February 14, 2020

Mr. Doug Clark
Executive Director
Patented Medicine Prices Review Board
Standard Life Centre, Suite 1400
333 Laurier Avenue West
Ottawa, Ontario K1P 1C1

Submitted electronically: PMPRB.Consultations.CEPMB@pmprb-cepmb.gc.ca

RE: SANOFI Canada Comments - PMPRB Draft Guidelines Consultation

Dear Mr. Clark:

SANOFI Canada (SANOFI) is one of the leading innovative biopharmaceutical companies in Canada. With an extensive and diversified product portfolio serving Canadian patients, SANOFI Canada has been a proud local and global health partner. From working with the University of Toronto on the manufacturing of insulins and addressing Diphtheria in the early 1900s, to the eradication of smallpox and global polio eradication efforts, our contributions in recent decades has continued thanks to partnership with various Canadian health agencies.

Our work in Canada spans the production and distribution of vaccines (nationally and to more 80 countries worldwide annually), important advancements in cardiovascular treatments, insulin therapy for patients with diabetes, innovation to patients struggling with cancer, multiple sclerosis, immunological conditions and treatments for rare diseases and rare blood disorders. During the next 5 years, SANOFI aims to bring even more therapeutic innovations to Canada, with at least 15 planned new medicines for patients suffering from illness and disease.

SANOFI is also proud to have maintained the largest and most consistent investment footprint in Canada from our sector – a figure which reached $120 million in 2018. Over and above this ongoing commitment, SANOFI was proud to secure a landmark global investment in 2017 of $570 million towards our Sanofi Pasteur Building 100 project – the largest single investment in Canadian life sciences history.

SANOFI is sensitive to the challenges facing the Canadian health system. A growing and aging population will continue to cost more and savings in the systems are required to ensure sustainability. Our industry has created many innovations for patients, helping them to live longer and more productive lives. Despite these innovations, drug costs have moderated or even fallen in some areas as patents expire and generic medicines enter the market[1], creating opportunities to integrate new and beneficial treatments into patient care. All stakeholders have a contribution to make to the overall sustainability of the system, while maintaining a focus on safeguarding the ability for patients to access the medicines they need.

Currently, Canada is an attractive place to invest for our sector with world-class doctors and scientists, clinical researchers, a diverse population base, and a legal and policy framework which encouraged a

[1] E.g. *Prescribed Drug Spending in Canada, 2019: A Focus on Public Drug Programs*, Canadian Institute For Health Information, December 17, 2019, pp. 12-13.

predictable market reflective of the long-term risks that are an inescapable reality of our business model. For example, we are proud that Canada was the first in the world to enrol patients in two new important Phase III clinical trials for our company in 2019.

It is against this context that we would like to offer solution-oriented comments to the PMPRB with respect to its ongoing efforts to modernize its Guidelines. SANOFI remains an active member of our industry associations, Innovative Medicines Canada and BIOTECanada, and fully endorses their submissions on this matter. On a complementary basis, we also feel it is important for all individual companies to express concrete examples of the challenges we face with implementing these proposed Guideline adjustments given our experience with different therapeutic areas and different product portfolios.

In this submission, SANOFI provides specific examples of challenges with the proposed Guidelines, potential impact to Canadians, and some solutions for PMPRB to consider in the areas of rare disease treatments, oncology treatments, vaccines, and stable supply of currently available medicines.

Example 1: Drugs for Rare Diseases

SANOFI pioneered and has a proud history in the research and development of drugs to treat rare disorders. Until recent times many of these diseases escaped diagnosis and treatment. Fortunately, many Canadian patients (including children) are today able to lead longer and productive lives because of the innovative treatments that have been developed and made available in Canada. We acknowledge the challenges being experienced by payers to identify an appropriate balance between providing timely coverage for patients in need of access to treatments while operating within the boundaries of finite healthcare budgets. We have successfully worked with governments in Canada over many years in finding appropriate and workable solutions to these challenges that serve the patient interest.

There is widespread agreement among economists and policymakers that the traditional approaches to health technology assessment (HTA) are inappropriate for the examination of drugs for rare and ultra-rare diseases. Clinical data is often limited, there may be no recognized standard of care, and patient populations are smaller, all of which challenges the use of clinical assessment and cost-effectiveness models.

As a result, throughout Europe and elsewhere, more innovative approaches to reimbursement and evaluation of these products are being developed and applied. Canada remains an outlier among developed countries in not having an established rare disease drug framework. Despite this, the federal government recently announced new funding for drugs for rare diseases. Key details are still yet to be determined, but the new funding should be available within the next two years. In addition, the Provincial-Territorial Expensive Drugs for Rare Disorders (EDRD) Working Group has explored options for a supplementary process for the assessment of rare disease drugs in recognition of the limits of existing HTA tools.

The proposed PMPRB Guidelines approach to managing the pricing of such drugs in Canada is rooted in a highly regulated approach based on the use of traditional HTA analyses. SANOFI would submit to PMPRB that this approach is inappropriate and unworkable, rooted in the discipline's fundamental unpredictability and the PMPRB's own case studies which suggested price reductions so dramatic that they would threaten the viability of commercializing many products. Understanding the limitations of using pharmacoeconomics in isolation of other relevant factors, the CADTH HTA process attempts to incorporate several other factors within a deliberative framework to determine whether a given product should be recommended for funding. These include unmet need, burden of illness, clinical evidence, quality of life metrics, patient values, clinician input, provincial input, adoption feasibility, and implementation considerations, in addition to economic evidence. These additional important factors are not adequately reflected within the PMPRB's approach to its Guidelines, which focus narrowly on cost alone.

The proposed approach is also inconsistent with best global practices in the funding and reimbursement of drugs for rare diseases. A major reworking is required to avoid the counterproductive outcome of new products for rare disease being delayed or deferred with corresponding impacts on patient care in Canada. It is inescapable that without effective therapies, many patients with a rare disease will die.

Consider the case of a new innovative therapy for a rare condition for which there is no recognized comparator – the kind of innovation which provide a high value to patients living in hope of access to treatment for their condition. First-in-class products of this type are often subject to increased uncertainty due to limited evidence. This would likely result in an HTA analysis recommending a substantial decrease in price. Even applying a "pharmacoeconomic premium" to a steeply discounted price, as contemplated by the proposed Guidelines, would be grossly insufficient to make the availability of the first-in-class product feasible. We believe this result is counterproductive and the worst possible outcome for the Canadian patient who may have no other therapeutic option.

- **Under the circumstances, we recommend that the PMPRB place any proposed guidelines as they would apply to drugs for rare diseases on hold, pending further development of (1) the federal funding initiative, (2) the provincial rare disease assessment initiative, and (3) a comprehensive review of best global practices for funding and reimbursement in other countries. SANOFI would be pleased to contribute to any open policy development process focused on appropriate price regulation options for rare disease medicines. In the interim, rare disease medicines will continue to be subject to all other regulatory requirements, including international price comparisons and reporting obligations to PMPRB.**

Example 2: Oncology

We have reviewed and analyzed the proposed guidelines in considerable detail with respect to their application to oncology products. Oncology is a key therapeutic area for SANOFI. Every day, we are seeing new advances in developing targeted treatments for various cancers that previously were inadequately treated or deemed untreatable. More Canadian cancer patients are now living longer with improved quality of life as a result of new oncology medicines, and the potential for further advances in the coming years is significant. Many of these advances include novel combination therapies in response to an increased scientific understanding of the complex pathology of many cancers.

By way of specific illustration, in some treatment contexts, a newer oncology medicine may be combined with either a second innovative treatment or an older, more established medicine. For purposes of informing public reimbursement of the new combined product, both CADTH and INESSS conduct HTA reviews and make recommendations for decision-makers. The HTA reviews take various considerations and criteria into account to evaluate the potential place in therapy and coverage of the combined treatment regime.

The proposed Guidelines will place significant emphasis on the narrow application of pharmacoeconomics to determine the maximum rebated pricing for many new oncology medicines as an up-front regulatory tool. Under the proposed Guidelines as written, the prices for some oncology treatments could be reduced to dramatically lower levels. In some cases, the mechanistic approach of the Proposed Guidelines would require that the medicine be sold free of charge, in order to meet an artificial and inappropriate cost-effectiveness threshold. By any reasonable, common sense standard, this type of regulatory barrier would result in an inability to commercialize a new treatment in Canada, further challenging those oncology patients in need of access to these treatments.

Determining the cost-effectiveness of combination oncology products does not translate well to the PMPRB's desire to establish a non-excessive price for the combined medicine under the proposed Guidelines. Different parts of the combination product may be subject to very different compliance standards as a function of time on the market and patent status. Unfortunately, the proposed Guidelines provide no additional guidance or clarity as to how the PMPRB would manage such real-world product circumstances (e.g. through the provision of detailed case studies). This information gap significantly reduces SANOFI's ability to predict the pricing approach for a new combination oncology treatment,

reducing the likelihood that our global operations will sanction a timely launch in Canada vs. other global markets which offer greater levels of regulatory clarity and certainty. Canadian patients will therefore be denied access to the latest advances in life-saving cancer treatments.

PMPRB has already acknowledged that both CADTH and INESSS will need to modify some of their methodologies and practices in order to accommodate the implementation of the proposed Guidelines. However, it is unclear at this juncture what specific changes PMPRB would be seeking to those other agency procedures, and we have no indication that either CADTH or INESSS has confirmed that such modifications are possible or appropriate.

As was already raised by the PMPRB'sTechnical Working Group, there is no apparent consensus in Canada on the appropriateness of applying pharmacoeconomic tests, nor on the most advisable methodologies to be applied, for the purposes of regulatory price-setting. It is for these fundamental reasons that no other international jurisdiction attempts to establish a regulated price based on pharmacoeconomics. Instead, HTA analyses (such as those conducted by CADTH and INESSS) which include pharmacoeconomic and other important analyses are used with the very clear purpose of helping to inform the overall decision-making of payers in their negotiations with suppliers on appropriate reimbursement terms and conditions.

- **In light of the significant uncertainty with respect to the future regulation of oncology products, we recommend that PMPRB set aside the application of pharmacoeconomic analysis to establish a maximum rebated price for oncology products in its Guidelines or, in the alternative, to defer development of such Guidelines until a more thorough review is conducted in consultation with all oncology stakeholders.**

Example 3: Vaccines

SANOFI is a global leader in the research, development and provision of innovative vaccines. Canadian governments have long recognized the value of vaccines to safeguarding public health and have developed specific and effective procurement programs to manage access to vaccines under acceptable terms and conditions.

To a large extent, publicly funded vaccines are supplied to Canadians through a structured evaluation and tendering process, with governments acting jointly to consolidate demand to ensure a balance between ensuring adequate supply at a competitive price. This market structure concentrates purchasing power through the federal Public Services and Procurement Canada (PSPC) agency, exposing vaccine suppliers such as SANOFI to rigorous and competitive requirements in order to secure access to Provincial immunization programs. In fact, the criteria in these contracts awards the bidder with the lowest price the majority share of the volume.

Under the terms and conditions of the PSPC tenders, volume awards are based on the relative price differential between the bidders with the two lowest bidders being awarded a split of the volume based on price, with the lowest of the two getting the majority share. As an example, a recent tender for an adolescent vaccine was issued to three manufacturers. The terms of the tender clearly indicated that only two suppliers would be awarded portions of the national demand. Additionally, in the Province of Quebec, the lowest bidder is awarded 100% of the tender. These approaches to vaccine procurement effectively eliminate the risk of excessive pricing by incentivizing competitive bids due to the large volumes and long-term nature of these public contracts. Prices are often locked in for 3 to 5 years due to the duration of the contracts, further preventing the possibility of significant price increases.

The reality of this operating environment means that vaccine manufacturers are subject to robust and highly effective checks which favour the purchaser by encouraging competitive pricing. Subjecting vaccines to the equivalent requirements as other patented medicines is therefore unwarranted and would only serve to substantially increase the regulatory burden on vaccine manufacturers with no actual or perceived benefit to Canadian consumers, including governments.

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In their current form, the proposed Guidelines provide no additional benefit to Canadian patients or purchasers of vaccines, while only increasing uncertainty and introducing new (and unnecessary) barriers to the future availability of vaccines for Canadians.

- **In light of existing reimbursement mechanisms and market circumstances, SANOFI would therefore recommend that the PMPRB apply a sound and explicit risk-based approach for vaccines by specifying their exclusion from the proposed Guidelines.**

Administrative Burden and Maintaining Stable Supply of Medicines

The current scope and complexity of administrative arrangements in Canada governing the pricing and reimbursement of medicines and vaccines are immense. The 2017 PMPRB Annual Report identified 1,311 existing patented medicines on the Canadian market. The overwhelming majority of these are subject to various contracts and other terms and conditions as a function of their reimbursement by both public and private payers. As a mechanism, Product Listing Agreements (PLAs) are utilized by many public jurisdictions to manage coverage terms and conditions. Similar tools exist and are increasingly being applied by private insurers to reimburse new medicines.

As each of these individual agreements can take months to arbitrate, it is important to highlight the increased administrative burden and risk to stable supply. Starting July 1st, 2020, Provinces and the private insurance industry must implement changes to the PMPRB Guidelines. To facilitate this, months of legal and administrative work will be required to update hundreds of agreements made over the past 10+ years. In SANOFI, for example, this could mean as many as 300 individual agreements to be secured with Provinces and private payers. This activity, in parallel to other manufacturers will put a massive strain on an already stretched administrative system. We fear that sufficient time has not been granted to patentees, nor the provinces or private payers who may not be equipped to manage this complexity, risking stability of supply of important medicines.

During the course of regulatory policy development and the drafting of updated Guidelines, we have been struck at the evident lack of consideration of many of these practical issues and the absence of sufficient case studies to illustrate the operation of the proposed approach. We would encourage the PMPRB to return to your initial aspiration to advance a modern, risk-based and "bright-line" approach. Fortunately, there is still some opportunity to make much needed adjustments in the Guidelines to realize a more predictable, efficient and effective pricing regime. The current proposals are far from the only available mechanisms to implement the recently adopted regulatory amendments for the PMPRB's mandate and role.

At SANOFI, we remain steadfast in our objective to ensuring Canadian patients are afforded timely access to our innovative medicines and vaccines. Accordingly, we strongly encourage the PMPRB to revisit its proposed Guidelines in the spirit of increased workability and clarity, alignment with best global standards, and protecting the interests of Canadian patients who depend on access to current and future innovative treatments for their health and quality of life.

We would be pleased to discuss the content of this submission with you and PMPRB staff at your convenience.

Sincerely,

Michael Mullette
President & CEO
Sanofi Canada