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Dear Ms. Reynolds,

Re: Canada Gazette, Part I, Vol. 151, No. 48 – December 2, 2017

GSK recognizes the need to address prescription drug access, affordability, and appropriate prescribing for Canadians in a stable and predictable manner. We acknowledge the targeted savings of $8.6B (NPV) over 10 years, in pharmaceutical prices[1], and as a committed and relevant stakeholder we stand ready, with our colleagues, to join governments in achieving this goal while minimizing negative implications for Canadians.

Addressing the "maximum ceiling price" is only one way to realize some of these objectives and the PMPRB is only one player in a complex but balanced system. Consequently, a singularly focused effort by the PMPRB to significantly lower prices of patented medicines, without consideration for the potential impact to the broader ecosystem, is short-sighted. While GSK supports the need for modest PMPRB regulatory reform, we believe the proposed regulations are excessive and unnecessary. They compel PMPRB to take on a role well beyond its capability and are based on assumptions developed from limited and incomplete data. As a result, the proposed changes significantly underestimate the potential impact to stakeholders, patients, and our economy. A more fulsome discussion between relevant government departments and the pharmaceutical sector is warranted to ensure that we can help deliver these savings while maintaining a vibrant Biosciences sector in Canada.

Assessing the PMPRB's role in the current system:

The mandate of the PMPRB, as established in the Patent Act, is to protect the interests of Canadian consumers from excessively priced patented medicines and prevent the exploitation of intellectual property exclusivity by the patentees [2]. The PMPRB is the price regulator responsible for protecting consumers by establishing the maximum, non-excessive list price for patented medicines. Whereas, health technology assessment (HTA) bodies work within that price ceiling to try to identify the relative value new patented medicines bring to society. Finally, payers (through pCPA and other negotiation vehicles) are responsible for using this combined information, along with other tools, to make access decisions based on their willingness and ability to pay. The proposed regulatory changes cause the PMPRB to overstep its mandate and usurp the role of established players within the system, unnecessarily creating duplication, excessive regulatory burden, and an unpredictable operating environment.

Recommendation: GSK recommends the PMPRB stay within its mandate by focusing on developing a practical and predictable price ceiling using "objective" measures without relying on "subjective" measures which are the purview of HTA and payer bodies.

Addressing the rationale for change:

In launching the regulatory reform, former Minister of Health, the Honourable Jane Philpott indicated that it was necessary because:

> *"Our price reviews were set up in a way that the deal was it would be fair to Canadians, that the pharmaceutical companies that were being paid high prices would invest in research and development, ...In increasing ways we haven't actually seen that come true, and we have not continued to have a fair system* [3] .

Subsequently, the government's cost-benefit analysis (CBA) identified that the economic impact of the proposed changes will be minimal (with the exception of some lost revenue by the industry)[4].

In summary, the government believes that drug prices remain excessive, industry investment is minimal and the negative economic impact of the proposed reforms will be limited. However, these three positions are not supported by the facts.

Position #1 – Excessive Prices: The PMPRB reports that the prices of patented medicines in Canada have been increasing in the past several years beyond acceptable levels. However according to the PMPRB's own data:

- Canada ranked fourth in drug prices of the seven PMPRB7 countries [5] placing it at the median of the PMPRB7, exactly as targeted.
- Patented medicine prices have actually been remarkably stable over time. The annual rates of changes (%) of the Patented Medicines Price Index (PMPI) have not exceeded 0.9% since 1992 [5].
- Canadian prices have declined relative to Canada's regulatory comparators: In 2016, the average international median price was 25% higher than Canadian prices (Vs 18% in 2015 and 11% in 2001) [5].

Since PMPRB's introduction, the industry has consistently abided by the established price ceilings, leaving little room for the argument that our prices have been too high by the standards of the day. However, we acknowledge the changing landscape and the expressed interest, by government, to lower price ceilings.

Position #2 – Minimal Investment: The PMPRB reports that per the approved definition of R&D, the industry's contributions amount to 4.3% of total sales, [5] which is well below the 10% "promised" by the industry when the PMPRB was first established. Therefore, as the logic goes, if prices are high and investments are essentially non-existent, then lowering prices would be expected to have no further impact on investments.

Currently, PMPRB uses a domestic tax credit, Scientific Research and Experimental Design (SR&ED), as a proxy for R&D. The tax credit was a progressive measure when first introduced but global approaches to R&D have changed significantly since then and so too should the formula for calculating investment. The basis of the SR&ED tax credit is that local money spent on research toward a specific molecule is considered R&D, but other contributions such as foreign direct investments (FDIs), joint ventures, venture capital investments in Canadian firms, university endowments, and investments in research incubators, etc., are not recognized. This is despite the fact that, from an economic development perspective, the government continues to encourage these investments which have a positive impact on the Canadian economy.

Using a more inclusive methodology, Ernst and Young recently identified that the Canadian pharmaceutical industry (IMC member companies) contributes approximately 9.97% of total sales to R&D. Furthermore, the Biosciences sector is the third highest sector in research intensity (a measure of R&D/sales) in Canada behind Aerospace and Software/Computer services[6]. Overall, an estimate of Canadian pharmaceutical R&D investment of 4.3%, based exclusively on SR&ED, significantly underrepresents the real industry investment which leads to economic stimulation, innovative medicines, and better patient access.

Recommendation: GSK recommends the formula for calculating R&D investment be modernized to reflect all relevant investments and that it should monitored by ISED. This information can then be provided to PMPRB to satisfy their statutory reporting requirements.

Position #3 – Limited Economic Impact: The purpose of the CBA was to provide clarity about the economic impact to all stakeholders, of the proposed regulatory changes. In theory, having this information would permit more meaningful submissions during the subsequent consultation process. However, some flaws and critical omissions with this analysis (vague assumptions, no economic impact, no lost tax revenue, limited administrative burden) call into question its utility in assessing actual costs and therefore the potential benefits of the proposed regulations.

The most important of these is that while lost revenue to industry is estimated to be $8.6B over 10 years (NPV) or $1.2B/year, the analysis also includes an unacceptably broad sensitivity range ($6.4B - $24.9B)[4], which is exclusively dependent on how the guidelines are interpreted by PMPRB staff. At the high end, this represents close to a 30% loss in revenue and not only makes planning and predictability a significant challenge but clearly exposes the sector to a highly inappropriate and unacceptable financial impact. This will be expected to have significant negative impact on employment (direct and indirect), investments, and access to innovative medicines.

Addressing a collaborative approach:

We recognize that the responsibility for PMPRB regulatory reform resides with the Department of Health, but we submit that the innovative pharmaceutical industry should meet with both the Minister of Health and the Minister of Innovation, Science, and Economic Development (ISED). Given that the Biopharmaceutical sector is important to both healthcare and economic development, it is imperative that we engage in joint discussions to level set on the facts and data which underlie these significant reforms and better understand their broader impact. A common understanding of the situation and potential changes will facilitate the development of a robust and pragmatic solution which will address each Minister's respective mandate by generating significant savings, and improving access for Canadians, while preserving a viable innovative pharmaceutical sector in Canada.

Recommendation: GSK recommends the innovative pharmaceutical industry meet jointly with both the Minister of Health and the Minister of (ISED) to develop a common understanding of the problem and a robust and pragmatic solution

With respect to the proposed regulatory changes we fully support the submission made by IMC, however we want to avail ourselves of the opportunity to address three specific elements.

1. Schedule of Comparator Countries

Consistent with GSK's submission from June 2017, we recognize the perceived need to modify the basket to address sustainable drug costs. However, as identified in the PMPRB Guidelines Scoping Paper [7], this is just the first of several factors designed to drive the prices to or below the median of the OECD basket of countries.

A major concern with the proposed comparator countries is how/why they were chosen. In particular, the methodology for applying the criteria appears inconsistent, and no attempts have been made to be transparent in the decision-making process. Consequently, there are several cases where the criteria contradict the inclusion/exclusion of a comparator country and cause one to question the validity of the decision. Per the CG1 document, the inclusion criteria include:

i. Countries with medicine pricing policies that are well aligned with the consumer protection mandate of the PMPRB although there is no mention of how the alignment of policies were applied to any countries.

ii. Countries with reasonably comparable economic wealth as Canada, as measured by GDP per capita.
   - Both Norway (~$71k) and Switzerland (~$78k) have significantly higher GDP per capita compared to Canada (~$42k), yet Norway was included and Switzerland was actively excluded, with no rationale provided.
   - Both Spain (~$26.5k) and South Korea (~$27.5k) have significantly lower GDP per capita compared to Canada yet both were included in the basket

iii. Countries with similar medicine market size characteristics as Canada, such as population:
   - Japan which has a population (127 M), almost four times the size Canada (36 M), is included
   - Both Norway (5.2M) and Sweden (9.9M) which are much smaller than Canada are included but Switzerland (8.4M) is actively excluded.

Moving Canadian prices to the median of the OECD basket would have the initial effect of reducing the average Canadian to foreign price ratio by 22% [8], however Canada is a G10 nation and should act as such. Even changing the basket to G10 (minus the US) would lower the comparator price ratio by 18%, generating significant savings, while maintaining our prices consistent with similar economic powers [8].

Currently, Canada ranks 4th highest among OECD countries in introducing new medicines to its population. PMPRB reports that 61% of new drugs launched in the preceding five years were made available to Canadian patients. This contrasts with newly proposed comparator countries such as Australia (40%), Japan (38%), Netherlands (36%) and Korea (33%) [5]. Due to the extent of international price benchmarking between jurisdictions, the predictable business decision is to delay market entry (viewed as launch sequence by the Industry) in markets with lower published prices. Consequently, if Canadian published prices move significantly lower relative to global comparators, evidence predicts the delayed or reduced launch of new products in Canada [9-13]. Naturally, this will reduce prices but there are other implications. It will negatively impact patient access and future clinical trial activity in Canada, if the

standard of care is not available on market for use in these new trials. This is not an intentional decision by industry to withdraw investment, rather simply a predictable consequence of the global business reality. Currently Canada "punches well above its weight" in clinical trial activity, which is a benefit to the economy, health system and patients.

Recommendation: GSK recommends that the new regulations should use a basket of G10 countries to assess price excessiveness. Removing the U.S. from the G10 would still achieve a substantial decrease in published prices and yet maintain competitiveness amongst other global economic leaders.

2. Pharmacoeconomics

GSK recognizes the role for pharmacoeconomics (PE) in a value discussion with HTA bodies and payers, but rejects the notion that it should be used to help establish a regulated price ceiling. A comprehensive and compelling rationale of this position is provided in the IMC submission. However, we will touch briefly on a couple of key elements in the following section.

One of the baseline principles under which the PMPRB must fulfil its mandate is to provide "fair, consistent, and predictable application of the Act" [2]. To do that, the rules under which the PMPRB operate must utilize clear and objective ("bright line") measures. Additionally, according to Health Canada, the PMPRB should apply rules that are consistent with international best practices and provide predictability to stakeholders" [14]. GSK believes the proposed use of PE by PMPRB contravenes these guidelines and principles:

i. The use of QALYs to determine price ceilings is not an international best practice. We are aware of no other jurisdiction which currently uses QALYs to establish price ceilings. There are many jurisdictions where QALYs are used but, as in Canada today, they are used by HTA agencies to provide guidance and recommendations to payers. Other jurisdictions recognize these tools should play no role in regulating price ceilings.

ii. Cost Utility Analyses (CUAs) are anything but clear and objective as they are subject to significant interpretation and variation amongst and between health economists themselves. It is common for CUAs developed by different parties to vary by an order of magnitude. Clearly, they are designed to add a quantitative element to an otherwise qualitative discussion, but their development and interpretation remains subjective. Even within Canada, the use of the QALY is not consistent between our two HTA agencies. QALYs calculated by CADTH and INESSS can differ significantly. In other situations, INESSS has opted to de-emphasize the economic value of a drug in favour of therapeutic value. In either case, this creates a significant difference in the decisions rendered by the two bodies.

iii. As discussed above, the use of QALYs introduces a significant amount of subjectivity. Under the new rules a manufacturer will not be able to predict the assigned QALY from the PMPRB and therefore will not be able to forecast a compliant price until well after market approval. Currently the objective rules allow a manufacturer to forecast their prices well in advance of NOC with a reasonable level of certainty. This will have a significant impact on business planning, and the introduction of new products, associated investments and patient access.

Additionally, regulated price thresholds based on highly variable and subjective measures would lead to a risk of fewer innovative products being launched in Canada, ultimately impacting access. Specifically, this would affect the future viability of rare disease and oncology treatments in Canada. Access to these treatments would be restricted by rigid cost-effectiveness thresholds since their QALYs are generally quite high. Under the current system these products are often adopted by payers because they address clear unmet needs. Finally, there is no consensus on what is an acceptable QALY for these innovative drugs, increasing unpredictability even more.

Recommendation: GSK recommends that PE analyses play no role in the PMPRB regulated price ceiling process, rather its use should be restricted to HTA analyses. This is consistent with international best practice and would prevent the misuse of a highly subjective tool and the resulting negative consequences.

3. Transition

The Federal Government seeks to address the prices of patented medicines in a predictable and sustainable manner. GSK, along with our industry colleagues, remains committed to making that happen. As it currently stands, in ten months, significant new guidelines will be imposed on the sector driving prices down to an unknown extent, by an unknown process using unknown criteria. We recognize and are willing to work within the timelines to deliver these savings, but we believe that a measured approach to implementation is necessary to minimize disruption to patients and the market and to maximize the ability of PMPRB to successfully implement the changes.

Our current business is built on the rules in place, which we have adhered to for thirty years. As a business, we have developed our plans and evaluated our investments based on our understanding of the market and these rules. Therefore, any changes to the regulations should not disrupt the work established under the current regulations. According to the CG1 documents, the intention to include or not include existing medicines is vague and would give the PMPRB significant authority to broadly implement guidelines that could harm the Canadian Biosciences sector. This will create uncertainty for many beneficiaries of our ongoing and future investments, and administrative chaos for many payers due to the multitude of existing negotiated product listings which would be subject to change. Consequently, we respectfully submit that the proposed regulatory changes should only affect new products with a Canadian date of sale after January 1st 2019. For the affected products, we also submit the need for a transition period that sequentially implements elements of the new guidelines. This is to allow manufacturers to remain compliant with the new reporting burdens.

Recommendations: GSK strongly recommends that all regulatory changes only affect new products with a Canadian date of sale after January 1st 2019. For the affected products, a transition period should be built in to sequentially implement elements of the new guidelines.

<u>Summary</u>

In the document entitled "Protecting Canadians from Excessive Drug Prices" introduced by the Minister of Health in May of 2017 it is clearly stated that "to the extent possible, the PMPRB should apply "bright line" rules that are consistent with international best practices and provide predictability to stakeholders". We believe that the proposed extensive changes fail to meet the standards set by the

Minister given the excessive room for interpretation, the lack of adherence to international best practices, and limited predictability available to stakeholders.

We acknowledge the targeted savings of $8.6B (NPV) over 10 years, in pharmaceutical prices and are committed to working together with industry and government to deliver on that objective while also preserving the standards set by the Minister of Health. While it may appear to be outside the scope of these guidelines, it is in fact integral to them, that our industry be able to meet jointly with the key departments. GSK, along with the innovative medicines industry, is prepared to discuss specific solutions for how the Patented Medicine Regulation changes can be revised in a way that contributes to health system affordability, patient access to new medicines and innovation strategy objectives.

Sincerely,

Patricia Gauthier

Vice President of Public Affairs and Reimbursement

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