February 14, 2018

Attention: Karen Reynolds, Executive Director
Office of Pharmaceuticals Management Strategies
Strategic Policy Branch, Health Canada
10th Floor, Brooke Claxton Building
70 Colombine Driveway, Tunney's Pasture
Ottawa, Ontario K1A 0K9

Dear Ms. Reynolds:

Enclosed, please find Hoffmann-La Roche Limited's (Roche Canada's) comment on proposed Regulations Amending the Patented Medicines Regulations published on December 2, 2017 in the *Canada Gazette, Part 1*.

As you will note in our submission, we have provided feedback on each of the proposed areas of amendments, but would like to also provide our perspective on the overarching process by which PMPRB changes are being proposed for implementation.

While we agree that a focus on access, affordability and appropriate use of medicines will help (1) reduce health spending on medicines that offer little to no value above the established standards of care, and (2) ensure our system is built for long-term sustainability, we fundamentally believe that further discussion and consultation is needed before we, as partnered stakeholders, agree on the core principles and provisions that will impact the future of our healthcare system.

We believe that the amendments proposed in the *Canada Gazette, Part 1* do not take into account previous input provided by our company, our industry, as well as other stakeholders. It is limited in focus, and views the cost of an innovative therapy in isolation of its true value to Canadians.

We also maintain that the current reimbursement framework in Canada is built on a pragmatic, step-wise approach, which offers the government various negotiation points starting with:

1. The assessment of whether the price of a new medicine is non-excessive through the PMPRB;
2. The opportunity to establish the clinical value and cost-effectiveness of a medicine (i.e., the clinical and societal impact the medicine will have in the real world) via the Canadian Agency for Drugs and Technologies in Health (CADTH) or *Institut national d'excellence en santé et en services sociaux (INESSS)*;
3. An opportunity for the federal, provincial and territorial drug plans to further negotiate this price through the pan-Canadian Pharmaceutical Alliance (pCPA); and
4. The added opportunity for each province to build their individual needs into a Product Listing Agreement (PLA) that ultimately enables a medicine to be funded by the public drug plans.

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The current access framework in Canada has built-in checks and balances, as well as a distributed approach by which medicines are funded, that allows the government and public drug plans to evaluate the price, value and patient impact of a medicine before it is reimbursed. Changing any one pillar of this framework will require a re-assessment of the entire process to ensure alignment within the system.

As we noted in our submission dated June 27, 2017, we believe Canada has the ability to lead on a global stage by becoming a prime destination for clinical research and innovative medicines. As a country, we have a long history of innovative thinking to better the lives of Canadians. Understanding that health system sustainability is and should be a priority for our society, we believe innovative ways of addressing affordability that go beyond price are achievable. But, we also believe that these changes must be made in partnership with all stakeholders currently involved in the delivery of care and maintenance of our healthcare system.

We hope you find our submission helpful in your review of the Patented Medicines Regulations. We look forward to your feedback and would welcome a dialogue about the perspectives we have shared both in this letter and within our formal response.

Regards,

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RESPONSE TO THE PROPOSED AMENDMENTS TO THE PATENTED MEDICINES REGULATIONS

Submitted by Hoffmann-La Roche Limited

February 14, 2018

Medicines change lives. Patients are able to live longer and have more productive lives thanks to medical innovations. Medicines do not change lives on their own: patients, their caregivers, volunteers, patient organizations, healthcare practitioners, researchers, institutions, industry and government all have a role to play in bettering the lives of Canadian patients. It is only through working together to invest in health that we can expect to see better outcomes in the future.

How can we hope to achieve better outcomes together? It will require us to optimize current processes or build better ones. We will need to break down silos and increase communication between players in each patient's care network. It will also require innovative thinking to overcome the financial barriers that stymie patient access: drug cost should not be a barrier to healthcare in Canada.

Roche agrees with the Government of Canada, and the Minister of Health, that medicines need to be "affordable, accessible, and appropriately prescribed". A healthcare system that cannot afford the medicines it adopts cannot be expected to be sustainable. At the same time, patients cannot expect the very best clinical outcomes if they do not have access to the best innovative medicines. We acknowledge that the Government's intent to address these challenges is valid, but we also caution that the proposed way it seeks to achieve these public policy objectives will have unintended consequences.

Sound public policy requires that all impacts be taken under consideration, including those on patients, caregivers and tax payers, as well as employees and employers. There is no question that healthcare system sustainability is of paramount importance. So is access to innovation. So is job creation. So is a sound and vibrant life sciences ecosystem, on which so much of our future depends. Roche is ready to tackle this challenge alongside equally concerned partners to ensure that all patients have access to innovative medicines and that the value of Canada's life sciences and pharmaceutical ecosystem is recognized and reflected in the Government's policy approach.

The current proposals to amend the Patented Medicines Regulations (Regulations) represent a well-intentioned attempt to move Canada towards a more sustainable healthcare system. Roche supports the ideals that have led to these proposed amendments, and our engagement during the consultations to date reflects this. Unfortunately, we strongly believe that the current proposals and the manner in which this reformation of the pricing of patented medicines in Canada has been conducted have lacked the holistic approach required to create a stronger Canadian system. Instead, due to its proposed approach to reducing drug prices, Health Canada is now on the brink of setting into motion changes that promise to add inefficiencies to the existing system and a climate of uncertainty that may have long-term implications for patients, patentees, and other players touched by the pharmaceutical industry. The purpose of this response to the Canada Gazette, Part 1 (CG1) consultation is to shine a light on our concerns regarding these changes and to propose a new direction that will benefit all Canadians.

RETHINKING THE REGULATIONS: MAKING SENSE OF THE PROPOSALS

A key concern of Roche and other industry partners is that the proposed regulatory changes will lead to excessive uncertainty or unreasonable comparisons. As noted in our previous submission (Hoffmann-La Roche Limited, 2018) and in the Innovative Medicines Canada submission to the CG1 consultation (Innovative Medicines Canada, 2018), we believe that the introduction of new economic factors and the introduction of the proposed set of comparator countries are ill-advised; such changes promise to introduce uncertainty that may lead to access challenges for Canadian patients. Here, we discuss four key concerns related to the proposed regulatory reforms: the inclusion of new economic factors, the lack of transparency and / or justification for change, the selection of new comparator countries and the need to review and revise the Regulations appropriately.

REGULATORY ISSUE #1: INCLUSION OF NEW ECONOMIC FACTORS

The Canadian market is unique in that it separates the regulation of the pricing of patented medicines from their reimbursement. Although Health Canada and the Patented Medicine Prices Review Board (PMPRB) may believe that changes to one side of this continuum will have a desired impact on the other, this remains uncertain. Choosing to lower prices based on economic factors does not guarantee that these medicines will be adopted by public or private payers quickly or at all. Such guarantees cannot be made as these powers reside outside of the federal government. Without such guarantees, the effect of these factors that are typically used by decision makers will merely be punitive to patentees. As such, we caution against the inclusion of the proposed economic factors to aid in the setting of Canadian drug price ceilings.

PHARMACOECONOMIC EVALUATIONS

As noted in our June 2017 submission, we believe that pharmacoeconomic evaluations should not be included in the assessment of excessive pricing for three reasons: pharmacoeconomic evaluations do not fit with the PMPRB's mandate; uncertainty is a key limitation of pharmacoeconomic evaluations; and, pharmacoeconomic evaluations are already a component of the Canadian access process.

We are troubled by the adoption of cost-effectiveness analyses by an agency that is only responsible for establishing maximum price ceilings and has no power to make enforceable decisions concerning drug reimbursement. One of the biggest challenges in this scenario is the attempt to re-engineer a tool that estimates efficiency into a tool that sets a price ceiling and/or determines affordability. A cost-effectiveness analysis gives a perspective on the efficiency of incremental resources attributed to a new health intervention. While it is possible to judge the acceptability of an intervention's efficiency, the preferences

> Cost-utility analyses represent a tool to help decision makers allocate resources efficiently; they are not designed to be used to set drug price ceilings.

(e.g., an efficiency threshold or willingness-to-pay) of the decision maker must be known. Therein lies the ultimate challenge.

To date, no jurisdiction has successfully developed a legitimate set of preferences. There is no consensus within the academic, government, payer, or policy communities on a cogent methodology. There remain numerous methodological and ethical challenges that have not been resolved. These include questions such as:

- Which is more legitimate: an empirical estimate of resources displaced, preference elicitation, implied precedence or another?
- Should future decisions be determined by past decisions?
- Whose preferences should be used: societal or individual?
- How does the threshold vary given that there are many factors that can influence it?[1]
- How does a threshold change over time?

Furthermore, many attempts at elucidating a threshold fail to measure if there is an intrinsic societal value to innovation. Citizens, patients, providers, academia, industry and government need more time and active engagement to resolve these challenges. For Health Canada and the PMPRB to anticipate that these questions will be addressed within a 6- to 8-month timeframe to support a durable, bespoke system for Canada seems to be overly optimistic.

Roche acknowledges that the setting of incremental cost-effectiveness ratio (ICER) thresholds sits outside of the responsibility of Health Canada; the PMPRB will ultimately establish thresholds should the regulations move forward as proposed. The quagmire that is to come can be avoided by removing pharmacoeconomic value from the Regulations instead of shoehorning cost-effectiveness analysis inappropriately into the exercise of setting price ceilings.

We are also troubled by the adoption of pharmacoeconomic evaluations despite their inherent variability. The ICERs generated by manufacturers often differ from those of health technology assessment (HTA) agencies. This is because the ICER is simply an estimate; an estimate that varies considerably due to a host of direct, indirect, medical and non-medical variables. The sensitivity analyses that are provided within pharmacoeconomic evaluations demonstrate the level of uncertainty, which can be wide ranging and independent of the price of the new medication. Manufacturers will not be able to appropriately assess their price prior to launch if this approach is adopted. This was confirmed by the PMPRB during its Outreach session; we are most likely to have clarity regarding our prices following the publication of an ICER by a

[1] These factors include, but are not limited to, end-of-life, type of disease, stage of disease, age of diseased, life extension vs. quality-of-life improvement, and level of wealth.

publicly funded Canadian organization, such as the Canadian Agency for Drugs and Technologies in Health (CADTH) and *Institut national d'excellence en santé et en services sociaux (INESSS)* (Patented Medicine Prices Review Board, 2018). This will be especially true for rare diseases, where small trial sizes can lead to models that are highly sensitive to changes in modeling assumptions. (Adkins, Nicholson, Floyd, Ratcliffe, & Chevrou-Severac, 2017) Although HTA is used around the globe, the use of ICER thresholds without consideration for other factors typically results in reduced access to innovative medicines. This is demonstrated by the adoption of the Cancer Drugs Fund in the United Kingdom. We do not believe that this is the right direction for a government that is moving to improve access to innovative drugs.

The use of pharmacoeconomic analyses will also be problematic given that not all analyses are specific to a single medicine. As combination therapy becomes more common, the HTA reports generated to study these treatment regimens will become less useful for pricing purposes. For example, if a combination therapy consisting of two drugs is being used to treat a rare cancer that was never treated by either of the therapies before, the ICER will not aid the PMPRB in its determination of the price of each individual drug, only the price of the combination. As such, use of pharmacoeconomic evaluations promises to complicate the pricing process rather than simplify it.

It is also unclear how the PMPRB, with its proposed powers, will address the scenario where a new medicine cannot be made to be cost effective at zero price. In a 2014 report "Assessing technologies that are not cost-effective at a zero price", Davis identifies multiple case studies that demonstrate how this challenge can arise (Davis, 2014). All of these scenarios, which are summarized in Appendix 1, can be distilled down to a common theme: the costs associated with helping patients live longer outweigh the additional quality-adjusted life years (QALYs) gained by these patients. Although the PMPRB has recognized the need to address treatments that extend life differently in its Scoping Document, with no clear local or international guidance on how best to achieve this, it seems unlikely that a suitable solution will be identified in time for the Regulations and Guidelines to be prepared prior to January 1, 2019; additional time will be required.

CANCER DRUGS FUND AND THE ICER THRESHOLDS OF THE UK

The National Institute for Health and Care Excellence (NICE), the United Kingdom's HTA agency, uses a threshold of £20,000 – £30,000 per QALY gained to determine whether a new medicine should be reimbursed. During the latter half of the 2000s, this threshold was effectively increased to £50,000 per QALY gained for drugs treating end-of-life conditions. Despite this change, numerous oncology drugs were rejected by NICE, as their ICERs exceeded these established thresholds.

By 2011, given the inequity that was being generated in the UK system where patients were being denied access to life-changing cancer medicines because of the use of ICER thresholds, the government of the day introduced the Cancer Drugs Fund (CDF). An ICER threshold was not used by the CDF.

Although ICER thresholds were introduced to the CDF in 2016, this was done in a manner that resolved price, access and uncertainty concerns rather than one single concern (e.g., price).

Inclusion of economic factors—Market size projections

Roche continues to believe that the therapeutic value of a medicine is the key determinant of whether or not it is excessively priced. The size of the population treated with a medicine should not be a consideration when establishing a maximum price threshold. Population size should only be a factor when payers work with patentees to determine how to reconcile their limited budgets with the challenge of providing patients with access to innovative medicines.

It should be noted that the Regulations are currently unclear as to what the definition of 'size of market' actually is. It has been assumed that this term refers to the projected market uptake of a given medicine for a specific indication or use. Multiple other possible definitions are possible. As mentioned later in this document, poorly defined terms within the updated Regulations will ultimately lead to confusion and poor decision making. Care must be taken when updating the Regulations.

Issue #2: Lack of transparency and / or justification for new regulations

Based on the information that Health Canada and the PMPRB have made publicly available, it appears that filing requirements for patentees are being increased without adequate planning and justification. In the absence of such justification, Roche recommends that additional time be spent ensuring that the new Regulations balance the need for relevant regulation with the needs of business. Two specific areas of concern for Roche are: the continued exclusion of therapeutic value from the Regulations and the inclusion of indirect rebate information (e.g., product listing agreements, PLAs) as part of mandatory reporting.

Continued exclusion of therapeutic value from the Regulations

Based on the proposed Regulations as presented, the therapeutic value of a medicine need not be a consideration with respect to the price of a medicine; only its pharmacoeconomic value should be considered. This is a flawed approach, especially given that the PMPRB Guidelines Scoping Document explicitly recognizes that therapeutic improvement over existing treatment options (i.e., therapeutic value) should be a consideration in its proposed risk-based approach to pricing review. We continue to believe that the primary and secondary factors considered in the assessment of level of therapeutic improvement should be detailed in the Regulations to provide guidance regarding the assignment of a given level of therapeutic improvement. At a minimum, we see the need for therapeutic value to be added to section 4.4 of the Regulations, to ensure that both the clinical and economic value of drugs are considered; this approach is consistent with HTA organizations in Canada.

Mandatory Inclusion of indirect rebate information

The justification for requesting mandatory access to indirect rebate information continues to remain unclear. As noted in our response to the previous Health Canada consultation, our concerns revolve around three concepts: confidentiality, incentives and logistics. Without additional information regarding how Health

Canada will address these concerns, Roche cannot support the adoption of mandatory reporting of indirect rebates.

Despite calls from stakeholders during the initial consultation on proposed regulatory changes for additional information regarding how third party pricing information will be used, patentees have been left relatively uninformed. The Regulatory Impact Analysis Statement included in the CG1 states the following:

> *The PMPRB currently regulates the non-excessive price of a medicine based on the prices of other medicines in the same therapeutic class for sale in Canada. Since that price information does not include third-party price adjustments, the prices of comparator products that subsequently enter the market are often inflated (as the price ceilings for those medicines are determined in relation to an inflated list price of the existing medicine, rather than the actual price paid in Canada). As a result, the therapeutic class comparison tests yield price maximums that are higher than they would be if the actual price paid were available to the PMPRB.*

Although this has been provided as a rationale for gaining access to third party pricing information, a tangible solution to address this issue has not been tabled. Roche rejects the notion of adapting the therapeutic class comparison tests to incorporate third party adjustments due to the risk of breaching confidentiality.

The efforts to add mandatory filing of third party rebates is of great concern to Roche given that the PMPRB Guidelines Scoping Document (PMPRB Guidelines Scoping Paper, 2018) asks individuals to reflect on the following question:

> *How should the PMPRB make use of confidential third party pricing information?*

This question suggests that either the regulatory burden of mandatory reporting of third party pricing information is being added without a purpose and sufficient planning or that the transparency associated with this consultation process is not being prioritized to ensure that all stakeholders can provide clear, meaningful feedback regarding the Regulations and future Guidelines. Neither of these scenarios seems appropriate if this exercise is to allow all Canadians, including industry, to contribute to the future state of our healthcare system.

REGULATORY ISSUE #3: SELECTION OF COUNTRIES

We continue to believe that clear criteria are required to determine the countries that should be used for international reference pricing purposes. At present, the rationale behind the addition or removal of some countries from the PMPRB7 to create the PMPRB12 remains unclear. In our previous submission, we provided criteria that could be used to select appropriate comparator countries. We also provided rationale for why both Switzerland (which meets Health Canada's proposed selection criteria) and the United States (with its marketplace that is most aligned and integrated with the Canadian marketplace) should be considered to be reasonable members of the countries used for international comparisons.

Operationally, we believe that a basket of countries based on the G7 is more appropriate than the PMPRB12 as Canada should be measured against its economic peers. To address concerns regarding having a basket of countries that is too small (i.e., less than 7 comparator countries), a basket based upon the G10, another internationally recognized economic group of countries, should be used. As shown in Figure 1, the G10 countries reflect all markets within the G7 and two-thirds of the markets referenced as part of the PMPRB12.

Group	CA	US	UK	FR	DE	IT	JP	BE	NE	SE	CH	NO	AU	KR	ES
PMPRB7		■	■	■	■	■				■	■				
G7	■	■	■	■	■	■	■								
PMPRB12			■	■	■	■	■	■	■	■		■	■	■	■
G10	■	■	■	■	■	■	■	■	■	■	■				

FIGURE 1: COMPARISON OF COUNTRIES WITHIN THE PMPRB7, G7, PMPRB12 AND G10.

G7 = Group of Seven. G10 = Group of Ten. CA = Canada. US = United States. UK = United Kingdom. FR = France. DE = Germany. IT = Italy. JP = Japan. BE = Belgium. NE = Netherlands. SE = Sweden. CH = Switzerland. NO = Norway. AU = Australia. KR = South Korea. ES = Spain.

We continue to strongly advise against the inclusion of countries that have access levels that are significantly below the OECD median as this could result in the level of access Canadians have to life-changing drugs being compromised.

REGULATORY ISSUE #4: ADDITIONAL REVIEW AND REVISION OF THE REGULATIONS IS REQUIRED

Although Health Canada has chosen to revise the existing Regulations to provide the PMPRB with additional powers to support the PMPRB's consumer protection mandate, it has failed to use this opportunity to ensure that the final regulations have been appropriately drafted both to modernize them and to ensure they are fully aligned with the Government of Canada's commitment to reduce the regulatory burden on companies. Four areas of concern for Roche are the following:

- Unclear definitions
- Inclusion of redundant regulation
- Lack of thoroughness with respect to revising outdated and/or ineffective regulation
- Patentee requirement to supply publicly available information

Details pertaining to each of these issues can be found in Appendix 2. Should these issues not be addressed at this time, Health Canada will miss an important opportunity to add clarity to the PMPRB's operations and provide the PMPRB with a modern view of the current pharmaceutical industry landscape.

A BALANCED APPROACH TO REGULATORY REFORM IS REQUIRED

Roche recognizes that the Regulations have not changed in 20 years, and therefore a review of the existing Regulations may be timely. We question, however, whether these amendments have been undertaken in a thoughtful, practical, and evidence-based way. A constructive approach to such sweeping changes would involve first and foremost those who are most impacted, as well as key thought leaders in industry and beyond, to facilitate a smooth and effective implementation.

Such an approach would set up all parties up for success, create realistic expectations, and limit regulatory burden. The current trajectory of change with its limited amount of consultation and the rush to implement changes promises to lead the impacted parties to an uncertain future at best.

The current trajectory of change with its limited amount of consultation and the rush to implement changes promises to lead the impacted parties to an uncertain future at best.

CONSULTATION ISSUE #1: INSUFFICIENT CONSULTATION TO UNDERSTAND THE PERSPECTIVES OF STAKEHOLDERS

As part of the Health Canada consultation on the proposed amendments to the Regulations held during the Spring of 2017, Roche, as well as Innovative Medicines Canada and its member companies, shared their perspectives through written responses. In our responses, we reiterated our long-standing position that a change to the formula presented in the current Regulations to calculate research and development spending in Canada is necessary. In addition, Ernst and Young showed the true level of investment made by member companies of Innovative Medicines Canada (Ernst & Young LLP, 2018). This was seemingly ignored. We called for the inclusion of therapeutic value in the new Regulations. This, too, was not considered. We now caution against not working with partners to explore the reasonableness and feasibility of their submitted arguments; if appropriate consideration of stakeholder views is not performed, we risk having the final results of this reform process diverge from the needs of Canadians.

With the initiation of the CG1 consultation, there are now three consultations that have been initiated since 2016 to understand how the PMPRB and the Regulations should be modified to improve upon the effectiveness of the PMPRB. Although we believe that the quantity of consultation has been appropriate, the quality of each consultation has been lacking.

Of note, the first consultation period launched by the PMPRB in 2016 outlined a well-designed process within the PMPRB Guidelines Modernization: Discussion Paper (Figure 2). Although Phase 1 was completed on

October 31, 2016 and received a high level of engagement (i.e., 66 submissions) and Phase 3 is expected to occur in the Spring of 2018, the critical second phase of the consultation has been largely ignored (PMPRB Guidelines Modernization – Discussion Paper – June 2016, 2018). The negative impact of this, given the previous announcement that representations in support of written submissions would be conducted, is two-fold:

- those drafting submissions with the intention of explaining and expanding upon their views were left without an opportunity to do so; and,
- respondents were unable to work with the PMPRB to ensure that their points were heard and understood.

In the end, the PMPRB's consultation process has fallen short of its guiding principles. (Consultation Policy, 2018) This consultation process should have been followed as planned prior to embarking on regulatory reform. By circumventing the process, Health Canada has been left without a robust understanding of the concerns of stakeholders. We urge Health Canada to collect and consider additional information in a more thorough manner prior to proceeding with the proposed changes.

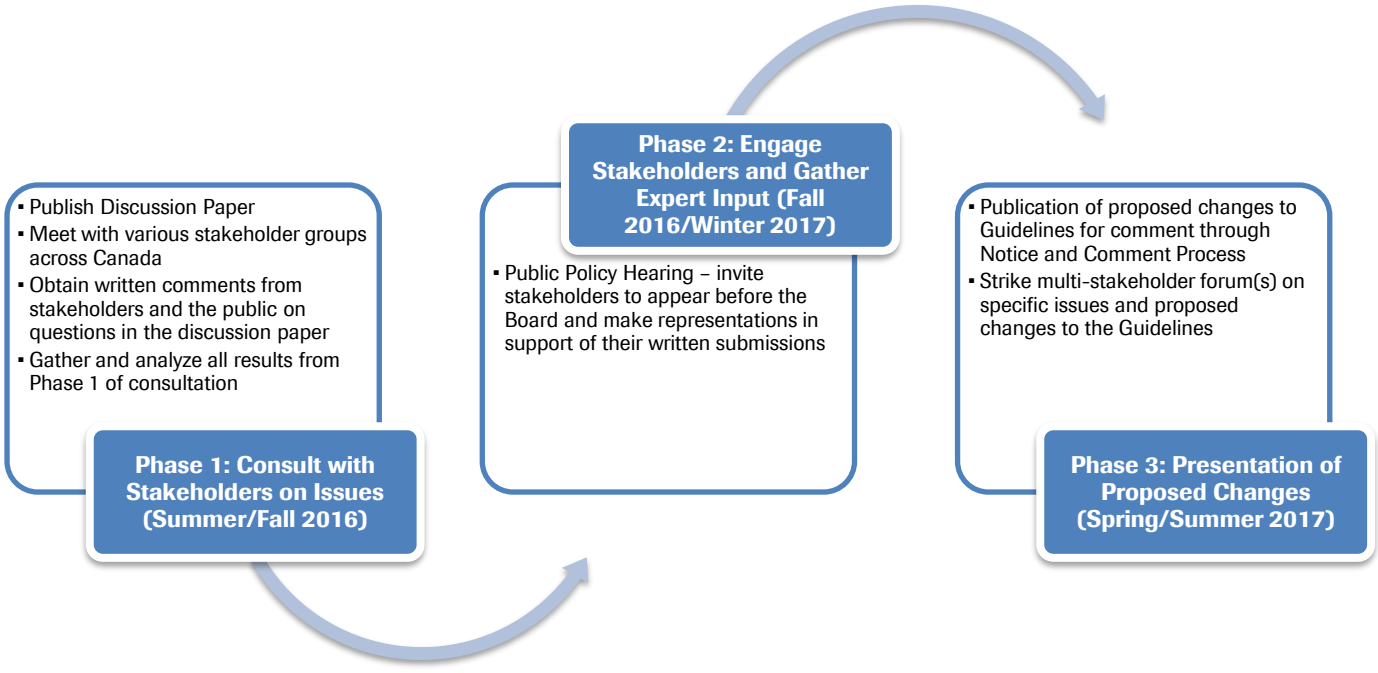

FIGURE 2. PUBLISHED PROCESS FOR PMPRB GUIDELINES MODERNIZATION CONSULTATION

CONSULTATION ISSUE #2: INSUFFICIENT TIME TO IMPLEMENT CHANGES

As part of the CG1, it has been stated that:

> *The proposed Regulations would come into force on January 1, 2019. This would allow patentees time to prepare for implementation of the new price regulatory factors and information reporting requirements on prices. January 1, 2019, was the date chosen to align the implementation with the PMPRB's reporting periods of January 1 and July 1.*

The current timelines for the draft and final PMPRB Guidelines, as well as the publication of the Canada Gazette, Part 2, have not been shared in detail with those who will be impacted most by these changes: patentees. It is assumed that final Regulations will be made available at the beginning of the second half of the year, to provide patentees with six months to prepare for the January 30, 2019 filing deadline. That timeline, however, adds a great deal of uncertainty to prices for both launch and in-market product planning today. As such, expecting that manufacturers will be able to comply with the new Regulations by January 1, 2019 when little is known about future prices is inappropriate.

To provide manufacturers with sufficient time to plan and prepare for the changes, a more reasonable implementation date that falls no earlier than January 1, 2020 should be used. The last time that a fulsome revision of the Regulations and Guidelines was performed, approximately four years of discussion and consultation occurred before the new Guidelines were implemented. At its current pace, the new Regulations and Guidelines will be revised within a two-year timeframe—half the time of the 2005 consultation. This is an exceptionally aggressive timeline. Attempting to consult with industry and other stakeholders within Spring 2018 alone to create clear, implementable guidelines given historical precedents promises to do a disservice to all involved parties while relying on a longer consultation period makes January 1, 2019 an unrealistic target.

A NEW DEAL FOR CANADA

We all play a part in making the Canadian healthcare system work. All Canadians have a vested interest in continuously striving to have the very best healthcare system available. As demonstrated by the results of the PMPRB's 2016 consultation on the Guidelines[1] and the engagement of stakeholders as part of the 2017 Health Canada consultation[2], there is a willingness to engage and help shape Canada's 'Better Tomorrow'.

In the absence of a forum in which all partners can collaborate to create a New Deal for Canada, Roche and Innovative Medicines Canada recommend that Health Canada limit its reliance on regulatory reform, leverage

[1] 66 individuals or organizations have publicly posted responses to the PMPRB's 2016 consultation.

[2] At least 46 individuals or organizations contributed to submissions to the Health Canada consultation based on those submissions that were made public through the PDCI Market Access website.

reform of the PMPRB Guidelines as an interim measure and engage with all Canadians to carve out a new path that will ensure that cost is not a barrier to appropriate care for Canadians and that patients receive the right medicine and the right time to make a meaningful impact on health outcomes.

If regulatory reform must be implemented, Roche and Innovative Medicines Canada recommend the following changes to the current Regulations:[1]

1. Elimination of annual price increases for existing patented medicines (i.e., section 85(d) of the Patent Act would only apply to new medicines)
2. Creation of a PMPRB9, based on the G10 countries that are part of the G10 with the removal of the United States.

These changes would be made in place of, rather than in addition to, the proposals found in the CG1. More specifically, neither the introduction of pharmacoeconomic value as a factor nor the mandatory disclosure of confidential third-party pricing information should be introduced to the Regulations. In addition, existing patented products should be grandfathered, meaning that existing products should continue to be managed based on the Regulations and PMPRB Guidelines as they are written today.

Both Roche and Innovative Medicines Canada recognize the PMPRB's view that adoption of a risk-based approach to price regulation will lead to a better deployment of resources. In that vein, we support the PMPRB's proposal to continue reducing the regulatory burden for low-risk drugs (e.g., patented generics, over-the-counter drugs, veterinary drugs, branded medicines following generic entry, etc.) and the move to determine how best to assess 'high-risk' medicines. The definition of 'high-risk' and 'low-risk' must be done with appropriate consultation to ensure that the resources of all involved parties are considered.

SHAPING CANADA'S 'BETTER TOMORROW'

Eliminate annual price increases for existing medicines.

Expand the comparator countries to the G10 and remove the US.

Limit the use of pharmacoeconomic value assessments and third-party pricing information to Canadian payers.

Adopt a risk-based approach to price regulation through the PMPRB Guidelines using agreed-upon definitions of 'high-risk' and 'low-risk'.

[1] These changes do not include the required housekeeping changes that have been mentioned elsewhere in this report.

These changes to the Regulations, along with appropriate changes to the PMPRB Guidelines, represent the first step towards reforming the Canadian healthcare system such that it will be better able to serve Canadian patients today and into the future.

Roche and the innovative medicines industry are prepared to discuss specific solutions beyond regulatory reform to contribute to health system affordability, patient access to new medicines and innovation strategy objectives. A key part of this discussion is a vision paper entitled *For Our Health, for Our Economy, Let's Aim Higher: A Made-in-Canada Approach to New Medicines.* The vision paper makes the case for more holistic and forward-looking strategies and policy options to address the government's stated priorities of access, affordability and appropriate prescribing while advancing the innovation agenda. The hope is that this paper will catalyze real solutions to the challenges facing patients, our health systems and our economy. (Please visit www.innovateforlife.ca for more information.)

CONCLUSION

Affordability and sustainability are, and will continue to be, significant concerns for payers within Canada's healthcare system. Both Roche and the larger innovative medicines industry recognize this. We need to ensure that all Canadians are able to access the innovations they need to lead healthier, longer, more productive lives. We also need to fuel the engine of innovation both at home and abroad to fill the gaps in care that currently exist. To achieve this in a successful and sustainable way, it will take a concerted effort by all stakeholders, including patients, industry and governments, to make this happen.

The existing plan to change the way that prices are regulated in Canada needs to be re-examined to improve the likelihood of improving access which enhancing affordability and sustainability. Roche would welcome the opportunity to meet with both the Minister of Health and the Minister of Industry, Science and Economic Development to highlight the risks associated with the current approach and to help find a way forward that supports the creation and deployment of innovative medicines while addressing the pressing issues of affordability and sustainability.

Our aim is to ensure that patients have the best access to life-changing medicines, that cost is never a barrier to patient health and well-being, and to ensure that the right patient gets the right treatment at the right time. We look forward to working together to make that happen.

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APPENDIX 1: ICERS AND THE CHALLENGE OF EXTENDING LIFE

By introducing pharmacoeconomic analyses that are published by public Canadian institutions as a mandated consideration for price assessments without consideration for intrinsic therapeutic value, future products similar to the ones mentioned by Davis and summarized below will effectively be blocked from entering the Canadian marketplace as manufacturers will be unable to determine whether a price above $0 is achievable in Canada (Davis, 2014). This uncertainty will lead either to patient access delays as negotiations with the PMPRB will be required or patients being denied access to life-changing medicines, as was seen in the UK prior to the necessary undermining of its HTA body through the introduction of the Cancer Drug Fund (CDF). Neither of these scenarios is positive for patients.

Scenario A: Additional time on best supportive care (Based on cinacalcet in end-stage renal disease)

- New medicine extends patient life.
- Patients still need to receive best supportive care (e.g., in the case of cinacalcet: dialysis).
- Cost of best supportive care during extended period of life renders treatment not-cost-effective even if the new medicine is given away for $0.

Scenario B: Additional time on intensive treatment (Based on pertuzumab for metastatic breast cancer)

- New cancer medicine, when taken in combination with existing treatments, extends patient time in a progression-free survival state.
- Treatment must be taken in combination with existing treatment(s) (e.g., in the case of pertuzumab: trastuzumab).
- Cost of the existing treatment(s) over the extended period of progression-free survival renders the new medicine not-cost-effective even if it is given away for $0.

Scenario C: Additional time in later disease state (Based on vinflunine for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract)

- New cancer medicine taken until disease progression.
- The new treatment extends patient life in the post-progression state.
- The extension of patient life results in increased costs that render the new medicine not-cost-effective even if it is given away for $0.

Scenario D: High cost events in period of extended survival (Identified through the example of cetuximab for head and neck cancer)

- New medicine extends the survival of a given patient.
- Patients live long enough to experience age-related high-cost health events.
- By allowing patients to live longer, they become more likely to experience expensive health events that render the new medicine not-cost-effective even if it is given away for $0.

APPENDIX 2: ADDITIONAL REVIEW AND REVISION OF THE REGULATIONS IS REQUIRED

UNCLEAR DEFINITIONS

The terms that have been included in the proposed regulations have not been clearly defined. As a result of this ambiguity, Board Staff and the PMPRB Panel can be expected to face challenges when interpreting the Regulations. Roche recommends that, should these terms continue to be included in the Regulations, the terms should be clarified prior to the finalization of the Regulatory text.

Some of the terms that remain poorly understood within the proposed text include:

Regulatory text	Issue(s) with Regulatory text
Issue: Definition of size of the market **Regulatory text:** The size of the market for the medicine in Canada and in countries other than Canada	It is unclear whether the size of the market must reflect the epidemiology of the disease area being considered, forecasted sales numbers, or some other data.
Issue: Definition of estimated maximum use of the medicine in Canada **Regulatory text:** 4.2 (1) For the purposes of paragraphs 80(1)(d) and (2)(d) of the Act, the information to be provided respecting the factor referred to in paragraph 4.4(b) is the estimated maximum use of the medicine in Canada, by quantity of the medicine in final dosage form, for each dosage form and strength that are expected to be sold.	It is unclear whether the estimated maximum use of the medicine in Canada must reflect the epidemiology of the disease area being considered, forecasted sales numbers, or some other data.
Issue: Limits of pharmacoeconomic value assessment **Regulatory text:** The pharmacoeconomic value in Canada of the medicine and that of other medicines in the same therapeutic class	It is unclear whether the PMPRB will only be able to assess the pharmacoeconomic value of <u>one</u> indication at any given time, as some products may have multiple indications and be members of multiple therapeutic classes.
Issue: Valid sources of cost-utility analyses **Regulatory text:** 4.1 (1) For the purposes of paragraphs 80(1)(d) and (2)(d) of the Act, the information to be provided respecting the factor referred to in paragraph 4.4(a) is 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.	It is unclear whether only CADTH and INESSS should be used as valid sources or whether hospitals, drug plans, universities and other publicly funded Canadian organizations should be considered to be valid. A broad definition will make compliance challenging. It is also unclear what the definition of 'published' is as it could be viewed as including any print or electronic media.

INCLUSION OF REDUNDANT REGULATION

Although we philosophically support the reduction of the regulatory burden associated with patented over-the-counter, veterinary or generic drugs, it remains unclear why such amendments to the Regulations are required. In the PMPRB NEWSletter – February 2017, Volume 21, Issue 1, the PMPRB indicated that it would move to a complaint process for patented generic medicines and that this would take effect as of the July-December 2016 reporting period (PMPRB NEWSletter – February 2017, Volume 21, Issue 1, 2018). This calls into question the rationale for consulting on the inclusion of this factor in the new Regulations; such changes can be and have been made using the Guidelines. Further, the PMPRB Guidelines Scoping Document suggests that the products that will be moved to a complaints-based approach will be expanded beyond the current regulatory proposal. Specifically, it states:

> *Drugs categorized as low priority,* ***because of the presence of a significant number of therapeutic alternatives in the market and/or generic competition****, would not be subject to an introductory or ongoing s.85 analysis and would be investigated on a complaints basis only. [Emphasis added]*

Roche is of the position that regulations should only be employed if they add greater clarity. The current approach to regulatory reform promises to create confusion for Board Staff and patentees for concerns that are required to move to Hearings or to the courts. As the PMPRB is already empowered to move products to complaint-based reporting and it is clear that the current regulatory proposal is insufficient to meet the PMPRB's proposed needs, this regulation should not be included in the current amendments.

In addition to the request to limit compliance responsibilities for certain classes of patented medicines to responding to the PMPRB upon request, it is also unclear why regulatory change is required to allow the PMPRB to access forecast data regarding the size of the market. Sections C.4.4 and C.4.5 of the existing Guidelines demonstrate that the PMPRB is able to use these data in the absence of regulatory reform (Compendium of Policies, Guidelines and Procedures – Updated February 2017, 2018).

> *C.4.4 Where there is no apparent single approved indication or use for which the new patented drug product offers the greatest therapeutic advantage, the approved indication or use representing, potentially****, the greatest proportion of sales*** *will be the basis for recommending its level of therapeutic improvement and selection of drug products to be used for comparison purposes.*
>
> *C.4.5 Estimates of potential sales can be based on several sources including* ***actual prescribing patterns (when available), epidemiological data (Canadian incidence and prevalence) and prescribing patterns in other countries.*** *[Emphasis added]*

Regardless of whether the regulatory changes are seeking to provide the PMPRB with access to epidemiology data or market forecasts, it would appear that the PMPRB already has this power. As such, the need to amend this component of the Regulations remains to be demonstrated.

LACK OF THOROUGHNESS WITH RESPECT TO REVISING OUTDATED AND/OR INEFFECTIVE REGULATION

With time comes experience. The PMPRB, during its 30 years of existence, has been able to amass a great deal of experience regarding the best way to manage the regulation of drug prices. Despite this available knowledge, Health Canada has neglected to modify all aspects of the Regulations to align them with current realities. Section 4(a) of the Regulations continues to require semi-annual reporting despite the PMPRB's previous call for such reporting to be changed to annual reporting (Notice and Comment: Regulatory Burden Reduction Initiative, 2018). Sections 5 and 6 of the Regulations concerning the reporting of research and development spending has been left untouched, despite calls from industry to rewrite the formula for such assessments and evidence from Ernst and Young that the current regulatory approach dismisses approximately 50% of industry's investment in Canada (Ernst & Young LLP, 2018). Technology has evolved and the PMPRB has moved to keep pace, rendering Section 7 of the current Regulations obsolete relative to current filing practices. Roche believes that adequate time and planning is required to ensure that the final Regulations are reflective of the reality that now exists 30 years after the creation of the PMPRB.

PATENTEE REQUIREMENT TO SUPPLY PUBLICLY AVAILABLE INFORMATION

As part of the regulatory reforms, it should be important to balance the positive expected outcomes of change with the increased regulatory burden. On the Government of Canada website concerning the "One-for-one" rule, it is stated that:

> *The government has committed to reducing the regulatory burden on businesses to better enable them to make needed investments in productivity and job creation.*

The requests made within the current and proposed Regulations for patentees to supply publicly available information seem to run counter to this approach; patentees should not be responsible for providing publicly available data.

The current Regulations do not require patentees to provide consumer price index (CPI) or exchange rate data for reference countries as these data are in the public domain. The proposed Regulations do not require patentees to provide gross domestic product (GDP) data for the same reason. With these new reforms, manufacturers will be required to collect information published by public institutions regarding cost per quality-adjusted life year (QALY)-based assessments. As this information is publicly available in the same way that CPI, exchange rate and GDP data are available, it is inappropriate for patentees to be required to supply this information.