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February 14, 2018

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Submitted via email: PMR-Consultations-RMB@hc-sc.gc.ca

RE: Regulations Amending the Patented Medicines Regulations released by the Government of Canada on December 2nd, 2017, in Canada Gazette, Part I

Dear Ms. Reynolds:

On behalf of the more than 750 employees working at AstraZeneca Canada (AZC) I am responding to the proposed *Regulations Amending the Patented Medicines Regulations* released by the Government of Canada on December 2nd, 2017, in Canada Gazette, Part I (CG1).

We were deeply disappointed to see that the draft regulations, the accompanying Regulatory Impact Analysis Statement (RIAS) and the Cost Benefit Analysis (CBA) do not address the serious concerns we, and many others, have raised multiple times, including in AZC's submission to the original policy consultation dated June 28th, 2017. With the CG1 publication, it is evident that none of the concerns raised by Canadian patient, professional or industry organizations in the spring consultation were addressed in any meaningful way.

These draft regulations are based on flawed reasoning, inaccurate assumptions and incomplete information presented in the RIAS and CBA. They will have negative economic implications, leading to reduced research and development (R&D) investments, less innovation in Canada and fewer jobs in our life sciences sector. Ultimately, though, it will be Canadian patients who suffer most from the changes being proposed. These reforms will see Canada shift from a 1st tier to a 2nd or 3rd tier health care system when it comes to accessing breakthrough medicines, resulting in both fewer new medicines being brought to Canada and much slower access to new medications.

The negative impact of CG1 for both Canadians and the health sciences sector is significant, and we are calling on the Government of Canada to:

1. **Postpone implementation of any element of the draft regulations until a full impact analysis can be undertaken, modelled in the context of the Canadian health system and life sciences ecosystem;**
2. **Establish a committee with representation from the innovative biopharmaceutical industry, the Ministry of Health and the Ministry of Innovation, Science and Economic**

Development (ISED) to jointly develop solutions to attract innovation and improve access, affordability, and appropriate use of medicines for Canadians.

AstraZeneca Canada fully endorses the comprehensive submissions from Innovative Medicines Canada and BIOTECanada to the CG1 consultation. We discuss many of the same concerns in the body of our CG1 submission, however, we believe three priority areas are particularly integral to the continued health and investment of Canada's innovative biopharmaceutical sector:

1. **Pharmacoeconomic Factors should not be implemented.** Adding these factors would be a significant departure from PMPRB's historic intent. They will impair our ability to bring new medicines to Canadians in the future, and may impact the continued availability of some medicines currently in market. International best practice shows that the national pricing regulator is not the appropriate body to impose value judgements to set a price. Health Technology Assessment (HTA) bodies, payers and patients are best positioned to consider value and willingness-to-pay. **No other jurisdiction globally uses pharmacoeconomic factors alone to set a national ceiling price**, and Canada should not be an outlier in this regard.

2. **Net Pricing Reporting should not be implemented.** Disclosing net prices to the PMPRB is not within their pricing or consumer protection mandate. It also does not serve Canadian patients well, as these lower prices are already negotiated by payers on their behalf. Mandating price discount reporting could hinder the ability for innovative pharmaceutical manufacturers to remain in or enter into Product Listing Agreements (PLAs) with public plans, which often serve more vulnerable populations. **This will ultimately limit patient access for those who need it most**. The ambiguity surrounding the inclusion of these factors has already caused significant uncertainty in business planning.

3. **Outdated R&D definition needs updating.** Much of the rationale for modernizing the PMPRB regulations rests on the fact that they are 30 years old. Yet, Health Canada has chosen not to update the R&D reporting methods the PMPRB uses, instead remaining with a definition that is very narrow, outdated and out-of-step with modern economies around the world. The way our industry invests in and supports the Canadian life sciences ecosystem has evolved markedly from the 'bricks and mortar' research model used 30 years ago. Indeed, other departments of the Government, such as Statistics Canada and ISED, recognize this and use a more modern definition of R&D. AstraZeneca Canada is proud to have invested more than $90M in R&D in Canada in 2017, representing 13.9% of our sales. We believe **Canadians deserve the full picture of innovative biopharmaceutical research investments in Canada through modernized reporting.**

We urge the Government of Canada to collaborate with our industry, Canadian patient and professional stakeholders to get this right for Canadians. We recognize that access, affordability and appropriate use of medicines must be addressed. As one of the country's leading innovative

companies, we believe we can improve affordability and access, while attracting more research investments, clinical trials and jobs if we work together.

The innovative medicines industry is prepared to discuss specific solutions for how the Patented Medicine Regulation changes can be revised in a way that contributes to health system affordability, patient access to new medicines and innovation strategy objectives. A key part of this discussion is a Vision Paper entitled *For Our Health, for Our Economy, Let's Aim Higher: a Made-in-Canada Approach to New Medicines*. The Vision Paper makes the case for more holistic and forward-looking strategies and policy options. We hope that this paper will catalyze real solutions to the challenges facing patients, our health system and our economy.[1]

However, if the Government continues to proceed unilaterally with these proposed PMPRB reforms, it will put Canadian lives and livelihoods at risk: these changes will most assuredly reduce investment in life sciences in Canada, impact knowledge economy jobs, and significantly delay or even prevent many new medications launching here. The reforms will have the consequence of denying potentially life-saving innovations to Canadian patients.

ASSUMPTIONS IN RIAS AND CBA

Many of the assumptions and data points that Health Canada relies on are inaccurate or incomplete. It is incomprehensible that the Government of Canada is forcing through major reforms to one of its top seven strategic economic innovation sectors[2] based on selective facts and a lack of openness to feedback from Canadian stakeholders.

Before addressing the assumptions in the RIAS and CBA, it is important to address the baseline from which the Government's case for change typically begins: that prices for innovative medicines are comparatively high and therefore unaffordable; and that the innovative biopharmaceutical sector is not investing enough in Canada. That narrative does not accurately characterize drug access and affordability in Canada, and none of the arguments put forward by the Government justify the haste with which they are pushing forward the PMPRB reforms:

- **Innovative drug costs are not driving healthcare spending overall nor are Canadian prices "some of the highest in the developed world**."[3] Spending on innovative medicines in Canada represented 6.7% of total public and private healthcare spending in 2016.[4] Furthermore, the PMPRB's own 2016 Annual Report (released after the Minister's May 2017 announcement) showed that Canadian prices are already at the mid-range of

[1] For more information please visit www.innovateforlife.ca
[2] Ministry of Innovation, Science and Economic Development website. Accessed February 13, 2018. https://www.ic.gc.ca/eic/site/098.nsf/eng/home
[3] Government of Canada (May 16, 2017) *Government of Canada taking action to protect Canadians from high prescription drug prices.* [Press Release]. Retrieved from https://www.newswire.ca/news-releases/government-of-canada-taking-action-to-protect-canadians-from-high-prescription-drug-prices-622584484.html
[4] Skinner, Brett J (2017). Facts about the cost of patented drugs in Canada: 2017 Edition. *Canadian Health Policy*, working paper December 8, 2017. Access to Innovative Medicines (AIM) series. Toronto: Canadian Health Policy Institute (CHPI). URL: www.canadianhealthpolicy.com.

the reference basket. PMPRB's own data also show that patented medicine price increases have been consistently below the Consumer Price Index for decades. The last time drug prices grew faster than the CPI was 1992.[5] Analysis of the Canadian Institute for Health Information (CIHI)'s health spending data shows that total drug-related costs have remained relatively stable, around 16%, for the last 15 years.[6] This figure is comprised of drug costs from all sources which includes: brand *and generic* drug costs, pharmacy and wholesaler mark-ups, drug plan administration costs, and over the counter medicines. Yet, it is used to target only innovative biopharmaceutical prices. This is a purposely misleading way to present the "facts" to Canadians on the issue. As stated above, innovative biopharmaceutical costs make up 6.7% of health spending.

- **Only a small minority of Canadians forgo medicines due to cost**. Contrary to news headlines and statements in Health Canada's consultation documents that are not referenced, the vast majority of Canadians actually do have access to some form of drug coverage. A recent Nanos[7] poll found that less than 1% of Canadians who needed a prescription did not take it because of cost. A subsequent policy paper by the Conference Board of Canada found that less than 5% of Canadians do not have drug coverage.[8] This remains an important and unresolved issue, however it is not the 10% to 20% figure often quoted by the Government.

- **PMPRB does not capture the entirety of industry investment in their reporting framework.** The traditional reporting mechanism used by the PMPRB does not accurately depict industry's ongoing contribution to R&D in Canada. At AZC we are proud of our commitment to scientific excellence, research and discovery, the jobs this R&D supports and the lives it saves. In 2017, AZC invested more than $90 million in Canadian health sciences research, focused in cardiovascular, diabetes, oncology and respiratory disease. This represents roughly 13.9% R&D to sales ratio; however, a significant part of this investment is not recognized through PMPRB's narrow and outdated 30-year-old definition of R&D. We are at a loss as to why the Government has not chosen to update the PMPRB's reporting definition of R&D, particularly when other Government departments such as Statistics Canada and ISED already use a more modern R&D reporting method that is more consistent with modern economies.

The underlying assumptions in the RIAS and CBA documents do not accurately reflect the realities of the Canadian biopharmaceutical sector or broader life sciences ecosystem. This

[5] PMPRB Annual Report (2016). Figure 7. Accessed online at http://www.pmprb-cepmb.gc.ca/CMFiles/Publications/Annual%20Reports/2017/2016_Annual_Report_Final_EN.pdf . p27

[6] Critchley, Wayne and Robert C. Owens (February 2018). The Unkindest Cut: How a new plan for slashing drug prices could harm the prosperity and health of Canadians. *MacDonald Laurier Institute*, A Better Path for Canadian Health Care series. p8.

[7] Nanos Prescription Use Survey Summary. November 2017. Accessed online at http://innovativemedicines.ca/wp-content/uploads/2018/01/2017-nanos-survey.pdf

[8] Sutherland, Greg, and Thy Dinh (December 2018). Understanding the Gap: A Pan-Canadian Analysis of Prescription Drug Insurance Coverage. *Conference Board of Canda.* Published in Canada. Accessed online at http://innovativemedicines.ca/wp-content/uploads/2017/12/20170712-understanding-the-gap.pdf

includes a significant under-estimate of the potential harm the CG1 changes will have to local, high-value jobs and the Canadian economy, as well as the harm to Canadian health care.

We reiterate our disappointment that nothing appears to have changed as a result of the many Canadian stakeholder submissions to the initial policy consultation in 2017 – submissions which Health Canada has refused to release publicly or respond to directly. As an affected stakeholder, as an oncologist, and as a Canadian, it is deeply disappointing to see the Government so patently disregard the thoughtful and substantive advice of knowledgeable stakeholders, many of whom will be the those most affected by these changes.

Irrelevance of Positive Economic Multiplier

Reviewing the Cost-Benefit tables in the RIAS and the CBA shows that the largest forecasted benefit from the proposed CG1 changes is attributed to the "health care system" and is not a direct result of reduced drug expenditures. According to Health Canada, reduced drug expenditures account for $8.6B in benefits while the "health care system" accounts for $12.7B added to the benefit side of the ledger.[9] However, the benefit is not enumerated or quantified or in any way based in the Canadian context. Rather, it is an estimate based on an economic multiplier calculated in a study of the economic impacts of healthcare expenditures prior to the European economic crisis in the late 2000s [10]. We believe it is imperative to have a Canadian model that can accurately estimate the positive and negative impacts of any pricing changes through PMPRB reforms.

The Conference Board of Canada published a study in 2013 which does describe a Canadian model of the impact of spending on pharmaceuticals. They concluded that for every dollar spent on pharmaceuticals two dollars were realized in societal and economic benefits[11]. Given this Canadian context, we argue that drug spending is a prudent use of healthcare funds, and that there is no guarantee that reductions in drug expenditures will deliver any added benefit to the rest of the healthcare system.

Lastly, the assumption that "savings" from reduced drug costs will be reinvested in healthcare is entirely unverifiable. Indeed, the Health Minister indicated as much in her May 2017 remarks, acknowledging that it would be up to the Finance Minister where any drug plan savings go.[12] Notwithstanding that PMPRB is not a payer or deliverer of healthcare – this assumption also ignores the fundamental fact that the vast majority of savings would not occur at the Federal level, regardless.

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[9] Canada Gazette Part I, Vol. 151, No. 48. (December 2017). Accessed online at http://www.gazette.gc.ca/rp-pr/p1/2017/2017-12-02/pdf/g1-15148.pdf. p4516.

[10] Reeves *et al.* (2013). Does investment in the health sector promote or inhibit economic growth? *Globalization and Health.* 9:43. Accessed online at https://globalizationandhealth.biomedcentral.com/articles/10.1186/1744-8603-9-43

[11] Hermus *et al.* (July 2013). Reducing the Health Care and Societal Costs of Disease: The Role of Pharmaceuticals. *Conference Board of Canada*. Accessed online at http://www.conferenceboard.ca/e-library/abstract.aspx?did=5598

[12] During the question and answer session at the May 16, 2017 announcement the Minister acknowledged she had no control over where drug plan savings would go. https://www.periscope.tv/HealthCanada/1djGXAwkXmEJZ at about minute 40-42.

It is a commitment they have no authority to make or enforce, and it means that even if the multiplier from the European model were valid, the concept itself is irrelevant and unrealizable in Canada. The only reinvestment from drug savings that could be promised by Health Canada is from its Non-Insured Health Benefits (NIHB) drug plan, and we have seen no such commitment.

Due to this critical flaw in the CBA we are calling on the Government to postpone any further progression of the PMPRB regulations until an authentic dialogue between industry, Health and ISED occurs.

Lack of Multiplier Factor for Negative Effects

The Government of Canada indicates there will be no negative ripple effects to the Canadian economy or jobs from reduced pharmaceutical revenues. This assumption is both unreasonable and incorrect, and undermines the credibility of the CBA. To assume little-to-no impact from significantly reducing Canadian prices for innovative medicines is to ignore the interconnected nature of investments, support services, research endowments, clinical trial infrastructure and distribution channels associated with a thriving innovative health/bio-sciences sector. It simply does not align with the reality of how our sector operates in and supports the Canadian life sciences ecosystem.

Numerous articles and letters from members of the Canadian ecosystem, such as BIOTECanada and multiple Bio/Life Sciences organizations across the country support our assertion that Health Canada's assumptions lack balance and as a result, greatly underestimate the actual impact these changes will have.

In addition to direct ripple effects from lost revenues, the RIAS and CBA also fail to contemplate that companies will alter their model of business in Canada. For Health Canada to assume it will be "business as usual" in the wake of fundamental reforms to the PMPRB's mandate is unrealistic.

As an example of how reduced revenues can significantly impact jobs in Canada, AZC went through a major restructuring from 2011-2014 as a direct result of substantial revenue decline after patent losses for several products. Restructuring included job reductions of over 50% of the workforce at the time (more than 500 jobs) and the divestiture of physical assets in Canada. The simple fact is that lost revenues in Canada affect Canadians as they lead to job losses and other investment reductions.

In addition to local impacts, global parent company investment in Canada could be at risk in the future if these reforms go through unchanged. For example, AstraZeneca's investment in the Canadian Cancer Trials Group (CCTG) at Queen's University by our global parent company is the largest single research investment by AstraZeneca in Canada. In fact, it is the largest investment that CCTG has received from any industry sector. Our partnership with this team of leading clinical experts is building its capacity and talent to deliver cutting edge cancer clinical trials in Canada and around the globe, in areas of high unmet need such as immunotherapy, combination

oncology therapies, and others. It is expected that if the proposed regulations are put in place Global headquarters will no longer be willing to make such meaningful and significant investments in Canada moving forward and would instead divert research investments to other countries with more favourable and supportive life sciences environments.

Based on our real world experiences, the economic impact of the proposed PMPRB changes will be significant and far-reaching in Canada, particularly across the entire health/bio-sciences sector. For the RIAS and CBA to outright dismiss and minimize any impact to Canadian jobs and the life sciences economy is unreasonable and an important miscalculation.

Due to this critical flaw in the CBA we are calling on the Government to postpone any further progression of the PMPRB regulations until an authentic dialogue between industry, Health and ISED occurs.

The Integral Link Between Pricing and R&D

Health Canada contends that "there is no causal relationship between domestic price levels and industry decisions on the location of investment, employment and R&D."[13] This is in direct contrast to the Organization for Economic Cooperation and Development's (OECD) who clearly state there is a link between sales revenues and investment.[14] This is a readily available OECD report, and Health Canada's decision to ignore it speaks to both a disregard for anchoring their proposed changes to validated facts and not appreciating the impact to the Canadian health sciences ecosystem and Canadian patients. It is ironic to see Health Canada use OECD median drug prices as a policy benchmark, while refusing to acknowledge analysis from the OECD showing a clear link between pricing environment and R&D investments.

We are concerned that no references have been given for Health Canada's categorical statements. The regulations proposed in CG1 represent the most sweeping changes to Canadian biopharmaceutical policy in more than 20 years. There is a lot at stake for Canadians, stakeholders and the health sciences ecosystem. We believe it is irresponsible not to offer balanced and credible information on the issue.

Future landmark global investments in Canadian institutions – such as the one AZC made in the Queen's University Canadian Cancer Trials Group – will be at risk in the future, should the regulations proceed as proposed. The impact will also be felt across the entire ecosystem: research partnerships will not be renewed, start-ups will not receive needed capital and leading clinicians will leave Canada – or not come in the first place – to work in countries like the United States and Europe where robust research investments by multinational biopharmaceutical

[13] Cost Benefit Analysis supplementing the Regulatory Impact Analysis Statement for the Amendments to the Patented Medicines Regulation (September 2017). Strategic Policy Branch, Health Canada. p29.

[14] Pharmaceutical Pricing Policies in a Global Market (2008). *Organization for Economic Coordination and Development.* Figure 6.1. Accessed online at http://www.keepeek.com/Digital-Asset-Management/oecd/social-issues-migration-health/pharmaceutical-pricing-policies-in-a-global-market_9789264044159-en#page192

companies are recognized and valued by governments as integral to both healthcare and the economy.

The dismissal of the innovative biopharmaceutical sector's economic importance also runs counter to Minister Navdeep Bains's Innovation Agenda.

Due to this unbalanced reasoning in the CBA we are calling on the Government to postpone any further progression of the PMPRB regulations until an authentic dialogue between industry, Health and ISED occurs.

Administration Costs

The purported administrative cost burden to industry is simply not credible. At a recent stakeholder consultation it was confirmed by Government officials that no attempt was made to verify these numbers externally. While this is by far not our most significant concern with the CBA, it speaks again to the lack of rigor, thoroughness and balance adopted by the Government when assessing the impact of the proposed changes. Moreover, it suggests that this exercise may simply be a formality for the Government with the end result pre-determined long ago. Canadians should be very concerned that their Government is not giving this review the proper consideration needed to get it right, particularly given what is at risk to health care in this country.

The Government asserts it needs more than $80M to operationalize these reforms over 10 years[15], while concluding that industry only requires $0.1M to implement the same reforms. This is unreasonable. Independent analysis shows the impact for the Canadian biopharmaceutical industry to be estimated at $10M to $40M over 10 years.[16]

Sensitivity Analysis

The Sensitivity Analysis in the RIAS and CBA spans an alarming range. While Health Canada uses $8.6B Net Present Value (NPV) over 10 years as its base case for reduced drug expenditures, the range is wide, from $6.4B to $24.9B NPV. The CBA states that "the maximum impact represents the highest projected patented medicine sales coupled with the *most aggressive guidelines reforms*"[17] (our emphasis added). Given this vague explanation, and the strong implication that guidelines could easily be more aggressive than the base case, industry must consider Health Canada's $24.9B upper limit as our "base case." This would represent an average annual revenue cut of $2.5B (NPV). There is simply no way the Canadian biopharmaceutical industry can sustain such a significant impact without any negative effects being felt locally. Further, independent

[15] Health Canada Presentation (January 10, 2018). Proposed Amendments to the Patented Medicines Regulations (PMRs): Cost-Benefit Analysis. Slide 6.

[16] Proposed Amendments to the Patented Medicines Regulations: A Critical Appraisal of the Cost-Benefit Analysis (January 2018. *PDCI Market Access.* Accessed online at http://www.pdci.ca/wp-content/uploads/2018/01/20180129_PDCI-Critical-Assessment-PM-Regs-Amendments_Report-Final.pdf

[17] Canada Gazette Part I, Vol. 151, No. 48. (December 2017). Accessed online at http://www.gazette.gc.ca/rp-pr/p1/2017/2017-12-02/pdf/g1-15148.pdf. pp4520-4522

analysis has concluded that even Health Canada's upper limit has underestimated the impact on industry revenues. PDCI calculates total industry impact at approximately $26.1B.[18] They further calculate that the overall impact resulting from lost industry revenues, lost research investments and lost taxation revenue to Canadian governments will result in a $35B negative impact.

The possible range of impact on industry and lack of transparency from the Government regarding their intent for the PMPRB Guidelines means that the fast-approaching implementation date of January 1st, 2019 has already introduced uncertainty and risk into the Canadian landscape.

In a world with interdependent global price referencing, the new and sudden instability introduced by the Government will force global companies to scrutinize the feasibility of bringing new products to market during such a volatile period. The Government's proposed changes highlight that Canada does not value innovation and is making important shifts towards becoming a 2nd tier health care system globally.

Putting internal processes in place to operationalize the changes come January 1st will be extremely difficult. The ambiguity, lack of meaningful dialogue, and refusal to discuss the intended functioning of the Guidelines, coupled with the accelerated implementation deadline could significantly impair our ability to conduct regular business operations in the interim.

This is yet another reason we are calling on the Government to postpone any further progression of the PMPRB regulations until an authentic dialogue between industry, Health and ISED occurs.

We do know that recent examples of Government-industry partnership exist: A recent joint announcement from the pan-Canadian Pharmaceutical Alliance (pCPA) and the Canadian Generic Pharmaceutical Association (CGPA) highlighted cost savings *as well as benefits for the generic industry.*[19] This is a clear example that industry and Government(s) can work together to achieve public policy goals while maintaining the viability of an important sector.

PHARMACOECONOMIC FACTORS

AstraZeneca Canada strongly recommends the removal of the new pharmacoeconomic factors from the regulations. We do not believe it is within the authority, accountability or consumer protection mandate of the national pricing regulator to use cost-effectiveness (CE) or willingness/ability to pay considerations to set prices in Canada. The addition of these factors is inappropriate: while well-established bodies like the Canadian Agency for Drugs and Technologies in Health (CADTH) and pCPA use pharmacoeconomic factors for the purpose of

[18] Proposed Amendments to the Patented Medicines Regulations: A Critical Appraisal of the Cost-Benefit Analysis (January 2018. *PDCI Market Access.* Accessed online at http://www.pdci.ca/wp-content/uploads/2018/01/20180129_PDCI-Critical-Assessment-PM-Regs-Amendments_Report-Final.pdf

[19] A Joint Statement from the pan-Canadian Pharmaceutical Alliance and the Canadian Generic Pharmaceutical Association (January 29, 2018). [Press Release]. Retrieved from https://www.newswire.ca/news-releases/a-joint-statement-from-the-pan-canadian-pharmaceutical-alliance-and-the-canadian-generic-pharmaceutical-association-671651014.html?tc=eml_mycnw

determining cost-effectiveness and willingness to pay, this is balanced with a clinical assessment in the context of reimbursement recommendations, not with the intent to evaluate price. Affordability can only be appropriately defined by the payer and consumer; the role of the national pricing regulator is to protect against excessive pricing and not to dictate a uniform definition of affordability to all payers and patients across Canada. We believe this to be significantly outside the bounds of PMPRB's mandate.

This is also clearly out of scope for a "consumer protection" mandate, given how subjective cost-effectiveness or ability/willingness to pay can be for each payer (private and public) and the patients they cover. Prices must reflect the values and preferences of the consumer, in this case Canadian patients and payers. The pharmacoeconomic assessments conducted by CADTH do not incorporate these considerations and the proposed regulatory changes make no attempt to include inputs for either of these stakeholder groups.

A cost effectiveness model is inherently subjective as it is highly dependent on the assumptions and inputs used. It is widely known that the goals of public plans are different than the goals for private plans and so their cost effectiveness (CE) considerations will be different. Indeed, in Canada, private payers, Quebec and CADTH all include different factors. Furthermore, the result of a cost-effectiveness analysis can vary significantly depending on the perspective adopted; even within Canada, different payers will require models to be submitted from different perspectives. As an example, the province of Quebec has its own HTA body that requires economic analyses be submitted based on a societal perspective. CADTH on the other hand requires models be submitted from a government public payer perspective only – hence, for the same new drug, different cost-effectiveness results will be generated.

Furthermore, it is important to note there are typically significant differences between the manufacturer-submitted incremental cost-effectiveness ratio (ICER) and CADTH-generated ICERs. For example, Forxiga (dapagliflozin) is a sodium-glucose co-transporter-2 (SGLT-2) inhibitor that was launched in Canada in 2015 for the treatment of Type 2 diabetes. At the time of launch, AZC submitted a cost-effectiveness analysis to CADTH that demonstrated Forxiga was cost-effective to the Canadian public payer, with an ICER of $25,762/QALY. CADTH used different assumptions in the same cost-effectiveness model and generated a result of up to $342,374/Quality Adjusted Life Year (QALY).

Health Canada indicated in their January 2018 stakeholder session that a $50,000/QALY threshold for primary care products was assumed in their analysis.[20] Under the current proposal, that would require a price reduction of up to 85% for Forxiga to be considered cost-effective. It is reasonable to assume that had we been required to price Forxiga at a price 85% lower than its current list price, the drug would not have been launched in Canada. Canadian patients would have been denied this important therapy which is currently helping 150,000 Canadians effectively manage their Type 2 diabetes. Forxiga is also being studied in the largest cardiovascular outcomes trial in the world, with more than 1600 Canadian patients participating.

[20] Health Canada Presentation (January 10, 2018). Proposed Amendments to the Patented Medicines Regulations (PMRs): Cost-Benefit Analysis. Slide 10.

AZC submitted cost-effectiveness	CADTH generated cost-effectiveness	Price Reduction Required to achieve $50,000/QALY
$25,762/QALY	$342,374/QALY	85%

The use of CE factors such as ICERs may also result in promising new medicines being delayed until clinical trial data is fully mature. This could particularly impact cancer patients with high unmet need. Currently, manufacturers will submit oncology products to CADTH – particularly for diseases with high unmet need like lung cancer and ovarian cancer – based on promising Progression Free Survival (PFS) data, along with immature Overall Survival (OS) data. If pricing for a new medicine was significantly reduced based on pharmacoeconomic assessment at the time of launch, AZC would likely delay our launch until OS data matures so that it would obtain a price that better reflects the true value of the product.

The examples above highlight the important gaps that are created by using such a subjective and inconsistent measure to regulate pricing. In addition, the lack of uniformity in cost-effectiveness assessments will no doubt result in delayed access to medications as the various parties attempt to reconcile information into a single reference point for the PMPRB and that patients are the most negatively impacted by the introduction of such factors.

In addition, using cost-effectiveness to determine pricing may also not always achieve lower prices. For example, medicines that reduce mortality, prevent life-threatening situations, or prevent events leading to high resource use will often result in very low ICERs. Is PMPRB proposing that the cost of these medicines would increase? Clearly not; further reinforcing that cost-effectiveness modeling is not an appropriate way to set prices.

We are concerned that Health Canada is proceeding down a path that would make it an outlier compared to all other major HTA markets. While Health Canada correctly notes in the consultation documents that other jurisdictions use cost-effectiveness as an element of drug reimbursement decision making, to our knowledge **no other jurisdiction in the world uses cost-effectiveness to set a price ceiling**. The discussion questions in PMPRB's December 2017 Guidelines Scoping Document[21] and the Health Canada stakeholder briefing in January 2018 indicate PMPRB intends to introduce a fixed QALY threshold to determine an excessive price ceiling. We strongly urge this approach to be discarded.

One relevant example which illustrates the perils of strict QALY threshold application is cancer outcomes in the United Kingdom (U.K.). It is reported that patients in the UK have more restricted access to oncology medications than in other European Union counties, which contributes to very poor patient outcomes:

[21] Patented Medicine Prices Review Board (December 2018.) PMPRB Guidelines Scoping Paper: High Level Overview of Potential New Framework. p9.

> A study of over 20 million cancer patients across the EU found survival in the UK to be worse than nearly every country in western Europe. In 9 of the 10 common cancers discussed, UK patients have worse 5-year survival rates than the European mean; UK survival rates for breast cancer and colon cancer are a decade behind other western European countries, including France, Germany, and Sweden.[22]

We also dispute that market size or GDP-per-capita are relevant or appropriate factors to consider in determining excessive price. Each are poor proxies for affordability and it is questionable whether they would be relevant at a payer level. We believe pricing should be established on discrete data, not forecasting data. We would also argue that o having PMPRB assess the affordability of products would make the role of pCPA redundant.

These new pharmacoeconomic factors are identified in the CBA as contributing the largest direct savings amount from reduced drug expenditures. This is concerning as few details about the scope and breadth of their application to current and future business are forthcoming from Health Canada or PMPRB, creating great uncertainty for our future investments and product launches in Canada.

For these reasons listed above, we are calling on the Government to postpone any further progression of the PMPRB regulations until an authentic dialogue between industry, Health and ISED occurs.

NET PRICING REPORTING

Our ability to comment meaningfully on the proposal to require manufacturers to report confidential pricing information to PMPRB is again limited by the significant lack of clarity or transparency from PMPRB related to how the information would be used.

It is evident from recent stakeholder information sessions (December 2017 and January 2018) that despite PMPRB giving no clear indication of how the information will be used, they are determined to mandate its collection. PMPRB has stated they need to see net prices to know whether prices are excessive, but this rationale makes little sense as any price lower than the excessive price ceiling set by PMPRB is, by definition, non-excessive.

PMPRB's insistence on obtaining data on net prices is a shift from a "price regulator" to a "price controller" mindset. This is clearly outside the scope of PMPRB. Moreover, the existence of Product Listing Agreements (PLA) with payers demonstrate that rebate reporting is unnecessary to ensure payers achieve value for the medicines they cover. PLAs allow manufacturers to provide broader access for Canadians by negotiating directly with payers. These confidential agreements are known to provide a further discount that reflects the value set by a competitive marketplace and the payers' willingness and ability to pay for a drug. Oversight by a price regulator is unnecessary since the discount is applied to a list price that has usually already been

[22] De Angelis R, Sant M, Coleman MP, *et al*. Cancer survival in Europe 1999-2007 by country and age: results of EUROCARE-5 – a population-based study. *The Lancet*. Published online December 5, 2013.

deemed non-excessive by the price regulator. Visibility to these discounts does not enable the PMPRB to better regulate prices and does not support or provide greater access to Canadians.

PMPRB has indicated that they would keep the net pricing information confidential. However, it is unclear how this information could be kept confidential and not used to lower the visible price. There are scenarios we can envision where net price information would be technically confidential but it would be used to reduce visible prices of a product either at launch or over time. Questions raised during the recent PMPRB Outreach Session in January 2018 highlighted that not enough consideration has been given to preventing confidential net price information being indirectly revealed.

We conclude that this would be another tool to drive towards a single price for all payers and patients. Such a rigid approach, mandated by the national regulator (who has no authority or accountability for local decision making or delivery of health care) will have real and negative consequences for new medicines and new research investments coming to Canada. It will also make it increasingly difficult for manufacturers to enter into – or remain in – PLAs with public payers.

To assume that a particular medicine has the same value across these varied populations is an assumption again not anchored in the Canadian context. In our multi-payer, multi-government Canadian healthcare context, this raises many questions about the need for PMPRB to require reporting of this net pricing information, and none of the answers serve to improve access or affordability for Canadians.

For all of the reasons listed above, we are calling on the Government to postpone any further progression of the PMPRB regulations until an authentic dialogue between industry, Health and ISED occurs.

NEW BASKET OF COMPARATOR COUNTRIES

The addition of new comparator countries in determining the price of new medicines – including Australia, Spain, Japan, and South Korea will not Canadian patients well. We would welcome the opportunity to work with Health Canada to develop a modernized reference basket that meets the Government's pricing needs while ensuring Canada's leading role in the G7 - and indeed the world - Is appropriately recognized.

The criteria and rationale to exclude the United States and Switzerland, but include South Korea and Japan are inconsistent. It is important to note that the Government of Canada is actively re-negotiating the North American Free Trade Agreement with the U.S.A. and also recently signed an agreement with Switzerland on "science and innovation that would promote growth and middle-class jobs," noting that the life sciences was a strategic sector.[23]

[23] Government of Canada (January 25, 2018). *Canada signs Joint Statement on Science, Technology and Innovation with Switzerland*. [Press Release]. Retrieved from https://www.canada.ca/en/innovation-science-economic-development/news/2018/01/canada_signs_jointstatementonsciencetechnologyandinnovationwiths.html

These are comparable countries in many respects, yet both have been removed from the proposed basket of countries included in the PMPRB12.

What is very disappointing is that all new countries in the proposed PMPRB12 basket have fewer New Active Substance (NAS) launches than Canada, and four of those countries have fewer NAS launches than the OECD median.[24] According to the PMPRB's analysis, Canada has launched 61% of new medicines, whereas Australia launched 40%, Japan 38% and South Korea 33%. Further supporting this link is independent analysis by the Canadian Health Policy Institute which shows that there is a statistically significant correlation between NAS launches and pricing environment.[25] Therefore, if Health Canada's goal is to drive Canadian drug prices to the OECD median, we should expect it will also drive new medicine launches down to the OECD median, which according to PMPRB's analysis is 45%.

The changes in the basket of comparator countries signals an intent by the Government to shift from a 1st class healthcare system to a 2nd or 3rd class healthcare system. The Government of Canada has decided to aspire to a lower benchmark for Canada's health care system. Particularly for products with few or no alternatives, patients will be most impacted in a commercial environment that does not adequately value innovation.

Canada was the 2nd country in the world (after the U.S.A.) to launch our latest cancer medicine, Imfinzi, for locally advanced or metastatic bladder cancer. Recently, AZC also achieved accelerated regulatory review for four oncology products in breast, lung and blood cancers. We were able to file these medical advances for regulatory approval ahead of other countries because Canada is currently viewed as a 1st tier country for new medicines. These are leading-edge advances in medicine that are reshaping the standard of care and saving lives. But these are the types of new medical innovations at risk of not launching here if Canada establishes a pricing regime that is arbitrary, rigid, and overall shows little value for new medical innovations.

PRIVATE PAYERS

It is well known that public and private payers tend to have different goals and cover different patient populations. Public payers tend to be concerned with more vulnerable populations, including seniors, those on social assistance and those needing catastrophic drug coverage. Private insurers tend to focus on the dynamic health needs of the working population, between the ages 18-65, including access to innovative medicines, wellness, workplace productivity and improving presenteeism/absenteeism.

Private insurers are also sophisticated for-profit financial institutions who have built-in mechanisms to adjust their assessments of risk and premium prices and remain profitable. The

[24] PMPRB 2016 Annual Report. Accessed online at http://www.pmprb-cepmb.gc.ca/CMFiles/Publications/Annual%20Reports/2017/2016_Annual_Report_Final_EN.pdf . p48.
[25] Skinner, Brett J (2017). Does Canada need a Patented Medicine Prices Review Board? *Canadian Health Policy*, October 26, 2017. Access to Innovative Medicines (AIM) series. Toronto: Canadian Health Policy Institute (CHPI).

majority of the savings to drug plans due to reducing visible list prices will only benefit these private institutions, as public payers routinely negotiate discounts below the PMPRB list price through the pCPA. Transparent net pricing, the new PMPRB12 basket and pharmacoeconomic factors will all lower prices for private insurers.

Furthermore, Health Canada openly concedes in the CBA that they cannot capture or assign any health system benefit for the savings private insurers will realize from PMRPB pricing changes. They are effectively admitting that these significant savings will benefit private insurers, with no benefits or return to the public interests of Canadians.

Private payers also have the ability to negotiate listing agreements with manufacturers to serve their clients' needs and many manufacturers, including AZC, have such agreements in place. What private payers lack is a mechanism to pass through drug price savings to individual employees or Canadians. There is no guarantee that a single Canadian under a private plan will see a reduction in premiums or out of pocket drug costs due to these reforms.

PLAs continue to be a tool used to offer a value proposition that fits payers' needs, but their utility is undermined by the proposed PMPRB reforms. Health Canada may believe these changes will increase access by lowering prices overall, however, it may do the opposite: reduce access for public drug plan patients due to an inability of manufacturers to participate in PLA pricing.

As such, the Government should not intervene to lower the input costs of one private business at the expense of another private business, with no tangible benefit to Canadian public interest. We are calling on the Government to postpone any further progression of the PMPRB regulations until an authentic dialogue with industry, Health and ISED occurs.

INVESTMENTS AND NEW R&D DEFINITION

At AstraZeneca Canada we are proud of our commitment to scientific excellence, research and discovery, the jobs this R&D supports and the lives it saves. In 2017, AZC invested more than $90 million in Canadian health sciences research, focused in cardiovascular, diabetes, oncology and respiratory disease. This represents roughly 13.9% R&D to sales ratio, however, a significant part of this investment is not recognized through PMPRB's outdated and narrow definition for R&D reporting.

Much of the rationale for modernizing the PMPRB regulations rests on the fact that they are 30 years old. Yet, Health Canada has chosen not to update the R&D reporting methods the PMPRB uses, instead remaining with a definition that is decades old and out-of-step with modern economies around the world The way our industry conducts research and delivers discoveries to patients has evolved considerably over the past 30 years, moving from 'bricks and mortar research model used 30 years ago to more external collaborations and partnerships, supporting academics and researchers, and investing in small biotechnology companies. This support comes from global and local funds, and benefits Canadian patients and the Canadian life sciences ecosystem directly.

Other government departments and agencies such as ISED and Stats Canada already use more modern criteria, based on the OECD definition, to capture the full picture of industry investment. We reiterate that the CCTG investment noted earlier would not be captured in PMPRB's outdated and narrow definition for R&D investment reporting. Ironically, nor would the recent requests for Super Cluster proposals from Minister Bains which were specifically designed to encourage innovation and R&D within Canada.

While Canada is a small market by international standards, making up only 1.9% of the global market in 2016 according to PMPRB[26], it has historically been an important destination for R&D related activities such as clinical trials. In fact, AstraZeneca Global recently selected Canada to become a global clinical hub for oncology, immuno-oncology and respiratory studies. As a result, we have tripled the size of our Clinical Study Team to more than 170 people in Canada. We are presently leading more than 30 global studies in such areas as severe asthma, and lung, head and neck cancers. In the competitive global research environment, this speaks to the quality of expertise that is housed in Canada – expertise that may migrate to more attractive research sites should future research funding be reduced as a result of PMPRB changes impacting the Canadian health/bio-sciences ecosystem.

This Global designation is a significant evolution for our company in Canada and should be leveraged to attract even more investment and clinical trials here. However, the PMPRB reforms as written will have the opposite effect and lead to reduced investment in Canada, again in line with OECD's analysis of the link between revenues and R&D investment.[27]

TRANSITION AND GRANDFATHERING EXISTING MEDICINES

When these reforms were unveiled, the Minister of Health characterized them as the "most significant suite of changes in over two decades in a comprehensive plan to protect Canadians from excessive drug prices."[28] Despite the magnitude of the proposed reforms, their wide-ranging impacts and the fundamental shifts to the Canadian biopharmaceutical and healthcare landscape they entail, there has been no meaningful dialogue with stakeholders.

It is common practice for governments to prescribe transition measures and/or grandfathering when implementing new policies or substantively changing existing ones. This is particularly important in a sector such as the innovative biopharmaceutical industry where human resource, research investment, and pricing discount decisions in PLAs are made on multi-year horizons based on a specific set of commercial circumstances, and an expectation of regulatory consistency.

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[26] PMPRB 2016 Annual Report. Accessed online at http://www.pmprb-cepmb.gc.ca/CMFiles/Publications/Annual%20Reports/2017/2016_Annual_Report_Final_EN.pdf . p39.

[27] Pharmaceutical Pricing Policies in a Global Market (2008). *Organization for Economic Coordination and Development.* Figure 6.1. Accessed online at http://www.keepeek.com/Digital-Asset-Management/oecd/social-issues-migration-health/pharmaceutical-pricing-policies-in-a-global-market_9789264044159-en#page192

[28] Government of Canada (May 16, 2017) *Government of Canada taking action to protect Canadians from high prescription drug prices.* [Press Release]. Retrieved from https://www.newswire.ca/news-releases/government-of-canada-taking-action-to-protect-canadians-from-high-prescription-drug-prices-622584484.html

As outlined above, any one element of the proposed PMPRB changes could have significant impacts and unintended consequences on the sector, and so transition measures must be included as part of any reform package. This is underscored by the accelerated implementation timeline proposed as well as the complexity of operationalizing any new price evaluation or reporting requirements.

We note that while the overall revenue reductions could be 20-30% industry-wide, individual product price reductions based on OECD median prices could be much greater. Such drastic changes would result in immediate negative consequences to jobs and investment, delays in launching new innovations and potential removal of products already here.

Given these points, we again call on the Government to postpone any further progression of the PMPRB regulations until an authentic dialogue between industry, Health and ISED occurs. Any changes would need to be accompanied by transition measures to ensure continuity of care for Canadians and that investment decisions made in good faith on a current set of rules are not undermined by unilateral action.

PATH FORWARD

As a physician who has cared for dying cancer patients, and as a researcher who has discovered new therapies, I cannot stress enough the importance of the innovative biopharmaceutical sector to our individual quality of life and our collective social and economic wellbeing. As a Canadian I want to see this sector thrive and be an even bigger contributor to Canada, but this is all at risk if we continue on the course set out by CG1.

The underlying assumptions and rationale in the RIAS and CBA are inaccurate and incomplete. Significant regulatory changes are being rushed through on an accelerated timeline with no guarantee that they will solve any of the access or affordability issues identified by the Government. In fact**, it is not clear what problem the Government actually hopes to solve through these reforms, as much of PMPRB's own analysis demonstrates there is not a crisis in drug pricing or access in Canada.**

We do appreciate that there is a desire on the part of Canadians to see some form of action taken to improve access and affordability of new medicines. We want to improve those things too.

However, the fundamental changes proposed to the mandate and operation of the Patented Medicine Prices Review Board (PMPRB) warrant an in depth and reciprocal dialogue between Government, stakeholders and industry. This has not occurred to date.

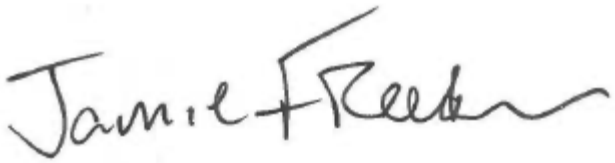
Therefore, we call on the Government of Canada to:

1. **Postpone implementation of any element of the draft regulations until a full impact analysis can be undertaken, modelled in the context of the Canadian health system and life sciences ecosystem;**

2. **Establish a table with representation from the innovative biopharmaceutical industry, the Ministry of Health and the Ministry of Innovation, Science and Economic Development (ISED) to jointly develop solutions to attract innovation and improve access, affordability, and appropriate use of medicines for Canadians.**

I am extremely proud of the daily impact AZC employees have on the lives of Canadians. That is why I am so concerned that these PMPRB reforms are moving us in the wrong direction: delayed and/or denied access to innovative medicines, less R&D investment, fewer knowledge economy jobs, and poorer health outcomes for Canadians. We believe Canada should aspire to more, and we want to be part of the solution to ensure that is the path forward.

Sincerely,



Dr. Jamie Freedman, MD, PhD
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