

Response by Eli Lilly Canada (Lilly) on Proposed Amendments to the Patented Medicines Regulations

Key Messages

- If implemented, Health Canada's regulatory proposals would result in significant changes to the PMPRB and fundamentally alter Canada's pricing regime for patented medicines.
- There are a number of unintended consequences related to the proposed PMPRB changes that have the potential to negatively impact F/P/T governments and their vulnerable populations, as well as research, innovation and life sciences stakeholders.
- Lilly Canada requests that there be a pause in the regulatory amendment process and reconsideration of the changes being proposed by Health Canada.

Introduction

This document represents Eli Lilly Canada's (Lilly's) submission to the consultation by Health Canada on the Proposed Amendments to the Patented Medicines Regulations. In brief summary, it is difficult to predict and assess the full range of impacts and implications and, so, provide a definitive response because the Consultation document lacks much detail regarding the Proposed Amendments, most notably how and when they would be applied in practice. Based on the information provided thus far, it would appear that the Proposed Amendments overstep the bounds for excessive pricing and create overlap and duplication with other agencies along the reimbursement continuum.

It is also not clear the degree to which Health Canada has carried out a broad-reaching impact assessment of the proposals, 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. We understand from our provincial government and life sciences partners in innovation and economic development that they have not been part of Health Canada's outreach.

For Lilly, this underscores the need for Health Canada and the PMPRB to slow down and ensure due diligence has been done to understand the impacts of the changes for all stakeholders. The consequences of a failure to do so could be severe. A six-week consultation window, marred by an unwillingness to meet with the full breadth of stakeholders, is out-of-step with a process determined to "get it right" in the interests of Canadian patients, business and innovation stakeholders, and provincial and territorial governments.

The following four issues are of special concern to Lilly: the need to align drug spend with the values of Canadians; the negative impact of a lower price ceiling on the ability of F/P/T drug plans to secure best value; the appropriate use of pharmacoeconomics; and the potential anti-competitive effect of reporting third party rebates. These issues set the frame for our responses to the specific questions asked by Health Canada.

I. Canadians and Their Health Care System

At risk of stating the obvious, "Canadians perceive health care as one of the most fundamentally important hallmark features of Canadian society....Canadians are very proud of their health care system and they

value health dearly.¹ Even in the face of increased cost, Canadians support improving the quality of Canada's health care system.² A survey by the Canadian Medical Association, just prior to Health Accord negotiations in 2016, reported that the top three priorities of Canadians for additional funding were: seniors' health, mental health services, and prescription drugs³.

It is no surprise, then, given the value Canadians place on their health care system, that Canada ranks high in health care spend compared to other OECD countries. In terms of patented medicines, Canada ranks 5th/6th in the PMPRB7 for new active substances, and 3rd in the OECD, behind the US and Mexico for all patented medicines. This is in line with its remuneration of physicians, where Canada ranks 2nd in the PMPRB7 and 4th in the OECD. For remuneration of nurses, Canada ranks 2nd in the PMPRB7 and 7th in the OECD, behind Luxembourg, US, Ireland, Australia, Denmark and Belgium. Canada's willingness to pay for health care is a measure of the value Canadians place on it. Canadians are striving for excellence, *not* the OECD median.

II. Changes to the Ceiling Price

Differential Pricing

The degree to which the Proposed Regulatory Amendments lower the ceiling price across all markets will have a redistributive effect that will benefit the private insurance industry while decreasing the size of the pool of resources available to provide confidential discounts to public payers responsible for the needs of Canada's most vulnerable populations.

Provincial and territorial (PT) governments, and now the federal government for the Non-Insured Health Benefits (NIHB) plan, currently negotiate high-value confidential discounts for their vulnerable citizens through the Pan-Canadian Pharmaceutical Alliance (PCPA). The PCPA has successfully negotiated 153 pricing agreements totaling roughly \$1B in annual savings. An additional 47 negotiations are underway. The ability of manufacturers to provide the highest value to public payers rests on the preservation of differential pricing between public and private markets: private markets pay up to the ceiling price while populations at greatest need receive a preferential discount. Since government-sponsored drugs plans already secure best value via PCPA, private payers would be the primary beneficiaries of a lower transparent ceiling price. Moreover, this transfer of value to private payers would put at risk the ability of the PCPA to negotiate best value for the vulnerable populations governments have elected to cover. A lower transparent price across all markets would mean a smaller overall pool from which to draw public payer discounts.

An analysis by Lilly, attached as an Appendix, shows the theoretical impact of a *modest* lowering in discounts (i.e., a 5-10% decrease) that would be available to public payers due to a drop in ceiling prices across all markets for two drug categories, direct anti-virals for the treatment of Hepatitis C and disease-modifying anti-rheumatic drugs (DMARDs) for rheumatoid arthritis. The analysis demonstrates that public

¹ Snowden et al. The Cost vs. Values in Health Care. Ivey International Centre for Health Innovation. Waterloo:2012.

² Ibid

³ Canadian Medical Association. 2016 National Report Card: Canadian's Views on the New Health Accord. Toronto: Ipsos. July 2016.

payers would lose upwards of \$150 million in negotiated savings to their budgets for these two drugs alone. Three provinces suffer a greater proportional loss – Saskatchewan, British Columbia and Manitoba – because of their drug plan designs, which were purposely crafted to protect their citizens from undue financial burden from illness. The additional loss comes about because their universal drug plan design means they have a smaller private market than in other provinces, with government covering a greater proportion of drug costs, particularly for higher cost drugs.

Of note: the federal government would suffer the greatest disbenefit, to a larger degree than any P/T government. This is because it offers first-dollar coverage to its beneficiaries, thus reimbursing all costs of listed products. As a result, all of the losses to NIHB and other publicly-sponsored federal plans would accrue as benefits to the private market through the lower ceiling price there: In essence, a redistribution away from vulnerable populations has occurred.

Differential Pricing as Equity

This redistribution of benefit away from the public plans warrants particular focus because it represents a fundamental disruption to the long-standing interpretation of equity by governments in Canada *to target benefit where it is most needed* – in this case, through differential pricing between public and private payers:

- The Prime Minister’s Mandate Letter to Minister Philpott stated the Government’s commitment “*to provide more direct help to those who need it by giving less to those who do not.*”
- Many government programs, including the recently announced joint federal-provincial child care agreement aimed at “families who need it most” have applied this ethical frame.

While the Patented Medicines Review Board (PMPRB) has referred to differential pricing as “discriminatory pricing”, the World Health Organization suggests an alternative interpretation: it could be viewed as “*equity pricing*”⁴. In this sense, differential pricing becomes *an explicit government policy to remedy differential abilities to pay and, so, differential access to medicines*.⁵ Lowering drug prices for private drug plans via Health Canada’s Proposed Amendments would reduce equity in this sense.

It can also be argued that F/P/Ts deserve preferentially-targeted benefits because they absorb upwards of 70% of all health care costs for all Canadians, including those with private insurances. In sum, it is difficult to see any injustice in public payers securing favoured pricing through confidential discounts.

Launch Sequence and Clinical Trials

Any of the Proposed Amendments that affect the ceiling price also have the potential to impact launch decisions for new products in Canada. A country’s pharmaceutical pricing policy 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.

⁴ WHO Collaborating Centre for Pharmaceutical Pricing and Reimbursement Policies. Glossary of pharmaceutical terms. Update 2013. Vienna 2013.

⁵ Vogler S, Lepuschutz L, Schneider P, et al. Study on enhanced cross-country coordination in the area of pharmaceutical product pricing. Brussels: European Commission: 2015.

Canada's current pricing regime, with a strong, competitive private market that offsets the low prices that public payers achieve for vulnerable populations, has resulted in manufacturers choosing to launch more new medicines in Canada, and in most cases, earlier than in other international markets. A change that makes Canada less desirable, such as a drop in pricing in the private market, would affect the number and timing of launches.

A recent study by PMPRB shows that Canada 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 UK, and Sweden launched ahead of Canada.

For Lilly, based on its particular portfolio of products, Canada typically launches in the "first wave" with leading markets, such as the US, Germany, the UK and Japan. The proposed changes to the PMPRB ceiling and its impact on the private market will change the attractiveness of Canada as an 'early launch' country.

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 so the accepted standard 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 2007⁶.

In instances where a new drug does not launch in Canada but does so in other countries, particularly the US, Germany and the UK, 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 these clinical trials. This impacts the clinical trial network as well as access for patients to what might be a life-saving therapy in the absence of any other 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 NA) 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%)⁷.

III. Economic Factors and Excessive Pricing

With respect to the pricing of patented medicines, two points are worthy of emphasis. First, while the Consultation Document talks about of the overall cost of pharmaceuticals, the emphasis for PMPRB must be squarely on price: its sole mandate. Cost speaks instead to utilization. Second, as per the submission by BioteCanada, "the PMPRB has reported that overall prices of patented drugs have been stable over the

⁶ HESA, Standing Committee on Health. Minutes of Proceeding, meeting 51. April 30, 2007.

⁷ 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.

past two decades, with annual average changes ranging between minus 2.2% and plus 0.7%. Relative to the countries in the current foreign basket, Canadian prices declined to their lowest level, 18% below the international median on average, in 2015.” For patented new active substances introduced between 2010 and 2014, Canadian prices in 2015 were not only below the foreign median, but were tied with Italy for fifth spot, lower than Germany, the U.K., Switzerland and the U.S. and only one percent above Sweden. These points must be front-and-centre in an evaluation of the need to implement Regulatory Amendments. What is the problem that the PMPRB is trying to solve?

While the *Patent Act* grounds the mandate of the PMPRB in the concept of non-excessive pricing, Health Canada’s consultation document on proposed Regulatory Amendments adds a layer of confusion to the meaning of “excessive” by speaking varyingly of “optimal pricing”, “willingness to pay”, and “ability to pay” (i.e., affordability), all of which are insufficiently restrictive for a price regulator setting a ceiling that must allow for different markets (private and public payers) with vastly different populations and, so variable willingness and ability to pay. Decisions about ability and willingness pay should remain with budget holders; provinces and territories hold constitutional accountability for these decisions.

Pharmacoeconomics: The QALY

Of greatest concern regarding the Economic Factors is the proposed use of the QALY as a “bright line” tool (i.e., “an unambiguous criterion or guideline... composed of objective factors”) in attempting to apply value-based pricing to setting the ceiling price. There is a large literature documenting the subjectivity of inputs into the QALY; assessments are based on a multitude of assumptions and small adjustments to the assumptions can cause large shifts in the QALY result.^{8,9,10} The QALY is no bright line. In Canada, both the Canadian Agency for Drugs and Technologies in Health (CADTH) and the Institut national d’excellence en santé et en services sociaux (INESSS) supplement it with additional value considerations to come up with a more robust assessment of value. Pharmacoeconomics (PE) is not a precise science. Nor, then, is it an appropriate tool for defining an excessive price: it would not account for any additional value ascribed by payers and their HTA agents through more thoughtful, broad-based deliberative reviews. The use of PE analysis in the establishment of a price ceiling would *reduce* the quality of pricing and reimbursement decision-making in Canada.

As important as the cost-effectiveness (CE) analysis by CADTH is as one of the factors public payers consider in making reimbursement decisions, negotiating pricing, and allocating their fixed resources, it would be prohibitively complicated to operationalize it across public *and* private markets, given the need for separate CE analyses for each, to incorporate different relevant inputs. As stated by Great-West Life, one of the “big three” 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 competitive edge over other

⁸ Pettitt DA, Raza S, Naughton B. et al. The Limitations of QALY: A Literature Review. *J Stem Cell Res Ther.* 2016.6;4.

⁹ Garau M, Shah KK, Mason AR, et al. Using QALYs in cancer. *Pharmacoeconomics* 2011.29: 673-685

¹⁰ 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

insurers, which may affect willingness to pay. In sum, this means there is no uniform determination of willingness and ability to pay, particularly across all markets.

A more appropriate way to manage the diversity across payers is through payer negotiations with manufacturers. Both public payers and private payers currently engage in negotiating price discounts¹¹; all public payers and private insurers engage in additional cost containment programs. It is unclear the additional role the PMPRB could play here.

IV. Information on Third Party Confidential Rebates

Given that the mandate of the PMPRB is protecting Canadians against excessive pricing, and its primary interest in the Consultation Document is stated to be the high cost of drugs, it is puzzling that the second trend highlighted as being of key importance is confidential rebates – i.e., “a growing discrepancy between public list prices and lower actual market prices due to increased use of confidential discounts and rebates.” (p.9) It is puzzling because third-party rebates take the price below the published (list) price and, so, should be of little interest to the regulator of excessive pricing. If anything, PMPRB should be primarily concerned with ensuring it does nothing to discourage such rebates. Of additional puzzlement, these rebates are not new. They began in Ontario in 2006 with the introduction of Bill 102, the only recent change being the growing role of PCPA in conducting joint negotiations on behalf of F/P/Ts. Indeed, for all of the reasons spelled out in section I of this document, there is every reason to support the use of confidential rebates so that public payers providing coverage to the most vulnerable, and likely highest cost, patients in the health system are preferentially targeted.

Of grave concern to Lilly is a potential other reason for Health Canada’s interest in third party rebate information. In her May 16, 2017, speech to the Economic Club of Canada, Minister Philpott stated, “We’re proposing a requirement to report rebates, discount & refunds to payers, *which could help set a fairer price ceiling*” [emphasis added]. This assertion by the Minister underscores the concern expressed earlier in this document that there seems to be growing confusion about the difference between excessive pricing – the PMPRB mandate as defined in the *Patent Act* – and “fair” or affordable” pricing, which is the purview of payers. Further, the intent to use the information collected about rebates in the manner suggested by Minister Philpott represents a high risk for breach of confidentiality to a manufacturer’s competitors around highly-sensitive financial information, for example through back calculation.

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 (as per the Minister’s comments), it would 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.

¹¹ 80% of private payers responding to a survey confirmed participating in negotiations with manufacturers; 56% of responding manufacturers reported successful private payer negotiations (PDCL, Private Payer Product Listing Agreements in Canada, 2016).

The appropriateness of the Proposed Amendment aside, the reporting of third party rebates would present multiple operational problems that render its use in price regulation highly impractical. These operational burdens will be detailed below, in Responses to Consultation Questions.

The Path Forward

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, they represent a step backward in many respects. Lilly acknowledges that a relatively small a number of patented medicines present a higher risk of excessive pricing, namely breakthrough medicines with no comparators. Health Canada may wish to consider establishing an Alternative Dispute Resolution (ADR) mechanism to aid the PMPRB in establishing price ceilings for medicines that have no comparators and a demonstrated high cost burden. An ADR mechanism for this category of medicines would allow for price ceilings to be negotiated by PMPRB staff and patentees beyond the Guidelines, but without the cost, time, and distraction of a formal quasi-judicial Hearing. Further, such a mechanism would address the risk this category of medicines poses in a targeted way, while avoiding the risk of negative unintended consequences for payers, patients and the life sciences cluster outlined above.

Responses to Consultation Questions on Proposed Amendments to the Regulations

Proposal #1: Introducing new factors to help determine whether a price is excessive

Question: Do you agree that a PE evaluation is an important factor for the PMPRB to consider when determining whether a drug is priced excessively? If so, how should the evaluation be considered?

Answer: No, Lilly does not agree. PE analysis, typically the QALY, is used by budget holders to inform reimbursement decisions and pricing negotiations in an attempt to optimize the allocation of scarce resources between therapies and within fixed budgets. It is not a price-setting tool.

There is a large literature criticizing the QALY, most notably the subjectivity in assumptions around inputs and the inherent discrimination against some populations (e.g., pediatric, disabled, and elderly). QALYs have been shown not to capture all dimensions of health benefits;¹² they 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.).

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 criteria¹³. QALYs cannot recognize that society values 'the rule of rescue,' meaning there is significant importance placed on rescuing people that need help. This is especially true for serious conditions, where breakthrough medications may be costly but burden of illness is high and there are limited treatment alternatives.

The strict QALY approach could additionally ignore other value-add components such as patient support, infusion clinics, and companion diagnostic testing provided by manufacturers, or the value of having more than one available drug to avoid drug shortages. These reflect important value-add factors that would not be captured by the QALY, yet might affect a payer's willingness to pay.

The limitations of the QALY have led CADTH and INESSS to incorporate their own additional measures of value. The Deliberative Framework for Review by PCODR explicitly considers "burden of illness", "need", "patient values", "economic feasibility" and "organizational feasibility" beyond the QALY.

Therefore, a price referenced to a QALY would be a step backwards, ignoring the significant work payers have done to date to identify a number of factors that they consider to add value over-and-above what the QALY measures.

In addition to being inappropriate, the use of the QALY is impractical. It would add significant burden to both the manufacturer and the HTA bodies, given the difference in inputs that would be required for public vs private insurance models. A private insurer's willingness to pay is driven by different variables, such as absenteeism, and additionally, the drive to gain edge in offerings over competitors.

¹² 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>.

¹³ Drummond M, Barbieri m, Glick HA et al. Transferability of economic evaluations across jurisdictions: ISPOR good research practices task force report." *Value in Health*. 2009, 12 (4): 409-418.

In sum, as per a 2013 report by the Institute of Health Economics¹⁴, “value-based pricing cannot be simply reduced to a mathematical algorithm. Rather, it would require the full participation and consent of representative societal actors who can deliberate and negotiate with information regarding how prices will affect the health and welfare of consumers, both now and in the future.”

Question: Do you agree that the size of the market for the drug in Canada and other countries is an important factor for the PMPRB to consider when determining whether a drug is priced excessively? If so, how should the size of the market be considered?

Answer: Lilly does not agree. It is unclear for what purpose and how this factor would be applied. Further, the *size* of the market speaks to affordability – it implies a fair price is one at which all eligible patients can be treated without excessive spend or being “unaffordable.” Fairness is clearly 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 above notwithstanding, the introduction of market size as a pricing regulation factor presents severe operational problems that render it impractical for general application. These are outlined in detail in the Innovative Medicines Canada (IMC) submission.

Question: Do you agree that Canada’s GDP and GDP growth are important for the PMPRB to consider when determining whether a drug is priced excessively? If so, how should GDP be considered?

Answer: Lilly does not agree. As noted within the Consultation Document, GDP would be used to assess affordability: affordability is not the mandate of the PMPRB. Most notably, the document fails to consider the variability in GDP across the country and how this variability would be managed by a national regulator. 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 provincial level: neither Health Canada nor the PMPRB is a budget holder for pharmaceutical spend in each of the PT jurisdictions.

Question: Are there any other factors that should be considered by the PMPRB when determining whether a drug is priced excessively? How should the factor(s) be considered and what information should be required from patentees?

Answer: Lilly recommends that the Regulations should be amended so as to codify therapeutic value as the primary factor in determining whether a drug is priced excessively. The factor should continue to be used in the manner outlined in the current Compendium of PMPRB Guidelines, independent of any link to cost effectiveness, which is not the concern of the PMPRB. No additional information would be required from patentees over and above what is provided now.

A paramount feature in determining the ceiling price of an innovative medicine is the level of therapeutic benefit it provides: the higher the benefit, the higher the potential price. Using therapeutic value as the

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.

major point for price determinations is consistent with the patent regime in which the PMPRB finds its home. Statutory factors in section 85 of the *Patent Act* reference “therapeutic class” when assessing an excessive price, clearly pointing to the importance of therapeutic value as a basis for pricing.

This is consistent with other jurisdictions – while pricing strategies may vary internationally, innovation is a key determinant in setting price. By ensuring a scaled recognition and reward for incremental benefits, clear and consistent expectations are signaled to the innovative medicines sector on what their research and development should deliver. This is commonly understood as the appropriate incentive and reward for bringing innovative medicines to market, which is consistent with the overall purpose of the *Patent Act*.

Therapeutic benefit is the same standard applied across the globe: we know of no jurisdiction that assesses the value of a medicines in another manner. For example, in both France and Germany the degree of therapeutic benefit an innovative medicine provides is first assessed, through the Commission d’Evaluation des Médicaments and the Federal Joint Committee (Gemeinsamer Bundesausschuss – G-BA), respectively, and only then is a pricing and reimbursement strategy assigned as a result of this assessment.

Alternative Dispute Resolution

Lilly acknowledges that a relatively small a number of patented medicines present a higher risk of excessive pricing, namely breakthrough medicines with no comparators. Health Canada may wish to consider establishing an Alternative Dispute Resolution (ADR) mechanism to aid the PMPRB in establishing price ceilings for medicines that have no comparators and a demonstrated high cost burden. An ADR mechanism for this category of medicines would allow for price ceilings to be negotiated by PMPRB staff and patentees beyond the Guidelines, but without the cost, time, and distraction of a formal quasi-judicial Hearing. Further, such a mechanism would address the risk this category of medicines poses in a targeted way, while avoiding the risk of negative unintended consequences for payers, patients and the life sciences cluster outlined herein.

Section 85 (2) (b) of the *Patent Act* currently gives the PMPRB the right to incorporate “Other Factors” as necessary, so the need for Regulatory Amendment to introduce additional factors is unnecessary.

Proposal #2: Amending the list of countries used for international price comparisons

Question: Are there other criteria that should be considered in revising the Schedule?

Answer: It is of concern that five of the seven countries being proposed for inclusion in the Proposed New Schedule sit at or below the OECD median of new medicine launches: South Korea – 33%; Netherlands – 36%; Japan – 38%; Australia – 40%; Belgium – 45%; Spain – 52%; Norway – 56%. Canadians place a high value on health care. They are not striving to be at the OECD median, and this is evident in Canada’s health care spend across the board.

Although the Consultation Document lists criteria for revising the Schedule, what is clear is that the Proposed New Schedule of price reference countries was specifically crafted as a means to lower prices to the OECD median price ratio (a 22% reduction, in aggregate). So, it is unclear the actual weight that was placed on the new factors in selecting the Proposed Schedule: no detailed analysis has been offered

by Health Canada. For example, it is not clear why Switzerland has been excluded; it is similar to Canada in economic standing and has a pricing regulation body that performs a function similar to the PMPRB.

What is obviously 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, PMPRB incorporate countries similar to Canada in terms of 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 expenditures¹⁵.

Overall, in lowering the ceiling price, the changes to the basket will create unintended and negative consequences that have not been appropriately considered.

Unpredictable and Unequal Impacts for Manufacturers

The proposed changes would not generate uniform price reductions in Canada. Its effect would be random, even haphazard, with every medicine in every class impacted differently. Older patented medicines, that have lost market exclusivity, and are rarely used, are more likely to be affected than newly launched ones.

Loss of Value to Public Payers

It is important to reemphasize, given the clear intent to lower the ceiling price to align with the OECD median, that the degree to which the Proposed Regulatory Amendments lower the ceiling price across all markets will have a redistributive effect that will benefit the private insurance industry while decreasing the resources available to provide confidential discounts to public payers responsible for the needs of Canada's most vulnerable populations.

The ability of manufacturers to provide the highest value to public payers rests on the preservation of differential pricing between public and private markets: private markets pay up to the ceiling price while populations at greatest need receive a preferential discount. Since government-sponsored drugs plans already secure best value, private payers would be the primary beneficiaries of a lower transparent ceiling price. This transfer of value to private payers would put at risk the ability of the PCPA to negotiate best value for the vulnerable populations that governments have elected to cover. A lower transparent price across all markets would mean a smaller overall pool from which to draw public payer discounts.

Launch Sequence and Clinical Trials

To reiterate, while there are a number of business and market dynamic considerations that affect launch sequencing, including market size and regulatory environment, price is a prime consideration. Based on an analysis by the PMPRB's National Prescription Drug Utilization Information System (NPDUIS), currently Canada is a "first wave" launch country, coming to market close behind the US, Germany, Sweden, and the UK. Canada also fares well in terms of the number of launches of new active substances (NAS), where

¹⁵ PDCI. International variations in Pharmaceutical Prices. Presentation to Northwinds Professional Institute. May 5, 2017.

it has one of the highest shares of NAS launched in the world at 61% vs the OECD median of 45% (the OECD has a foreign-to-Canadian price ratio of 0.78).

Proposal #3: Reducing regulatory burden for generics with a patent

Question: Do you agree that patentees of generic drugs, i.e. drugs that have been authorized for sale by Health Canada through an ANDS should only report information about the identity of the drug and its pricing in the event of a complaint or at the request of PMPRB?

Answer: Yes, Lilly Canada agrees that patentees of generic drugs should be moved to complaints-based regulation. In the spirit of risk-based regulation, Lilly Canada further recommends that this approach be extended to a broader range of patented medicines with a low risk of excessive pricing, in particular, patented branded medicines without market exclusivity.

It should be understood, however, that moving to complaints-based regulation reduces the regulatory burden mainly for the PMPRB. It does not reduce regulatory burden for patentees in any meaningful way, as they must still deploy highly skilled staff, or hire specialized vendors, to ensure that all product DINs remain compliant with pricing regulations and guidelines.

Proposal #4: Modernizing reporting requirements for patentees

Question: Is the information sought in relation to the new factors relevant and sufficient? Is this information generally available to patentees?

Answer: With respect to PE evaluations in other countries, there are important operational and implementation considerations that restrict their usability beyond the country in which the analysis originates; there are always generalizability and transferability issues/restrictions across different settings. Drummond et al¹⁶ conducted a review of national guidelines and found that the majority stress the potential for differences in clinical parameters that minimize the successful transferability of results. The majority also recommend the use of context-specific information on utility values, resource use, costing, routine clinical practice/standard of care, patient populations, and subpopulations of interest, and comparators.

A recent study by Nicod¹⁷ documents the substantial difference in coverage recommendations across countries for the same drugs. In five EU countries, six out of ten drugs received diverging HTA recommendations. Reasons for cross-country differences included heterogeneity in (a) the evidence (b) interpretation of the same evidence, and (c) different ways of dealing with the same uncertainty. These may have been influenced by agency-specific evidentiary, risk and value preferences, or stakeholder input.

¹⁶ Drummond M, Barbieri M, Cook J et al. Transferability of economic evaluations across jurisdictions: ISPOR good research practices task force report. Value Health. 2009, 12 (4): 409-418.

¹⁷ Nicod, E. Eur J Health Econ. Why do health technology assessment coverage recommendations for the same drugs differ across settings? (2017) 18: 715.

The collection of this information would impose a significant burden on patentees; it is not readily available, nor is it information that would be otherwise collected, given its irrelevance to the Canadian setting.

With respect to market size, its introduction in Canada and other countries as a pricing regulation factor presents several operational problems that render it impractical for general application. These are outlined in detail in the Innovative Medicines Canada (IMC) submission.

Proposal #5: Providing information related to third party rebates

Question: Are there any reasons why patentees should not be required to disclose to the PMPRB information related to third-party rebates?

Answer: Lilly is strongly opposed to the proposed requirement to disclose third-party rebates to the PMPRB. Moreover, it is puzzling why PMPRB should have interest in them, because third-party rebates take the price below the published (list) price and, so, should be of little interest to the regulator of excessive pricing. If anything, PMPRB should be primarily concerned with ensuring it does nothing to discourage such rebates. That the substance of third-party rebates is of interest to Health Canada and the PMPRB is profoundly concerning.

In her May 16, 2017, speech to the Economic Club of Canada, Minister Philpott stated, “We’re proposing a requirement to report rebates, discount & refunds to payers, *which could help set a fairer price ceiling*” [emphasis added]. This underscores the constant thread throughout this submission by Lilly Canada that there is a failure to recognize or acknowledge the critical difference between excessive pricing – the PMPRB mandate as defined in the *Patent Act* – and “fair” or affordable” of “optimal” pricing, which is the purview of payers. Further, the intent to use the information collected about rebates in the manner suggested by Minister Philpott represents a high risk for breach of confidentiality to a manufacturer’s competitors around highly-sensitive financial information, for example through back calculation.

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 (as per the Minister’s comments), it would 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.

The appropriateness of the Proposed Amendment aside, the reporting of third party rebates would present multiple operational problems that render its use in price regulation highly impractical. While internal rebate accruals are calculated monthly, payers invoice on a variety of schedules (quarterly, semi-annually or annually), with varying lag times for the preparation of invoices. Invoicing schedules would inevitably cross PMPRB reporting periods, creating rebate calculation challenges.

From time-to-time, the data supplied in invoices are 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 product listing agreement structures are in place in Canada, for example, tiers, hard caps, soft caps and indication-based pricing. Such listing agreement structures result in changes to the net price of a product from one year to the next. In the future, if outcomes-based pricing becomes more prevalent, there would be further challenges, as rebates and net prices would fluctuate based on measured patient outcomes.