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February 14, 2018

Patented Medicines Consultations
Karen Reynolds, Executive Director
Office of Pharmaceuticals Management Strategies
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By e-mail: PMR-Consultations-RMB@hc-sc.gc.ca

**Re: Health Canada Consultation on Proposed Amendments to the Patented Medicines Regulations – Lilly Canada Submission**

Dear Ms. Reynolds,

Please find attached the response of Eli Lilly Canada Inc. (Lilly) to the Consultation on Proposed Amendments to the Patented Medicines Regulations.

Lilly stands with Canada's federal, provincial, and territorial governments in the belief that no Canadian should be without a necessary medicine because of affordability, and we support the commitment of the Government of Canada to ensure that Canadians most in need receive preferential support. We are committed to working alongside government to identify and deliver appropriate solutions for the affordability of medicines.

However, as outlined in our response to the Proposed Amendments, more time and attention is required by Health Canada in its consideration of changes to Canada's pricing regime for patented medicines to ensure they do not put at risk the ability of government-funded drug plans to secure best value for the vulnerable populations they have elected to cover. The potential impact of these proposed regulatory changes on access to new, innovative medicines also justifies a closer look at unintended consequences for the health outcomes of Canadians.

We would request that our response be reviewed in detail by Health Canada, and we would further request the opportunity to discuss our concerns in person with appropriate Health Canada staff. I may be reached directly at 416-699-7446 or e-mail: fischer_lauren@lilly.com.

Sincerely,

Lauren Fischer
Vice President, Corporate Affairs

FEBRUARY 14, 2018

# ELI LILLY CANADA SUBMISSION ON THE PROPOSED AMENDMENTS TO THE PATENTED MEDICINES REGULATIONS (CG-1)

ELI LILLY CANADA INC.
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## KEY POINTS

This document represents the Eli Lilly Canada Inc. (Lilly) response to the Proposed Amendments to the Patented Medicines Regulations ("Proposed Amendments"), as published in Canada Gazette, Part 1 on December 2, 2017. As a fundamental basis for our submission, Lilly asserts that the Health Canada analysis informing the Regulatory Impact Assessment Statement (RIAS) and Cost Benefit Analysis (CBA) lacks the depth and breadth required to guard against the unintended negative consequences that are certain to occur if the Proposed Amendments are adopted in present form. The analysis overestimates the benefits of the proposed regulatory amendments and underestimates the negative impact for public payers and the vulnerable populations they support, as well as Canadian patients more broadly, and life sciences stakeholders engaged in research and innovation.

This assertion regarding the Health Canada analysis is supported by strong counterevidence presented by PDCI[1] and Innovative Medicines Canada (IMC) in their respective submissions. The quality of the Health Canada analysis is of paramount concern, given the profound redefinition of excessive pricing represented in the Proposed Amendments. At the same time, given the broad discretion that the Proposed Amendments allow PMPRB in writing the Guidelines, it remains difficult to predict the exact range and scope of both intended and unintended impacts of the proposed regulatory changes. *This alone justifies a suspension of the CG-1 process, pending greater transparency and meaningful consultation with vested stakeholders.*

While many aspects of the Proposed Amendments are troubling, FIVE points are of the utmost concern:

**KEY POINT #1:** The impact of the Proposed Amendments to the calculation of excessive pricing will be a sharp lowering of the Canadian ceiling price that applies to all markets. This will force a redistribution to private insurers of a portion of the benefits that public payers currently receive through confidential discounts. This is at odds with the direction in the Prime Minister's Mandate Letters to his Cabinet: *"We are committed to provide more direct help to those who need it by giving less to those who do not."*

- The pCPA negotiates upwards of $1.3 billion annually in confidential discounts on behalf of public payers. Through pCPA, public payers are already achieving amongst the lowest prices in the world. These prices are only possible because of differential pricing between the public and private market. A lower transparent price across all markets would mean a smaller overall pool from which to draw public payer discounts.
- The manner of discount to the list price – *confidential* price reductions – mimics what occurs in other jurisdictions. Two recent studies of international payers, including Canada, concluded that payers are unwilling to give up the benefit they gain through confidentiality in order to benefit others payers.[2,3]
- While Health Canada and PMPRB have referred to differential pricing as "discriminatory pricing," the World Health Organization (WHO) suggests it could be seen as "equity pricing", used as an explicit government policy to remedy differential abilities to pay and, so, differential access to medicines. In this sense, the lowering of prices for private drug plans reduces equity for vulnerable populations served by public plans in Canada.

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[1] PDCI. Proposed Amendments to the Patented Medicines Regulations: A Critical Appraisal of the Cost-Benefit Analysis. January 2018. This analysis, commissioned by Innovative Medicines Canada (IMC), was conducted and reported independently by PDCI Market Access.

[2] Morgan SG, Volger S and AK Wagner. Payers' experiences with confidential pharmaceutical price discounts: A survey of public and statutory health systems in North America, Europe, and Australasia. Health Policy 2017.

[3] Vogler S. et al. How Can Pricing and Reimbursement Policies Improve Affordable Access to Medicines? Lessons Learned from European Countries. Appl Health Econ Health Policy (2017) 15:307–321.

- A growing number of private payers, including the recently formed Blue Cross pricing alliance, negotiate prices with manufacturers. In a 2015 PDCI survey, 41% of private payer respondents reported negotiations with pharmaceutical companies.

**KEY POINT #2:** In Canada, PE analysis, most typically the QALY/ICER, is used by HTA agencies and public budget holders to *inform* value-based reimbursement decisions and pricing negotiations. While it is a priority factor for public payers, it is not the sole input for their decision making. Used in price regulation, the QALY would be peremptory to public payers assigning their own nuanced assessment of value.

- Surprisingly, given the expressed intent by Health Canada to use the QALY threshold to set price ceilings for high-cost drugs with few or no comparators, this is exactly the category of drugs where the QALY appears to be *least useful*, given that the price of many drugs for rare disorders will never fall inside a threshold, yet almost universally, society places high value on the rule of rescue and, so, the funding of high-cost drugs in exceptional circumstances[4,5]. Public payers have identified these drugs to be their main pricing problem; pricing rules built around a QALY threshold are of little practical help.
- Ivacaftor (Kalydeco), is one example, where a positive reimbursement recommendation was provided by CADTH despite a manufacturer-submitted QALY of $700,000 and CADTH's own QALY range of approximately $2 million to $9 million[6].
- Even in the UK, where QALY thresholds are applied most rigidly, NICE emphasizes that other factors might affect the upper limit of willingness to pay. While strict economists decry allowing claims by "special pleaders" for exemptions[7], Sir Andrew Dillon, Chief Executive of NICE, says the balance of what is considered in determining value should *not* be left to economists: the correct decision, he says, emerges from a deliberative process.[8]
- This conclusion is in line with the one made in a study commissioned by Health Canada to evaluate options to enhance PMPRB's ceiling price regime. The authors concluded that: "*Value-based pricing is not a mechanism to lower prices that are unaffordable; neither is it a mechanism to contain costs... Value-based pricing requires a negotiation mechanism that is fair and transparent. This is best informed by deliberative processes that include all relevant experts and policy actors...Value-based pricing must involve purchasers...Finally, value-based pricing cannot be simply reduced to a mathematical algorithm.*"[9] It is evident in the Proposed Amendments that Health Canada did not heed this advice.
- Finally, in a diligent assessment of whether or not to apply the QALY in France, the National Authority for Health conducted a thorough assessment of global methods for determining QALY thresholds and concluded that, in most cases, there was no obvious or explicit rationale for the choice of a particular threshold level. Further, there was a wide range of explicit or implicit thresholds across countries of similar economic backgrounds.

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[4] Carrera P and MJ J. IJzerman (2016) Are current ICER thresholds outdated? Valuing medicines in the era of personalized healthcare,Expert Review of Pharmacoeconomics & Outcomes Research, 16:4, 435-437.

[5] Vogler et al. ibid.

[6] CADTH. Final CDR Recommendation IVACAFTOR (Kalydeco). February 20, 2013.

[7] McCabe C, Claxton K, Culyer AJ. The NICE cost-effectiveness threshold: what it is and what that means. Pharmacoeconomics. 2008;26(9):733-44.

[8] Dillon A. Carrying NICE over the threshold. National Institute of Clinical Excellence. February 19, 2015.

[9] Husereau D. and Jacobs P. Investigation and analysis of options to enhance Canada's patented medicine price ceiling regulatory regime. Edmonton AB: Institute of Health Economics, 2013.

**KEY POINT #3**: It is inappropriate to apply a single price threshold across all markets – private and public – each with different motivations and abilities/willingness to pay. Under the federated system, each P/T is responsible under statute for allocating budgetary resources to its priorities, based on affordability and willingness to pay. Private payers, with entirely different populations and motivations for coverage, add an additional and untenable complication: there is no objective "bright line" that anchors the disparate markets together as one.

- The differential assessment of ability to pay and affordability across private and public payers is made plain by the difference in the number and type of products listed by each one. While public plans typically list 4,000-4,200 DINs, private plans cover 7,200-9,000 DINs.
- In part, the difference occurs because private payers operate in a highly-competitive marketplace where individual insurers seek an edge over competitors through enhanced product offerings. Drug benefits may be a loss leader to gain the life insurance and pension business of employers.
- Private payers recoup their costs through premiums; public payers operate under fixed budgets. In 2011, CHLIA reported $34.4B in health premiums vs. $25.6B in payouts (a surplus of $8.8B) and in 2016, $40.9B in premiums vs. $32.5B in payouts (a surplus of $8.4B). The gap between revenue and payout has not changed appreciably in more than 10 years.

**KEY POINT #4:** The Proposed Amendments would impose a complex regime based on subjective price review factors that does not allow businesses to predict allowable ceiling prices prior to launch or over time, post-launch. As such, it moves away from the PMPRB's own stated principles of regulatory fairness, transparency, openness, and predictability.

- The current PMPRB regime relies on objective, verifiable information in price reviews, namely international and Canadian list prices. As a result, patentees can reasonably estimate an allowable price ceiling at least a year in advance of drug launch, and plan launch resourcing accordingly. This regime has been successful in achieving voluntary compliance, with a very low level of investigations and hearings.
- Under the new regime that would be created by the Proposed Amendments, it would be impossible for a patentee to predict its price ceiling prior to launch, or even to know how the allowable ceiling may change over time. **NB: It cannot be appropriate for a regulatory regime to deny companies this most basic requirement for the normal conduct of its business operations.**
- For example, the CADTH PE analysis is not available until after a new drug launch; the ICER value is built off many assumptions and is generally given as a range of values. Market size forecasts are also based on assumptions; moreover, they are subject to fluctuations, not all of which could be reasonably predicted, much less controlled, by the manufacturer – e.g., if a competitor is pulled off the market for safety reasons. And, clearly, a manufacturer does not have insight into rebates paid by competitors, and cannot therefore predict the outcome of a therapeutic class comparison that may reference (inappropriately so, we believe) this confidential business information.
- Price tests associated with the three new "economic" factors would serve to exert additional downward pressure, bringing price ceilings below the level established via the application of the proposed new Schedule of reference countries. It is nowhere explained by Health Canada why new pricing factors would be needed, given that the Schedule has already been engineered to achieve government's stated objective of prices at the targeted level relative to international prices (i.e. OECD median). The need to inject additional complexity and uncertainty for manufacturers has not been justified.

**KEY POINT #5**: Confidential pricing does not relate to excessive pricing thresholds. Rather, it is related to marketplace activities which occur <u>below</u> those thresholds and, so, should be of no consequence to PMPRB in determining excessive pricing. In fact, the use of third party rebate information would result in a fundamental shift in the role of the PMPRB from making a determination of excessive price to one of imposing price control, with little connection to either the existing pricing factors or the proposed new economic ones. Given the murkiness surrounding the purpose and use of this confidential information by PMPRB, Lilly is opposed to reporting it.

- The intent to use the information collected about rebates in the manner suggested by PMPRB, to lower prices of new comparator products, presents a high risk for breach of confidentiality to a manufacturer's competitors, for example through back calculation.
- Furthermore, requiring manufacturers to disclose confidential rebates to the PMPRB is potentially anti-competitive. We are being asked to release information that we wouldn't ordinarily disclose. If the PMPRB uses this information to force a low price on a competitor as a result of receiving this competitively-sensitive information, it may have an anti-competitive effect.
- In addition, a competitor is now seized with competitively-sensitive pricing information that they would not ordinarily have *but for the amendments to the Regulations which require its disclosure*.
- The reporting of third party rebates also presents multiple operational problems that are administratively burdensome for companies and PMPRB. For example, while internal rebate accruals are calculated monthly, payers invoice on a variety of schedules (quarterly, semi-annually or annually), with varying lag times in the preparation of invoices. Invoicing schedules would inevitably cross PMPRB reporting periods, creating rebate calculation challenges. Additionally, the data supplied in invoices are sometimes found to be inaccurate, resulting in back-and-forth communication to resolve the issue that, in Lilly's experience, can last more than a year after the original invoice has been issued.

Finally, (and ironically, given government's objective to lower prices to the median OECD level) including confidential rebates (i.e., pricing rebates) in calculating the Canadian price will make apples-to-apples comparison with other countries impossible. Purchase rebates are used in all developed countries and they are always confidential. [10]

[10] Critchley W and Owens RC. The Unkindest Cut: How a new plan for slashing drug prices could harm the prosperity and health of Canadians. MLI. February 2018.

## Regulatory Impact Analysis Statement (RIAS) and Cost Benefit Analysis (CBA) – Inaccuracies and Errors

Based on the information and statements contained in the RIAS and the CBA, it is clear that Health Canada has not carried out an in-depth impact assessment of the proposals, most notably the potential unintended negative consequences for public payers, patients, the life sciences cluster, and Canada's research and clinical trial infrastructure across the country.

### The Impact on Public Drug Plans

Innovative Medicines Canada (IMC) has provided a comprehensive accounting of the inaccuracies and errors found in the RIAS and the CBA. Of importance from Lilly's perspective, Health Canada has underestimated the benefits already provided to Canada's public payers and, in doing so, has overestimated the size of prospective benefits from the Proposed Amendments to the regulations. This is because the benefits that would accrue to the private payers through a drop in the ceiling price are not "new" dollars, but rather represent a transfer in benefit that public payers currently receive through the upwards of $1.3 billion annually in confidential rebates negotiated by the pCPA. The drop in ceiling price across all markets would mean a smaller pool overall from which to draw these rebates for public payers.

In addition, some public payers, by virtue of their drug plan design, would incur additional disbenefits. Saskatchewan, British Columbia and Manitoba would be additionally penalized because of their universal drug plan designs and, so, higher share of high-cost drugs absorbed by the public plans. The federal Non-Insured Health Benefits plan (NIHB) would experience the greatest disbenefit because it offers first-dollar coverage to its beneficiaries.

In sum, the current system affords Canada's public payers, which represent Canada's most vulnerable populations, prices amongst the lowest in the world, with the size of the rebates related to the degree of differential pricing between the public and private market. In distributing the largest benefit to those who need it most, the current system of differential pricing is aligned with other government programs.

This system of targeting preferential benefit based on need is the same approach that is applied in many government programs, such as: the federal Child Tax Credit and Senior's Old Age Pension Income Supplement; Ontario's Postsecondary Tuition Subsidy Program; and Alberta's income-tested Low-Equity Loan Program for seniors.

The Proposed Amendments put at risk the ability public drug plans to secure the best value for the vulnerable populations they cover.

## The Role of the PMPRB and Excessive Pricing

Patents exist to reward innovation. In Canada, the *Patent Act* affirms the inherent value of innovation to society by awarding a period of exclusivity – a statutory monopoly – to the patent holder. In creating the PMPRB with a mandate to ensure that prices charged by patentees for their innovation are not excessive, it also recognizes a potential for an abuse of monopoly power that could occur without a countervailing check of those rights. This duality – fostering innovation while providing consumer protection from excessive pricing – sets the context for establishing the Patented Medicines Regulations.

The Proposed Amendments to the Regulations would result in a significant shift in the interpretation of "excessive pricing" and would mark a fundamental departure from the intent of the *Patent Act* in terms of abuse of monopoly power. Of concern, the Proposed Amendments shift the interpretation of "excessive" away from the *relative therapeutic contribution of a new medicine* – the fundamental basis

for assessing innovation – to criteria tied to affordability and willingness to pay – the exact purview of payers.

Given the evolution in Canada's Health Technology Assessment (HTA) and reimbursement systems, which appropriately apply these measures at the payer (i.e., budget holder) level, the rationale for the shift by PMPRB is unclear. Funders of medicines, including public and private insurance plans, assess value and their ability and willingness to pay in making decisions. Moreover, they have developed robust, sophisticated systems to do so, including the HTA programs delivered by the Canadian Agency for Drugs and Technologies in Health (CADTH) and the Institut national d'excellence en santé et en services sociaux (INESSS) and the price negotiation processes used by all F/P/T public drug plans and, more recently private insurers. Since payers fulfill these functions, for which they are, in fact, appropriately accountable, it is unclear what benefit intervention by PMPRB into this space would add.

**Determining the Non-Excessive Price**

***Therapeutic Value***

The paramount feature in determining the ceiling price of an innovative medicine must be the level of therapeutic benefit it provides *relative to comparators* in its therapeutic class: the higher the benefit, the higher the potential price. Using relative therapeutic value as the basis for price determinations is consistent with the innovation mandate of the *Patent Act*. It is also consistent with the majority of jurisdictions across the globe where it is the primary factor in determining value.

In this context, the PMPRB Board's own categorical rejection of economic interpretations of value tied to "therapeutic class" in the recent hearing in the matter of Soliris, is important. The Board made plain that medicines were to be compared to those in a relevant *therapeutic class,* grounded in clinical factors and *not* economic ones. The PMPRB failed this first test in its proposed rebranding of excessive pricing.

**Proposed Economic Factors**

**Pharmacoeconomic Value**

In Canada, PE analyses represent one among many considerations that inform assessment of value in drug funding decisions, albeit a highly significant one. CDR, pCODR, and INESSS all supplement the ICER with additional value considerations – though each with somewhat different ones - to deliver a robust assessment of value. This approach allows for additional value ascribed by payers and their HTA agents through a thoughtful, broad-based, deliberative process, similar to what Husereau and Jacobs[11] described in their work for Health Canada advising on a new regulatory regime for PMPRB. The use of PE analysis in the establishment of a price ceiling would act to reduce the autonomy and rightful authority of payers to complete their own assessment. In this determination – and particularly for high-cost drugs with few or no comparators, the QALY serves as a base, rather than a ceiling.

As a final important point about cost-effectiveness (CE) and in particular a single QALY threshold, it would be prohibitively complicated and inappropriate to operationalize it across public and private markets, given the very different relevant inputs. As stated by Great-West Life, one of the larger private insurers in Canada, "CADTH assessments consider the needs and perspectives of the health care system and not the impact of drug products on productivity-related costs, such as absence, disability and presenteeism that matter to employers." They also do not consider a key factor that distinguishes private insurers from public payers: the drive for a competitive edge over other insurers, which may affect willingness to pay.

[11] Husereau and Jacobs, ibid.

***Limitations Inherent to the QALY***

While the RIAS states that cost-utility analyses are a "gold standard" approach to considering the economic value of new medicines, there is a large body of literature documenting the subjectivity of inputs into the QALY; assessments are based on a multitude of assumptions and small adjustments to any of the assumptions can cause large shifts in the QALY result.[12,13,14] Simply put, the QALY is not the bright line that the PMPRB is seeking.

QALYs have been shown not to capture all dimensions of health benefits.[15] This key limitation was raised by stakeholders in the Spring 2017 consultation conducted by Health Canada. QALYs do not appropriately measure interventions that reduce short term-disabilities and many undesirable health states and difficult conditions for patients (e.g. nausea, vomiting, pain associated with use of contrast agents, postoperative recovery, etc.). A QALY framework has been demonstrated to present risks that the clinical benefits of interventions for a pediatric population will be underestimated, will result in artificially high ICERs, and could adversely impact innovation and the number of products that come to market for these populations.[16]

Similarly, ICERs are not a relevant metric for drugs for palliative care and rare diseases. Most of the orphan drugs appraised to date have QALYs well above the generally 'accepted' thresholds and would not be reimbursed according to conventional criteria.[17] QALYs do not recognize that society values 'the rule of rescue,' meaning there is significant importance placed on rescuing people who need help. This is especially true for serious conditions, where breakthrough medications may be costly, but the burden of illness is high and there are limited treatment alternatives. Ironically, these are the very medications that Health Canada, through the *Scoping Paper*, has targeted for the use of ICER in determining a ceiling price.

Furthermore, ICERs are greatly impacted by the methods used, such as the time horizon and clinical comparators selected. Although there are guidelines on conducting economic analyses, there can be high variability in assumptions between individuals and this may have serious consequences in the final analysis.

***Limitations of Maximum and/or Fixed Cost per QALY Threshold in Canada***

The RIAS also notes that the cost-utility analyses would enable the PMPRB to "consider the introduction of the concept of a maximum cost per QALY threshold in Canada." However, it is important to emphasize that very few countries have identified fixed QALY thresholds that are rigidly applied, and there is not a single instance where they are used for price setting.

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[12] Pettitt DA, Raza S, Naughton B. et al. The Limitations of QALY: A Literature Review. J Stem Cell Res Ther. 2016.6;4.

[13]Garau M, Shah KK, Mason AR, et al.Using QALYs in cancer. Pharmacoeconomics 2011.29: 673-685

[14] Husereau D and Jacobs P. Investigation and analysis of options to enhance Canada's patented medicines Price Ceiling Regulatory Regime. Edmonton: Institute of Health Economics. 2013

[15] Knapp M. "Economic outcomes and levers: impacts for individuals and society" *Int Psychogeriatr.* 2007 Jun; 19(3):483-95, https://www.ncbi.nlm.nih.gov/pubmed/17391570.

[16] Quality-adjusted life-years lack quality in pediatric care: a critical review of published cost-utility studies in child health. *Pediatrics* 115(5):e600-614.

[17] Drummond M, Barbieri M, Cook J, Glick HA, Lis J, Malik F, Reed SD, Rutten F, Sculpher M, Severens J: "Transferability of economic evaluations across jurisdictions: ISPOR good research practices task force report." *Value in Health*. 2009, 12 (4): 409-418.

To reiterate from earlier in this document, the Canadian health care system is highly decentralized across private and public payers – each with different motivations and abilities/willingness to pay.

- The differential assessment of ability to pay and affordability across private and public payers is made plain by the difference in the number and type of products listed by each one. While public plans typically list 4,000-4,200 DINs, private plans cover 7,200-9,000 DINs.
- In part, the difference occurs because private payers operate in a highly competitive marketplace where individual insurers seek an edge over competitors through enhanced product offerings. Drug benefits may be a loss leader to gain the life insurance and pension business of employers. Public payers, on the other hand, must make trade-offs within restricted and fixed budgets.

**A single representative QALY should therefore not be used to assess value for all Canadians. A more appropriate way to manage the diversity across payers is through payer negotiations with manufacturers. Both public payers and private payers currently engage in negotiating conditions for coverage and confidential rebates; all public payers and private insurers engage in additional cost containment programs.**

The rigid application of a QALY threshold by NICE has come under public criticism, as it has resulted in NICE refusing to fund life-extending cancer drugs that exceed the QALY thresholds. As a result of the sharp threshold, patients in the UK have more restricted access to oncology medications than in other EU counties, which has contributed to poorer patient outcomes:

- A study of over 20 million cancer patients across the EU found survival in the UK for certain cancers to be worse than in every country in Western Europe; only patients in Eastern Europe fared worse;
- In 9 out of 10 cancers, UK patients had worse 5-year survival rates than the European average;
- UK survival rates for breast cancer and colon cancer are a decade behind other western European countries, including France, Germany, and Sweden.

**The Size of the Market in Canada and Countries Other than Canada**

The size of the market speaks to affordability – it implies a fair price is one at which all eligible patients can be treated without it being considered an excessive spend or being "unaffordable." Fairness is a decision that belongs to budget holders: there is no empiric test of affordability and determining what is affordable will depend on what budget is available in individual public plans as well as what private plans and out-of-pocket consumers are willing to pay. Determining an arbitrary threshold for affordability has ramifications for all payers and stakeholders that are beyond the purview of the PMPRB.

The previous notwithstanding, the introduction of market size as an economic factor presents significant operational challenges that render it impractical for general application. Before going to market, patentees rely upon available statistics and information on the prevalence (number of people with a disease) in a given country and incidence (estimated number of new cases each year) to develop a sales forecast. In many cases, robust and/or reliable epidemiologic information in not readily available. This is further complicated with the introduction of new medicines into a market, or for new indications, where there is often no publicly available information from which to determine potential market size.

Finally, this tool would introduce inappropriate bias, as it would be used uniquely to lower price. If, for example, public drug plan access were not achieved, resulting in lower than expected market size, it would be impossible from a practical standpoint to raise a price that had already been established in the market.

**Gross Domestic Product (GDP) and GDP Per Capita**

As noted in the RIAS, GDP per capita would be used as a "proxy for buying power at the level of the individual" and would "provide the PMPRB with measures of ability to pay for medicines at the individual and national level." As per the *Patent Act*, affordability, as measured by ability and willingness to pay, is not the mandate of the PMPRB. Further, GDP per capita is not a measure of personal income, and therefore not reflective of an individual's ability and willingness to pay. To reiterate the above, affordability and willingness to pay are highly variable constructs; the use of a single measure, such as GDP per capita, in the determination of whether a medicine's price is non-excessive, is incapable of adequately reflecting these individual, jurisdictional and market differences.

GDP per capita also does not take into account income distribution variations within a country. In the RIAS, here is no indication of how the PMPRB, as a national regulator, would manage and account for the variability in GDP and per capita GDP across the country, and amongst public and private payers, employers and individuals residents. For example, in 2016, Alberta's Real GDP declined by 3.8% and Saskatchewan's dropped by 1.0%. In contrast, Ontario was a growth leader, with a real GDP increase of 3.0%. Managing the consequences of these fluctuations can only be done at the P/T level: neither Health Canada nor the PMPRB is a budget holder for pharmaceutical spend in each of the P/T jurisdictions.

While GDP and GDP per capita are not appropriate economic factors for use in the determination of non-excessive price, per capita GDP could be useful when determining which countries Health Canada should include in its Schedule of Countries for International Price Comparisons, because of its ability to show countries' relative performance in terms or productivity and economic output.

**New Comparator Basket – PMPRB 12**

The Proposed Amendments include an updated list of countries set out in the Schedule used by the PMPRB for international price comparisons. The selection criteria for the updated Schedule noted in the RIAS includes:

- Pricing policies "aligned with the consumer protection mandate of the PMPRB ... such as ... national pricing containment measures to protect consumers from high medicine prices."
- Reasonably comparable economic wealth as Canada, "such as ... measured by GDP per capita."
- Similar medicine market size characteristics as Canada, "such as population, consumption, revenues and market entry of new products."

Based on the criteria noted by Health Canada in the RIAS, the table below has been compiled to reflect the proposed Schedule, as well as Switzerland and the United States, which have been removed as part of the Proposed Amendments.

| Country | Price Regulation, Cost Containment Measures | GDP per capita[18] (2016, USD, current prices, current PPP) | Population Size, thousands (2015)[19] | New Medicine Launches[20] | Health Expenditures as a % of GDP 2016[21] |
|---|---|---|---|---|---|
| **Canada** | **National price regulation through PMPRB** | **51.7** | **35,950** | **61%** | **10.6** |
| Australia (N) | National purchasing and pricing negotiations through Pharmaceutical Benefits Scheme | 56.2 | 23,800 | 40% | 9.6 |
| Belgium (N) | Pricing, reimbursement and access controlled by the national government. Products with added therapeutic value can obtain a price premium over standard of care. | 73.1 | 11,288 | 45% | 10.4 |
| France | Pricing, reimbursement and access controlled by the national government. Price negotiated with economic committee after innovation and value assessments by separate committees | 66.7 | 64,457 | 45% | 11.0 |
| Germany | Price negotiated by national payer following assessments about added therapeutic benefit by Federal Joint Committee (G-BA) and IQWiG. | 59.9 | 81,708 | 69% | 11.3 |
| Italy | Price controlled by national payer, the Italian Medicines Agency (AIFA). Decisions and negotiations based on innovation ratings and HTA results. | 54.4 | 59,504 | 57% | 8.9 |
| Japan (N) | National price negotiated through Ministry of Health | 46.8 | 129,975 | 38% | 10.9 |

[18] http://stats.oecd.org/index.aspx?DataSetCode=PDB_LV

[19] https://esa.un.org/unpd/wpp/Download/Standard/Population/

[20] *Meds Entry Watch, 2015,* Patented Medicines Prices Review Board. April 2017

[21] https://data.oecd.org/healthres/health-spending.htm

| Country | Price Regulation, Cost Containment Measures | GDP per capita[18] (2016, USD, current prices, current PPP) | Population Size, thousands (2015)[19] | New Medicine Launches[20] | Health Expenditures as a % of GDP 2016[21] |
|---|---|---|---|---|---|
| | Labor and Welfare (MHLW). | | | | |
| Netherlands (N) | Pricing primarily controlled by government. Specialty products face risk-based HTA. | 67.3 | 16,938 | 36% | 10.5 |
| Norway (N) | Reimbursement decisions are made by the Norwegian medicines Agency (NoMa) based on budget impact assessments | 77.9 | 5,200 | 56% | 10.5 |
| South Korea (N) | Price negotiated by national health insurance (NHIS) based on HTA and reference price factors selecting lowest global prices | 27.1[22] | 51,010[23] | 33% | 7.7 |
| Spain (N) | Price controlled by national government, with some regional involvement, based on innovation level and budget impact. | 52.2 | 46,398 | 52% | 9.0 |
| Sweden | Pricing decisions are made by the TLV expert Board. | 61.0 | 9,764 | 60% | 11.0 |
| United Kingdom | Pharmaceutical Price Regulation Scheme (PPRS), a voluntary agreement between manufacturers and Department of Health | 52.7 | 65,397 | 62% | 9.7 |
| Switzerland (R) | Federal Office of Public Health regulates price based on international price comparison and value for money against comparator | 67.8 | 8,320 | 49% | 12.4 |

[22] Source: World Bank
[23] Source: World Bank

| Country | Price Regulation, Cost Containment Measures | GDP per capita[18] (2016, USD, current prices, current PPP) | Population Size, thousands (2015)[19] | New Medicine Launches[20] | Health Expenditures as a % of GDP 2016[21] |
|---|---|---|---|---|---|
| United States (R) | Free pricing with confidential negotiated discounts and rebates. Mandatory discounts in federal programs vary. | 69.6 | 319,929 | 84% | 17.2 |

*(N) – New countries, (R) – Removed countries

If one considers the above, it is not clear, for example, why Switzerland has been removed from the Schedule; it is similar to Canada in economic standing, and its price regulation system applies standards, approaches and objectives similar to the PMPRB.[24] Further, it is of concern that five (5) of the seven (7) countries being proposed for inclusion in the updated Schedule sit at or below the OECD median of new medicine launches.

While not explicitly stated within the RIAS, the updated Schedule demonstrates Health Canada's intent to ensure the comparator countries included in the updated Schedule will serve to lower prices in Canada to the OECD median price ratio (a 22% reduction, in aggregate). The full set of criteria used and the relative weighting afforded to each criteria, remains unclear in the selection of the new Schedule; no detailed analysis has been provided by Health Canada in either the RIAS or CBA.

Price tests associated with the new economic factors would serve to exert *additional* downward pressure on price below the level achieved via a new Schedule. Nowhere in the RIAS or CBA, does Health Canada explain why new economic factors would be required, given that the proposed PMPRB12 Schedule has been engineered to achieve government's stated objective of ensuring Canadian prices are at the OECD median level.

More importantly, the aim (or intent) to lower pricing for patented medicines in Canada to the OECD median is highly concerning and inappropriate. Canadians place a high value on health care. Expenditure on health labour force for physicians and nurses ranks in line with Canada's ranking for spend on patented medicines. Canadians are not striving to be at the OECD median, and this is evident in Canada's health care spend across the board. What is missing from a set of relevant criteria is the degree to which a country values health care. For Canada, the health care system stands in the top three elements that Canadians report as fundamental to their identity as Canadians. It seems reasonable, then, that in revising the Schedule, Health Canada incorporate countries similar to Canada in terms of their valuation of health care, as evidenced by expenditures in health care. A recent analysis of foreign-to-Canadian price ratios vs. health expenditures as % of GDP demonstrates a moderate relationship between drug prices and health expenditures[25].

[24] https://www.baerkarrer.ch/publications/BK_Briefing_New_Regulations_Regarding_Drug_Pricing.pdf
[25] PMPRB 2016 Annual Report, World Bank.

**Reporting of Indirect Price Adjustments, Including Third Party Rebates**

The Proposed Amendments contain measures that expand the scope of the PMPRB to require the reporting of indirect price adjustments, such as third-party rebates paid under confidential product listing agreements (PLAs) with F/P/T governments' public drug plans. Given that the mandate of the PMPRB under the *Patent Act* is to protect Canadians against excessive pricing, it is unclear why the PMPRB, as a regulator of prices, should have access to price adjustments, including third-party rebates (which take a price below the ceiling price), and use this information in the determination of whether a price is excessive. In fact, the use of third party rebate information would result in a fundamental shift in the role of the PMPRB from making a determination of excessive price to one of imposing pure price control.

Moreover, Lilly believes that requiring manufacturers to disclose confidential rebates to the PMPRB is potentially anti-competitive. We are being asked to disclose information that we wouldn't ordinarily disclose; if the PMPRB uses this information to force a low price on a competitor as a result of receiving this competitively-sensitive information, it may have an anti-competitive effect. In addition, the competitor would be seized with sensitive pricing information that they would not ordinarily have *but for* the amendments to the Regulations.

The appropriateness of the Proposed Amendments aside, the use of third party rebates to determine a ceiling price would create uncertainty for manufacturers launching new medicines in Canada. As proposed, the PMPRB would use confidential third party rebate information to determine the price ceiling for new drug entrants; this is information that a launching manufacturer is not privy to, making it impossible for a patentee to predict the allowable price ceiling.

The reporting of third party rebates present multiple operational problems that render its use in price regulation highly impractical and administratively burdensome. For example, while internal rebate accruals are calculated monthly, payers invoice on a variety of schedules (quarterly, semi-annually or annually), with varying lag times in the preparation of invoices. Invoicing schedules would inevitably cross PMPRB reporting periods, creating rebate calculation challenges. Additionally, the data supplied in invoices are sometimes found to be inaccurate, resulting in back-and-forth communication to resolve the issue that, in Lilly's experience, can last more than a year after the original invoice has been issued. We have also encountered data reliability issues, particularly in the oncology space, where internal rebate accruals are based on utilization and no data are available until the invoice is issued. A variety of PLA structures are in place in Canada (e.g. tiers, hard caps, soft caps and indication-based pricing), which result in changes to the net price of a product from one year to the next. As the prevalence of outcomes-based pricing increases, there would be further challenges, as rebates and net prices would fluctuate based on measured patient outcomes.

**Impacts of the Proposed Regulations Amending the Patented Medicines Regulations**

Based on the information and assertions contained in the RIAS and the CBA, it is clear that Health Canada has not carried out an accurate or in-depth impact assessment of the Proposed Amendments, most notably the negative unintended consequences for public payers, patients, the life sciences sector, research and clinical trial infrastructure across the country, and on Canada's international trade obligations.

**Access to New Innovative Medicines for Canadians**

Access to new medicines benefits Canadians. In the RIAS, Health Canada notes feedback received from patient organizations that "patient access to medicines in a primary concern." While the RIAS notes that the intent of the Proposed Amendments is to lower prices for patented medicines, there is no assessment in either the RIAS or the CBA related to the impact that a lowering of prices would have on the availability of new medicines in Canada. It appears there is an underlying assumption that Canada would see the same level of access to new medicines that it presently enjoys under the current pricing regime. What this fails to acknowledge, however, is that a country's pharmaceutical pricing policy and approach to determining the price of patented medicines is a key factor taken into consideration by manufacturers when they are making decisions on when – or if – to launch a new medicine in a jurisdiction.

Canada's current pricing regime - consisting of the PMPRB, national and regional HTA bodies and listing negotiations by public and private payers - has established a balance that protects Canadians from high prices while allowing manufacturers to launch more new medicines in Canada, and in most cases, earlier than in many other international markets. A recent study by PMPRB shows that Canada currently has one of the highest shares of new medicines launched in the world (at 61% vs. 45% OECD median, 45% in France, 40% in Australia, and 33% in Korea; only 13% of new medicines launched in New Zealand). Further, in terms of launch timing for all new active substances, only the United States, Germany, the United Kingdom, and Sweden launched ahead of Canada.[26] For Lilly, based on its particular portfolio of products, Canada typically launches in the "first wave" with leading markets, such as the United States.

In countries where pricing reforms have significantly lowered the price of patented medicines, there have been delays in the launch of new medicines, and in many cases, new medicines were not launched at all. There is evidence that shows that drug launches are less likely to follow launch in a low-price country with launch in a high-price country. Moreover, countries with lower expected prices or smaller expected market size due to cost containment measures, technology assessment, and other pricing and reimbursement hurdles have fewer launches.[27,28,29,30,31] The negative impact of pricing reforms on access to new medicines is clear; and most notably in the Schedule of countries that Health Canada has selected for international price comparison:

- **Australia:** Australia has implemented a series of cost-containment measures. For example, in 2015, it was announced that the price of all products listed on the Pharmaceutical Benefits Scheme (PBS) would be arbitrarily reduced by 5% after five years of listing, and applied retroactively to medicines already assessed as being cost-effective by the PBS review process. An independent review of Australia's Therapeutic Goods Administration's (TGA) medicines and

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[26] *Meds Entry Watch, 2015,* Patented Medicines Prices Review Board. April 2017

[27] I Cockburn, J Lanjouw and M Schankerman, Patents and the global diffusion of new drugs *Am Econ Rev*, 106, 136-164 (2016).

[28] Danzon, Patricia & W Mulcahy, Andrew & Towse, Adrian. Pharmaceutical Pricing in Emerging Markets: Effects of Income, Competition, and Procurement. *Health economics*. 24.10.1002/hec.3013. (2015).

[29] P.M. Danzon, and M. F. Furukawa. International Price and Availability of Pharmaceuticals. *Health Affairs*, January 2008.

[30] Margaret K. Kyle. Pharmaceutical Price Controls and Entry Strategies. *Review of Economics and Statistics*; Volume 89, Issue 1.p.88-99. February 07, 2007.

[31] Danzon PM, Wang YR, Wang L. The impact of price regulation on the launch delay of new drugs--evidence from twenty-five major markets in the 1990s. *Health Econ*. 2005 Mar; 14(3):269-92. 2005.

medical devices regulatory framework found that Australians wait up to 15 months longer to access new breakthrough drugs than in the United States or Europe as a result of launch delays.[32]

- **Germany:** With the adoption of Germany's Pharmaceutical Market Restructuring Act (AMNOG) in 2011, new medicines are subject to a rigid early benefits assessment, where prices have been lowered through forced negotiation or through therapeutic price referencing. The impact of AMNOG on the access to new medicines has been significant: 23% of medicines (40 products) that received approval from the European Medicines Agency (EMA) were not launched in Germany between 2010 and 2015. This is compared to just 5% (8 products) prior to AMNOG coming into force, between 2006 and 2010.[33]

- **Japan:** Prior to 2010, Japan had a highly selective review process that manufacturers had to undergo for new medicines to qualify for reimbursement, and utilized a drug reimbursement approach that lowered the prices of all products bi-annually. In 2004, it took an average of 3.8 years for a new drug to be launched, more than two years longer than it took in the United Canada[34] Access to new, innovative medicines was also curtailed, with only 34% of new drugs launched between 2008 and 2012 in Japan.[35]

- **Korea:** In Korea, reforms have been implemented that have reduced drug prices to less than half of the average price for new drugs across the OECD.[36] Between 2008 and 2012, less than 30% of new drugs launched globally had launched in Korea.[37]

- **Spain:** Spain has undertaken a series of national and regional pricing and cost containment reforms, including price cuts through the revision of the reference price system and the imposition of mandatory discounting.[38] These reforms have lowered the price of many existing products, and have resulted in the delayed launch of new drugs. In a report from the Spanish Association of Manufacturers of Orphan and Ultra-orphan Drugs (AELMHU), it was found that of 94 orphan-designated drugs approved by the European Union (EU) between 2002 and 2016, only 49 have subsequently been launched in Spain.[39] Additionally, of the 136 medicines receiving EU marketing authorization between 2011 and 2014, only 55 were available in Spain.[40]

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[32] PhRMA Special 301 Submission, 2017

[33] IHS Global Insights; September 18, 2015. German innovative drug makers' association highlights considerable reduction in centrally approved drugs launched after AMNOG

[34] Tsukamoto, E. Japan's Drug Lag and National Agenda. *Regulatory Affairs Professional Society*, January, 2011.

[35] IMS Institute for Healthcare Informatics. *Global Outlook for Medicines Through 2018.* November, 2014.

[36] EK Lee. Price comparison among OECD countries. 2014

[37] IMS Institute for Healthcare Informatics. Global Outlook for Medicines Through 2018. November, 2014.

[38] IMS Concise Guide. Spain 2017.

[39] APM Health Europe, Press Release February 22, 2017
https://www.apmhealtheurope.com/freestory/10/54866/reimbursement-of-23-new-orphan-drugs-on-hold-or-denied-in-spain-over-high-price

[40] EFPIA. The Patients W.A.I.T. Indicator, 2014 Survey. November 2015.

The current PMPRB regime relies on objective, verifiable information in price reviews, namely international and Canadian list prices. As a result, patentees can reasonably estimate an allowable price ceiling at least a year in advance of drug launch, and plan launch resourcing accordingly. The Proposed Amendments would result in a decrease to the price a manufacturer is able to charge, and through the adoption and application of new, highly subjective economic factors and reporting requirements, would create an unacceptable level of uncertainty in determining a ceiling price at which to launch a new medicine. These two factors, taken together, would affect Canada's attractiveness as an 'early launch' country, resulting in fewer launches and significant delays in the launch of new medicines in Canada.

**Clinical Trials in Canada**

Though the link between launch sequencing and future clinical trials may not be intuitively obvious, there is a worrisome connection, particularly for clinical trials in areas within oncology and other diseases where science and innovation, and the accepted standards of care, are changing rapidly. Dr. Jennifer Knox, an oncologist with the University Health Network and Princess Margaret Hospital first raised the alarm regarding the impact of delayed access to new medicines on Canada's role in research to the federal Standing Committee on Health in 2007.[41]

In instances where a new drug does not launch in Canada but does so in other countries, particularly the United States, Germany and the United Kingdom, the new drug becomes the "standard of care" for comparing the effectiveness of the new innovation in clinical trials. Because Canada would not have the accepted "standard of care," it would be excluded from being eligible for these clinical trials. This impacts the Canadian clinical trial network as well as access for patients to what might be life-saving therapies in the absence of any other treatment alternatives.

With respect to clinical trials more generally, Canada is recognized globally for the high quality of its clinical trial infrastructure, capturing 4% of global clinical trials. However, in recent years, competition for clinical trials has grown especially fierce. Countries such as Japan have been actively pursuing an environment to attract a larger share of the clinical trial market. By all accounts, in the last 10 years, the growth in clinical trials has shifted markedly away from traditional growth areas (Europe and North America) to Asian countries, including low-and middle-income countries. An examination of 205,000 registered clinical trials from 2005 onward showed that the absolute increase in numbers was greatest for Asia (489%) and Latin America/Caribbean (112%); the smallest increase occurred in North America (9%).[42] In this competitive environment, it is imperative that Health Canada ensure its pricing regime continues to support the launch and entry of innovative medicines that are considered standard of care.

**Alternate Solutions to Addressing Affordability of Medicines in Canada**

Lilly agrees with F/P/T governments that Canadians should have timely access to the medicines they need without affordability as a barrier, and that industry must stand with government in the co-creation of solutions. Lilly does not agree that Health Canada's Proposed Amendments are the right path forward; in fact, the Proposed Amendments will negatively impact F/P/T drug plans and the vulnerable populations they support, as well as life sciences stakeholders engaged in research and innovation.

Lilly supports the solution framework proposed by Innovative Medicines Canada (IMC) to support governments and Canadians in ensuring they have access to new, innovative medicines, while ensuring

[41] HESA, Standing Committee on Health. Minutes of Proceeding, meeting 51. April 30, 2007.

[42] Drain PK, Robine M, King KH and Basset, I. Global Migration of Clinical Trials in the Era of Trial Registration. *Nat Rev Drug Discov*. 2014 March ; 13(3): 166–167.

the long term sustainability of the health care, life sciences and investment environments in Canada. The alternatives proposed by IMC are consistent with PMPRB's mandate and would significantly lower patented drug prices for all Canadians. Specifically, IMC proposes: a pre-existing, cohesive group of comparator countries for the Schedule, more reflective of the value Canadians place on health care; a price freeze for existing medicines; and, co-creation with PMPRB of new price tests for medicines that present a higher risk of excessive pricing, namely, those that represent a substantial therapeutic improvement or breakthrough, with no comparators. IMC's proposal addresses this risk directly, while avoiding unintended and unnecessary disruption for payers, patients and industry noted above.

Lilly further notes that, in contrast to the IMC proposal, the Proposed Amendments would not address what F/P/T drug plans have identified as their most pressing problem: managing drugs with no comparators that present a potential high cost burden. As noted above, these drugs present the greatest risk of excessive pricing, but do not fit within the bounds of a QALY threshold and so, require a more nuanced approach to decision-making, which payers currently apply in assessing appropriate reimbursement and pricing.