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Karen Reynolds, Executive Director
Office of Pharmaceuticals Management Strategies
Strategic Policy Branch
Health Canada
Brooke Claxton Building, 10th Floor
70 Colombine Driveway, Tunney's Pasture
Ottawa, Ontario K1A 0K9

Re: **Shire Canada Response to Canada Gazette, Part I published December 2, 2017, Regulations Amending the Patented Medicines Regulations**

Dear Ms. Reynolds,

I am writing this submission to the consultation process currently underway regarding the Regulations Amending the Patented Medicines Regulations published in Canada Gazette, Part I on December 2, 2017. We have significant concerns that the regulations as proposed will have negative consequences to both the pharmaceutical industry and to patient care. We urge Health Canada to engage a cross section of health stakeholders to work together to build solutions that meet our mutual goals of accessible and affordable care.

Shire works to enable Canadians with life-altering conditions to live better lives. Founded more than 30 years ago, we believe we have a unique opportunity to champion underserved patient communities. Today, as the global leader in rare diseases, we are determined to build on this foundation as we go forward.

Shire has been present in Canada since 1999. Today, we have over 200 employees, with our place of business recently relocated to downtown Toronto. Shire Canada focuses on the areas of Hematology, Immunology, Neuroscience, Ophthalmics, Lysosomal Storage Disorders, Gastrointestinal/Internal Medicine/Endocrine, Hereditary Angioedema, and Oncology.

Patients living with rare disease deserve timely treatment. Half of those living with rare disease are children, and 25% of those will not live to see their 10th birthday. Only 60% of treatments for rare disorders make it into Canada and most get approved six years later than in the USA and Europe. This results in a significant number of Canadian patients with a debilitating rare disease living without access to treatments that could save or significantly improve their quality of life and prolong their life expectancy. We believe that the proposed regulations in Canada Gazette Part I will have unintended consequence of adding to this delay in access for many therapies, including those specifically for rare diseases.

Today, the major policy concerns raised by federal and provincial health ministers focus on the "affordability, accessibility and appropriate use" of pharmaceuticals. These factors are interrelated. We support these objectives and conduct our business with patient-centricity at top of mind. The proposed amendments to the Patented Medicines Regulations attempt to address only the affordability component of broader policy issues; if addressed in isolation, there is risk that a policy change in this area will produce

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unanticipated and negative impacts on patients and other elements of the life sciences ecosystem.

Shire and many other stakeholders have made submissions in response to the May 2017 consultation document for consideration when drafting regulations. While the receipt of these submissions is acknowledged in the RIAS (Regulatory Impact Assessment Statement) and Health Canada's CBA (cost benefit analysis) document (September 8, 2017), they have not been reflected in the CG1 regulations. Contrary to the purpose of consultation, the Proposed Regulations are nearly identical to the proposals in the initial consultation document with the exception of some minor changes regarding international filing requirements and other modest modifications. The lack of meaningful consultation is concerning to those who contribute to the life science ecosystem, and to those who benefit from it.

Shire is concerned that the RIAS and CBA grossly underestimate the impact of change on the overall ecosystem as the impact of some of the significant components of proposed regulations have not been fully examined. Furthermore, the impact only seems to have been calculated with a siloed approach rather than in a holistic context. To that end, we believe, Health Canada should consult further with FPT drug programs and agencies and other stakeholders to build solutions for drug pricing reform in a broader context than looking only at the PMPRB.

As noted in its June 2017 submission, Shire strongly opposes the proposal to use pharmacoeconomic analyses (PE) to regulate prices of pharmaceutical agents in Canada. The prolonged timeframe to confirm a price coupled with the uncertainty of PE results make this element of the proposed regulations untenable. We believe pharmacoeconomic evaluation in a price review is outside of the scope of the PMPRB mandate and would create unnecessary overlap and duplication with CADTH and INESSS. There are numerous underlying assumptions that contribute to an HTA assessment, and this often results in a wide range of results. Currently, health technology assessments (HTA) by CADTH and INESSS are conducted to inform the reimbursement processes of the participating public drug programs; HTA assessments for private payers may differ, as they must be tailored to the perspective and needs of the plan sponsor. Such duplication, or misplacement of the PE analysis use, would delay or reduce the overall availability of innovative medicines in Canada, in addition to inefficient use of resources.

The role of PE during the HTA process is to inform the stakeholders regarding decisions around a combination of factors including but not restricted to patient population, healthcare system costs and the clinical data present. There is considerable uncertainty in PE analysis around any pre-specified cost per QALY threshold based on interpretation of underlying clinical data, uncertainty of benefits (utilities) and measurement of relevant costs. Uncertainty extends to other health economic evaluation variables like perspective (heath care vs. societal), time horizons, indications and relevant confidence levels of the data. Utilizing PE as a factor in price determination can produce establishment of a maximum non-excessive price open to interpretation without a concrete set of calculations (rather based on assumptions, such as data generalized from non-Canadian sources to a Canadian population).

Furthermore, PE analysis may bias against a favorable assessment of severe conditions

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with great unmet need and small patient numbers. With the small population in rare diseases, it is difficult to generate the level of evidence required to demonstrate relative and cost-effectiveness[i]. PE analysis and Incremental Cost Effectiveness Ratios (ICERs) should be adapted to consider values such as disease severity, unmet need (availability of alternatives), disease prevalence, public policy choices and societal preferences.[ii] Evaluations of rare disease medications need to take into account a different set of benefits or value than simply a cost-effectiveness threshold. Many countries (UK, France, Germany, Italy and Sweden) have recognized that the usual methods of health technology assessment are inappropriate and have introduced pricing and reimbursement exemptions for rare and serious diseases. Patients living with rare disease could have more restricted access to therapies if cost effectiveness were introduced as a component to the PMPRB's price review.

These proposals have far-reaching and significant impact. We believe the current consultation process is too short given the complexity of the issues and potential impacts on the regulated industry, patients, public and private payers, and ultimately, access to health care. To that end, we invite Health Canada to undertake a thorough analysis of the impact of the proposals with consultation from stakeholders, including other federal departments, share them in a transparent manner, and carefully review all the unintended consequences of the proposed regulatory changes before moving ahead with the process that is underway. We also propose that any new regulations should only be applicable to new medicines. Existing medicines should continue to be guided by current regulation and guidelines. Furthermore, we propose to postpone the implementation of these regulations until at least two years after the guidelines are finalized and enacted, as our pricing strategies for soon to be approved medicines are finalized at least 24-36 months in advance.

We appreciate the opportunity to contribute to this important consultation and look forward to further meaningful opportunities as policies are refined to reflect the input that has been provided by multiple stakeholders.

Sincerely,

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[i] Tordrup D et al. RARE Journal 2014;1(3):83–97
[ii] Gutierrez et al. 2015