February 14, 2020

Dr. Mitchell Levine
Chairperson, Patented Medicine Prices Review Board
Box L40, Standard Life Centre
333 Laurier Avenue West Suite 1400
Ottawa, Ontario
K1P 1C1

Dear Dr. Levine:

RE: Gilead Sciences Canada, Inc. (Gilead Canada) Response to PMPRB Draft Guidelines Consultation

Thank you for the opportunity to provide feedback into the proposed PMPRB Guidelines. At Gilead, we support efforts to optimize patient access to innovative medicines in a sustainable manner, and to ensure a predictable business environment in Canada that enables decision-making around the launch of new clinical innovations and investment in research and development.

The global mission of Gilead Sciences, Inc. (Gilead) is to advance the care of patients suffering from life-threatening diseases. Through our medicines, we have helped transform the lives of patients around the world with HIV/AIDS, Hepatitis C and B and hematological malignancies. Gilead has led the development of antiretroviral therapy for HIV/AIDS, helping transform HIV infection from an often fatal and debilitating disease into a chronic, manageable condition for many. We are actively engaged in treatment and cure-focused research in HIV, HBV, hematology and oncology. With newer treatments available today, it has become much easier to cure chronic HCV in most patients with the use of direct acting antivirals (DAA's). Gilead is fully committed to the World Health Organization's ambitious goal of eliminating viral hepatitis by 2030 by actively supporting the efforts of governments, patient organizations, payers and healthcare providers to increase awareness, drive screening and facilitate linkage to care.

Complementing this work, we have endeavored to support Canada's goal of creating a vibrant life sciences sector. Based on the PMPRB's published statistics, our Canadian R&D-to-sales ratio has exceeded 10% since 2005. Approximately 500 Canadians are employed by Gilead across the country, supporting both our development of new, innovative therapies at our research and process manufacturing facility in Edmonton, Alberta, and our pharmaceutical business that provides Canadians with access to our medicines. Gilead also leverages Canadian contract manufacturing capabilities to serve both local and global production. Fully one third of worldwide Gilead tablet requirements are produced via Canadian contract manufacturing.

As a company that has demonstrated its commitment to helping to improve patients' lives and strengthening Canada's life sciences sector, we support the industry's position, as stated by BIOTECanada (of which we are a member), on the proposed changes to the PMPRB Guidelines. We have serious concerns that the proposed guidelines do not support the types of innovations that are expected to become standards of care in the future and will lead to fewer innovative medicines entering the Canadian market. Our greatest concerns include:

- the inappropriate application of cost-utility analyses,
- changes regarding net price confidentiality,
- disincentives created by the guidelines for curative and transformational single and short-term treatments (SSTs), and
- the increase in business uncertainty due to a lack of price predictability.

Inappropriate application of cost-utility analyses

We support the common position of BIOTECanada and Innovative Medicine Canada that pharmacoeconomic value should not be used in the Guidelines to establish net price ceilings. Cost-utility analyses (CUAs) are built

upon a collection of assumptions that have the potential to significantly impact the pharmacoeconomic price (PEP) that the PMPRB wishes to use to determine a medicine's Maximum Rebated Price (MRP). Health Canada has concluded that only CUAs developed by publicly funded institutions are acceptable sources of data for price assessments; however, this proposed system does not provide an independent means of validating the assumptions used by these institutions. This is structurally unfair and can result in highly conservative and potentially improbable clinical assumptions being made that will impact the net price of future medicines.

Further, overreliance on pharmacoeconomic value to define the price of a medicine potentially devalues the medicine in question. Several key agencies and associations that specialize in pharmacoeconomic analysis have recognized that value extends beyond pharmacoeconomic value. The table found in Appendix A identifies five of these organizations (ISPOR, CADTH, INESSS, ICER and NICE) and their respective positions. The ISPOR flower, for example, suggests that a multifactorial approach can and should be pursued that includes: quality-adjusted life-years, net costs, productivity, adherence-improving factors, reduction in uncertainty, fear of contagion, insurance value, severity of disease, value of hope, real option value, equity, and scientific spillovers. Indirect economic costs like family and caregiver burden and productivity gains from returning to work must also be included to give a full picture of a drug's value to Canadian society. We firmly believe that the PMPRB must establish a working group with industry representation to determine the most appropriate manner to integrate pharmacoeconomic value into the new PMPRB Guidelines.

Confidentiality

Confidential net pricing creates flexibility for patentees and payers to deliver sustainable access for Canadian patients.

Countries have found that protecting the confidentiality of reimbursement negotiations with payers is a matter of public interest which outweighs the public interest in the disclosure of such information.[1] Moreover, many competition authorities have cautioned that mandating such disclosures can harm competition in the market.[2]

Most importantly, from a health care system perspective, a country forcing disclosure of sensitive net price information which can then be used by other countries in their international reference pricing mechanism, ultimately prevent that country from getting pricing and reimbursement arrangements tailored to their local contexts, which can result in reduced patient access to treatments.[3]

We believe that any disclosure of product-specific net price ceiling information, whether it is revealed directly by the PMPRB or indirectly through its publicly-disclosed methods, compromises confidentiality. Further, having this information in the public domain will significantly change the risks associated with launching products in Canada; a change that global organizations will need to consider when determining where and when to launch innovative products. With efforts to allow the importation of Canadian medicines into the United States gaining traction, it is important to create safeguards that protect the Canadian market; confidentiality is one such safeguard.

Confidentiality is a cornerstone of effective negotiated agreements, both from a local and a global business perspective. The efforts being undertaken by the PMPRB, when combined with the changes these efforts will require HTA agencies to implement, promise to expose the magnitude of Canadian pharmaceutical rebates at a

[1] The Irish Information Commissioner upheld a refusal by the Irish Health Service Executive to hand over reimbursement records relating to the price negotiations with Vertex for Orkambi (Decision of 20 April 2018, Ms X and the Health Service Executive).
[2] The European Commission has recognized this risk in its Final Report of the Pharmaceutical Sector Inquiry when discussing price transparency in the context of tendering procedures: "… making the prices available to the general public allows health insurers not engaging in the tender process to free ride on the efforts of the other insurers and reduces the scope of competition between them."(para. 1485). See also: T. Koslov and E. Jex, "Price Transparency or TMI?" Federal Trade Commission, July 2, 2015.
[3] A recent study concludes: "In the absence of global purchasing agreement on tiered pricing by region and market (which would have to include the United States), the effect of price transparency will be to both slow the diffusion of innovative products to middle- and low-income countries, thereby reducing access, and, consequently, to reduce the returns to innovation." See Berdud et al. (2019) "The Future of Global Health Procurement: Issues around Pricing Transparency - Working Paper 507". (available at: https://www.cgdev.org/publication/the-future-global-health-procurement-issues-around-pricing-transparency)

product-specific level to the world. Estimation of the net price ceiling of Category I drugs will be possible given public disclosure of the following information:

- Cost of new treatment, as reported by CADTH/INESSS
- Time Horizon and Discount rate, as disclosed by CADTH/INESSS
- Incremental Cost, as reported by CADTH/INESSS
- Incremental Quality-Adjusted Life Years (QALYs), as reported by CADTH/INESSS
- ICER threshold (i.e., $60,000 per QALY), as published by the PMPRB
- Market Size Discounts, as published by the PMPRB
- Units Sold, as reported by various third-party vendors

In addition to the potential public exposure of net price ceilings in Canada for Category I drugs, the confidentiality of the current net prices of grandfathered products also appears to be uncertain based on the proposed Guidelines. As stated in paragraph 59 of the proposed Guidelines:

> *The [Maximum List Price, MLP] for all grandfathered patented medicines will be set at the lower of (i) the [Median International Price, MIP] for the PMPRB11 countries for which the patentee has provided information, or (ii) the patented medicine's ceiling under the Guidelines applicable prior to the issuance of these Guidelines.*[1]

Current price ceilings are based on all data shared with the PMPRB, which includes as per Subsection 4(4) of the Regulations:

> *…any reduction given as a promotion or in the form of rebates, discounts, refunds, free goods, free services, gifts or any other benefit of a like nature and after the deduction of the federal sales tax…*[2]

Should the PMPRB move forward with establishing the MLP of grandfathered products using current average transaction price-based ceilings (e.g., through use of the Non-Excessive Average Price), all the aforementioned confidential information would be revealed in the new list price of certain grandfathered drugs. This would represent inappropriate public disclosure of information that was reported under confidentiality.

Disincentives for curative and transformational single or short-term treatments (SSTs)

It is our strong belief that the proposed guidelines create a system that undermines the entry of single or short-term transformative therapies (SSTs) into the Canadian market. These treatments include one-time treatments such as cell therapy and gene therapy, as well as potential cures such as those offered to individuals with HCV infections. The Institute for Clinical and Economic Review (ICER) group, with support from CADTH and NICE, has recognized the unique challenges associated with these types of treatments and has taken steps to find a solution that is appropriate for the American healthcare system.[3,4] We believe that similar work is required here in Canada to create a solution that works for patients and our payer groups.

With the coming age of SSTs, fewer new drugs will have the gradual sales curves of the past. We all wish for society to have access to curative therapies that can provide individuals with long, healthy lives while eliminating the underlying disease. In the case of SSTs, this will require an initial outlay of funds to start treating the prevalent population followed by a rapid decline in healthcare spending as fewer and fewer individuals present with the condition. SSTs require short-term spending; however, the benefits are expected to last for a lifetime. An example of the difference between the financial impact of chronic medicines versus SSTs is provided in

[1] PMPRB Draft Guidelines Consultation, https://www.canada.ca/en/patented-medicine-prices-review/services/consultations/draft-guidelines.html. Last accessed February 11, 2020.
[2] Patented Medicines Regulations, https://laws-lois.justice.gc.ca/eng/regulations/SOR-94-688/page-1.html. Last accessed February 11, 2020.
[3] ICER Value Assessment Framework, https://icer-review.org/methodology/icers-methods/icer-value-assessment-framework-2/, Last accessed February 11, 2020.
[4] Valuing A Cure, https://icer-review.org/topic/valuing-a-cure/, Last accessed February 11, 2020.

Appendix B. Although we understand the need for a sustainable healthcare system in Canada, reliance on simple price reductions due to high SST usage is a suboptimal solution.

To encourage the further development of SSTs and to make Canada a preferred country for their launch, it will be important to develop policies that support those goals; the proposed PMPRB Guidelines fall short of this objective. For example, although a cure that is administered once to a patient may be preferred by the patient and by those involved in the patient's care, the PMPRB's proposed system encourages the development of treatments that are taken chronically. This is true because the PMPRB's proposed system makes its market size adjustment based on annual sales rather than a more customized duration aligned with the key properties of the medicine in question.

More appropriate methods of managing healthcare spending that recognize the long-term benefits of these therapies need to be explored; such approaches may extend beyond that which falls under the PMPRB's remit[1,2,3] As has been noted in the literature, the challenges posed by the initial outlay of funds to pay for SSTs can be overcome in a number of creative ways that look at affordability rather than price. This includes the amortization of costs over a longer timeframe or the implementation of outcomes-based agreements. To find the right path forward, working groups that have representation from the PMPRB, HTA agencies, payers, academia, patients and industry, are needed to find effective solutions to appropriately value SSTs.

Increased business uncertainty due to lack of price predictability

Canada has historically provided patentees with a reasonable level of certainty regarding the price of patented medicines and patient access to those medicines. This has helped position Canada as a stable and predictable market for global organizations when determining when and where to launch new products. The proposed guidelines introduce significant uncertainty into the Canadian market as summarized by the following excerpt from the Draft Guidelines:

> *In accordance with subsection 96(4) of the Act, these Guidelines are not binding on Staff, the Chairperson, Hearing Panels or patentees... The enforcement decisions of Staff and the ultimate resolution of issues will depend on the particular circumstances of the matter in question.*[4]

Based on this text, it is impossible for a patentee to have any level of certainty regarding how to operate in a compliant manner. This represents a departure from the previous guidelines, where Staff were obliged to follow the Guidelines:

> *Board Staff carries out the day-to-day work of the PMPRB including the administration of the Patented Medicines Regulations (the Regulations) to ensure compliance with the prescribed filing requirements. The review of prices of patented medicines is carried out in accordance with the Guidelines, which are approved by the Board.*[5]

By permitting Board Staff to evaluate compliance based solely on the Guidelines, the PMPRB was able to create a stable, predictable environment for those patentees providing Canadians with access to their medicines. Board Staff should continue to be bound by the Guidelines to maintain fairness within the PMPRB system. If greater flexibility is required to support the use of "common sense" solutions by

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[1] Comer B, Six drug pricing models have emerged to improve product access and affordability. https://www.pwc.com/us/en/industries/health-industries/library/6-drug-pricing-models.html. Last accessed February 11, 2020.
[2] Kleinke JD, McGee N. Breaking the Bank: Three Financing Models for Addressing the Drug Innovation Cost Crisis. *Am Health Drug Benefits*. 2015 May;8(3):118-26. PMID: 26085900; PMCID: PMC4467013.
[3] Schaffer SK, Messner D, Mestre-Ferrandiz J, Tambor E, Towse A. Paying for Cures: Perspectives on Solutions to the "Affordability Issue". *Value Health.* 2018 Mar;21(3):276-279. PMID: 29566833.
[4] PMPRB Draft Guidelines Consultation, https://www.canada.ca/en/patented-medicine-prices-review/services/consultations/draft-guidelines.html. Last accessed February 11, 2020.
[5] Compendium of Policies, Guidelines and Procedures – Updated February 2017, http://pmprb-cepmb.gc.ca/view.asp?ccid=492&lang=en, Last accessed February 11, 2020.

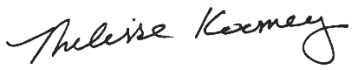
Board Staff, the rules that Board Staff should follow under these special cases should be determined through a working group and defined within the Guidelines.

Next Steps

As we move into the final phase of the PMPRB's reforms, we believe that it is critically important that working groups be established as soon as possible to solve the operational and access-related challenges that stem from the proposed Guidelines. Collaboration between the PMPRB and industry will be crucial if we are to implement changes that benefit all Canadians. We are committed to remaining engaged in this process and look forward to participating in future opportunities to create a sustainable system that works for everyone.

Should you have any questions regarding Gilead's feedback on the PMPRB Guidelines, please feel free to contact Patrick Douglas, Senior Manager, Market Access and Pricing at marketaccesscanada@gilead.com.

Best regards,



Melissa Koomey
Vice President and General Manager, Gilead Sciences Canada, Inc.

Appendix A: Examples of commentary or policy regarding assessment of value issued by selected agencies and organizations specializing in the evaluation of medicines

The following table presents examples of commentary made by or active policies followed by various organizations that specialize in the evaluation of medicines. This list is neither exhaustive nor comprehensive; however, it provides a window into general areas of sensitivity expressed by various relevant groups. These positions stand in direct opposition to the PMPRB's proposed Guidelines as the PMPRB has developed a system that states that the price of a new medicine can be no greater than its estimated pharmacoeconomic value. Gilead agrees with the sentiments of the organizations listed below, which suggest that factors beyond the pharmacoeconomic value and net costs should be considered and that pharmacoeconomic value does not represent a ceiling price.

Organization	Example of Commentary or Policy regarding Assessment of Value	Reference
International Society of Pharmacoeconomics and Outcomes Research (ISPOR)	From the abstract of Defining Elements of Value in Health Care—A Health Economics Approach: An ISPOR Special Task Force Report: *…We aim to broaden the view of what constitutes value in health care and to spur new research on incorporating additional elements of value into cost-effectiveness analysis (CEA). Twelve potential elements of value are considered. Four of them—quality-adjusted life-years, net costs, productivity, and adherence-improving factors—are conventionally included or considered in value assessments. Eight others, which would be more novel in economic assessments, are defined and discussed: reduction in uncertainty, fear of contagion, insurance value, severity of disease, value of hope, real option value, equity, and scientific spillovers…*	https://doi.org/10.1016/j.jval.2017.12.007 Last accessed: January 29, 2020
Canadian Agency for Drugs and Technologies in Health (CADTH): Pan-Canadian Oncology Drug Review (pCODR)	From the pERC Deliberative Framework: *…The framework provides an outline of all the elements that should be considered by pERC during its review, and reinforces that no single element over-rides another, but rather that pERC uses the sum of all elements to formulate a funding recommendation…*	https://www.cadth.ca/sites/default/files/pcodr/The%20pCODR%20Expert%20Review%20Committee%20%28pERC%29/pcodr_perc_deliberative_frame.pdf Last accessed: January 29, 2020
Canadian Agency for Drugs and Technologies in Health (CADTH): Common Drug Review (CDR)	From the CDR Process in Brief: *[Canadian Drug Expert Committee] CDEC is an advisory body to CADTH that makes drug-related recommendations and provides drug-related advice through the CADTH CDR and therapeutic review processes. CDEC's recommendations and advice are provided to CADTH to inform the drug plans and a range of stakeholders. CDEC members' deliberations take into account patient group input, clinical studies demonstrating the safety, efficacy, and effectiveness of the drug, therapeutic advantages and disadvantages and cost and cost-effectiveness relative to current accepted therapy.*	https://www.cadth.ca/about-cadth/what-we-do/products-services/cdr/common-drug-review-submissions/process-in-brief Last accessed: January 29, 2020

Institut national d'excellence en santé et en services sociaux (INESSS)	From the document Evaluation of drugs - a change of approach: *Determining the advisability of listing a drug in light of the purpose of the public plan is therefore based on all the considerations necessary for assessing fairness and reasonableness. This involves weighing all the assessments of the six criteria examined, namely:* • *The identification of the unmet health need in the intended patient population and the determination of the level of this need;* • *The drug's ability to provide a clinical benefit;* • *The drug's efficiency;* • *Level of impact of the medical condition and the drug on the health of the general population;* • *The drug's level of burden on the system's budget;* • *The system's organizational ability to offer the drug.* *In addition to these considerations are other elements that may be useful for the deliberations, such as:* • *Information on social values and priorities, such as results of citizen and stakeholder consultations, which are published or implemented by INESSS. The quality and representativeness of the consultation mechanisms are assessed according to the relevant standards;* • *A targeted review of the literature on the ethical or social issues and concerns, whose quality is assessed according to the relevant methodological and theoretical standards as well;* • *The approval and listing decisions made by other authorities;* • *The impact on the persons covered by the private portion of the public plan.*	https://www.inesss.qc.ca/index.php?id=1237&L=1 Last accessed: January 30, 2020
National Institute for Health and Care Excellence (NICE)	From NICE's Principles document: *NICE's recommendations should not be based on evidence of costs and benefit alone. We must take into account other factors when developing our guidance. We also recognise that decisions about a person's care are often sensitive to their preferences. We support personalised care and shared decision-making and provide information and tools to help with this in and alongside our guidance and standards.*	https://www.nice.org.uk/about/who-we-are/our-principles#takeaccount Last accessed: January 30, 2020

Institute for Clinical and Economic Reviews (ICER)	From the ICER 2020-2023 Value Assessment Framework: ***Recognition that what matters to patients is not limited to measured "clinical" outcomes.*** *The inclusion of an explicit domain of value labeled "other benefits or disadvantages" demonstrates that the ICER value framework fully acknowledges that all too often what matters most to patients is poorly captured in the available clinical trial data. Sometimes this occurs because the clinical outcomes measured do not reflect what is most important to patients' day to day quality of life. Even when trials do capture the clinical outcomes that matter most to patients, there are other aspects of the treatment regimen that have a significant impact on the overall value of the treatment. This can be related to the complexity of the treatment regimen or the impact of care options on the ability of patients to return to work, on family and caregivers, on overall public health, or on other aspects of the healthcare system or society.[i] The ICER value framework identifies these "potential other benefits or disadvantages" as important elements of any overall judgment on long-term value for money, and all ICER reports have separate sections in which evidence and information pertaining to these elements are presented.* *i For further insight and examples a useful resource is the FasterCures and Avalere Health work on "Integrating the Patient Perspective into the Development of Value Frameworks" available at http://www.fastercures.org/assets/Uploads/value-coverage-framework-March-2016.pdf*	https://icer-review.org/material/2020-value-assessment-framework-final-framework/ Last accessed: January 30, 2020

Appendix B: HCV Case Study: Implications of proposed changes on curative therapies

When breakthrough drugs become available, price cannot be the only lever to ensure sustainable access. Health system sustainability is only possible with the early and continual involvement of all stakeholders, including drug companies, patients, payers, governments and providers.

Curative therapies like direct acting antivirals (DAAs) for HCV have disrupted health systems (see Figure). Unlike chronic therapies, which align payment to benefit over a long-term horizon, delivery of a curative therapy requires up-front costs and short-term budget impact for a long term or lifetime benefit. Learning from the DAA analogue, curative therapies can also result in a short-term accelerated bolus of demand as patients who are diagnosed and linked to care actively seek the cure in the immediate post launch period, further exacerbating the short-term budget impact associated with the long-term curative benefit.

Based on the draft PMPRB Guidelines, a curative therapy runs the risk of being deemed a Category I drug and would be subject to the most stringent sequence of price tests to determine the maximum allowable price.

Seeking to manage affordability of a cure with a lens strictly on the up-front cost of therapy is a model that fails to acknowledge or address the disruptive factors at play. Counterintuitively, this approach serves to disincentivize investment in the development of a cure in favour of investment in the development of chronic, long-term therapies.

Innovative models, such as those that amortize the cost of benefit over a longer time span, are more appropriate for application in a cure model both from the lens of affordability as well as health system value.

An innovative payment model of this nature is best defined directly with the payer to ensure that system needs and considerations are appropriately met and that value and affordability are better balanced.