/2017/2017-05-27/html/reg2-eng.html; Health Canada's Corded Window Coverings Regulations – employs 3% discount rate: http://gazette.gc.ca/rp-pr/p1/2017/2017-06-17/html/reg7-eng.html; Environment Canada, Prohibition of Asbestos and Asbestos Products Regulations – employs 3% discount rate http://gazette.gc.ca/rp-pr/p1/2018/2018-01-06/html/reg3-eng.html#rias.

[29] CADTH, "Guidelines for the Economic Evaluation of Health Technologies: Canada (4th Edition): What's new" https://www.cadth.ca/sites/default/files/pdf/CADTH_Economic_Guidelines-3rd_vs_4th_Editions.pdf

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[67] Health Canada, "Proposed Amendments to the Patented Medicines Regulations," Presentation December 13, 2017, slide 8.

[68] Canada Gazette Part I, Vol. 151, No. 48, pp 4531. Proposed regulatory text, Paragraphs 4(4)(a) and (b):

> (a) in calculating the average price per package of a medicine, the actual price obtained by the patentee must be used, taking into account any adjustments that are made by the patentee or any party that directly or indirectly purchases or reimburses for the purchase of the medicine and any reduction given to any party in the form of free goods, free services, gifts or any other benefit of a like nature; and
>
> (b) in calculating the net revenue from sales of each dosage form, strength and package size in which the medicine was sold in final dosage form, the actual revenue obtained by the patentee must be used, taking into account any adjustments that are made by the patentee or any party that directly or indirectly purchases or reimburses for the purchase of the medicine and any reduction given to any party in the form of free goods, free services, gifts or any other benefit of a like nature."

[69] As one recent example, we would highlight Alberta's "Pharmaceutical Partnership Committee" (PPC)—a formal collaboration framework to enable the joint development of product listing agreements (PLAs) between Medavie Blue Cross, Alberta Blue Cross, and Pacific Blue Cross (February 1, 2018).

[70]Canada Gazette Part I, Vol. 151, No. 48, pp 4532; [4.1 (1)].

[71] Ibid.To provide the PMPRB with information to conduct the market size analysis required by subsection 4.4(*b*), the Proposed Regulations introduce several broad reporting requirements under new section 4.2.

[72] Ibid, pp 4499.

[73] See s.6(1), Certificate of Supplementary Protection Regulations, SOR/2017-165 September 1, 2017. It should also be noted that while the U.S. and Switzerland are proposed to be removed from the PMPRB's basket of national comparators, both nations are included in the CSP Regulations' schedule of nations for the purposes of determining whether a patentee has filed for a CSP in a timely manner.

[74] Bank for International Settlements, https://www.bis.org/list/g10publications/

[75] Tsukamoto, E. Japan's Drug Lag and National Agenda. Regulatory Affairs Professional Society, pp 35-41. January 2011.

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