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Regulatory Decision Making in Canada—Exploring New Frontiers in Patient Involvement

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ABSTRACT

Recent legislative amendments aim to enhance the transparency of the regulatory review processes about drugs, and provide public information about Health Canada's review decisions. There is also growing recognition of the value, with respect to regulatory benefit-risk assessment, of information that could be gathered from patients—the direct users of these products. Patients can provide unique insights into practical aspects of living with their disease and its treatments—as well as gaps in treatment needs. An enhanced understanding of patients' experiences and perspectives can contribute directly to better-informed decision making about these products by regulators. Health Canada is currently exploring and examining the most effective ways to collect and consider patient input in the evaluation of therapeutic products. As part of this process, Health Canada is assessing the suitability of other existing models through environmental scans, discussions with other health authorities, and pilot projects. Lessons learned from these models can inform best practices and opportunities for patient involvement when designing a model to meet Canada's needs and context. Health Canada launched a Patient Involvement Pilot Project in 2014 to simulate how input from patients, their caregivers, health care professionals, and patient groups could be collected and incorporated in the drug submission review process. This ongoing experience and continuous learning will define better how to incorporate patient input into benefit-risk assessment and regulatory decision making throughout the life cycle of therapeutic products in Canada.

Keywords: benefit-risk, health policy, patient-centered care, therapeutic products, regulatory review.

Introduction

Health Canada's Health Products and Food Branch is the national regulatory authority responsible for evaluating and monitoring the quality, safety, and efficacy of therapeutic products in Canada. Regulatory benefit-risk assessments underpin Health Canada's decisions across the life cycle of a therapeutic product. These assessments are based on core evidence and judgments regarding the intrinsic, practical value of each drug's potential positive effects, in contrast to their potential negative effects, in treating disease in real life.

Given their direct experience of disease and treatments, patients and their caregivers are increasingly recognized to be in a unique position to enrich traditional drug development and regulatory communities' understanding of drug performance measurement, value, and context, from early drug development and clinical trials planning stages onward. At the same time, as patients and their caregivers become increasingly interested in and knowledgeable about their diseases and available treatment options, a cultural shift has arisen that requires enhanced transparency and timely access to information on therapeutic products [1–3]. This demand has been associated with a desire to have an input into the regulatory evaluation of these therapeutic products.

Although regulators agree that patient involvement is important, how, when, and to what extent to use patient input effectively in benefit-risk assessment continues to be an evolving field and regulators are at various stages of maturity in this process. Furthermore, the nature and scope of patient information that could be gathered is also still in early days of development. The current use by stakeholders of numerous terms to describe the concept of patient feedback, with incompletely overlapping meanings—for example, involvement, engagement, input, voice, experience, participation, perspectives, and preferences—reflects the potential scope and diversity of envisaged input, as well as the breadth of possible engagement approaches.

Canadian Context

In Canada, recent legislative amendments and the introduction of Health Canada's Regulatory Transparency and Openness Framework aim to enhance the transparency of the regulatory review processes, and to provide public information about Health

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Canada's review decisions [2,4]. These modernization initiatives also provide opportunities to advance in the area of seeking and considering patient perspectives throughout the life cycle of therapeutic products.

Canada already has an established practice, albeit implicit and often *ad hoc* thus far, for including patient perspectives in both operational and policy-based regulatory decision making.

Health Canada is also extending its efforts to explore the most effective ways to involve patients in the benefit-risk assessment of therapeutic products to meet this country's needs, taking into account geographic, demographic, and resource considerations [5]. Public knowledge about the activities of other regulators, such as the US Food and Drug Administration and the European Medicines Agency, and Health Canada's involvement in various international regulatory activities to align regulatory frameworks place additional expectations about incorporating patient perspectives in the regulation of health products. However, given the legal system and environment in various countries, differences may exist in how alignment of such regulatory frameworks is to be accomplished.

Canadian Examples of Patient Involvement

Scientific/Expert Advisory Committees

Historically, patient advocates have been serving as members of Health Canada's standing Scientific and Expert Advisory Committees. Patient advocates, along with all other committee members, are educated on the regulatory process so that they may understand the scientific as well as the regulatory context within which Health Canada makes decisions.

These therapeutic area–specific or therapeutic class–specific committees meet to provide medical, technical, and/or scientific advice, as well as practical and contextual perspectives, to help resolve issues related to regulating these therapeutic products.

In addition, Health Canada may ask patient advocates to participate on ad-hoc Expert Advisory Panels that it establishes on an as-needed basis to provide advice on specific drug submissions or on emerging and/or controversial issues that arise postmarket. Examples where Health Canada has included patients in such deliberations include 1) an expert panel to advise on the use of insulin of animal origin and its place in the treatment of type 1 diabetes mellitus; 2) a public forum on selective cyclooxygenase-2 inhibitor nonsteroidal anti-inflammatory drugs; and 3) focused consultation with patient safety groups to discuss risk minimization options regarding acetaminophen overdose and liver injury. Such activities provide targeted opportunities for patient participants to learn about the review process and to help inform decision making. Health Canada can use these opportunities to explore both potential outreach strategies, such as online engagement and face-to-face meetings, and administrative/governance structures, such as multistakeholder steering committees, to focus and optimize next steps for public involvement.

Patient Involvement Pilot Project

Health Canada also launched a Patient Involvement Pilot Project in 2014 that explored the value and feasibility of such input specifically in the orphan drug context. Given the limited information that is known about rare diseases and the fact that patients may be experts on their own diseases, orphan drugs may present a good starting point for providing systematic, structured opportunities for patients to help inform Health Canada's benefit-risk assessment and the management of these products. The Pilot Project simulated how input from patients, their caregivers, health care professionals, and patient groups could be collected and incorporated in the drug submission review process [5].

Input was sought through an e-mail sent to known patient groups and health care providers. The e-mail notified the groups about the pilot, provided access to online questionnaires, and requested them to identify patients who would be willing to participate. There were four online questionnaires, one for each of the patient definition subgroups— patients, caregivers, health care professionals, and patient groups. E-mail links to the questionnaires were then sent to patients and caregivers who were identified as either living with the target rare disease/disorder or providing care for someone who was. The questionnaires were designed to gather qualitative information on the following:

- the impact of a rare disease on an individual patient's quality of life;
- their experience with currently available therapies (e.g., experience with providing care for patients using the drug under review or personal experience with the drug), if any;
- unmet medical need (e.g., does the drug under review fulfill any unmet patient needs that have not been sufficiently addressed by other drugs or treatments); and
- the patient's level of risk tolerance (e.g., what type of adverse effects or potential risks/harms would a patient be prepared to live with).

The pilot applied to two drugs, one biologic and one pharmaceutical, and was implemented at the stage of application for market authorization. Preliminary results from the Pilot Project include the following:

- Patient education on regulatory review and decision-making processes and reviewer training on when and how to best consider patient input in these processes is needed.
- The timing of when reviewers receive patient input is important because the review process is subject to strict performance targets.
- Additional experience would be valuable because the Pilot Project involved only two drugs.

Opportunities and Future Prospects

Current legislative and regulatory modernization initiatives in Canada present opportunities to establish criteria and programs for when and how to engage patients, as well as optimize the nature and value of their input. Innovations in drug development, regulatory science, and big data [6] both here in Canada and abroad can also be leveraged to optimize the collection and assessment of the diversity of patient experiences, both positive and negative, across product life cycle. Last, the rising tide of empowered patients who are increasingly forging strong collectives and seizing innovations in patient-centered research initiatives and social media technology—and who are willing and eager to add their voice to discussions with regulators and other institutional decision makers—will greatly facilitate regulatory developments.

Building on the experience gained from the Patient Involvement Pilot Project and existing *ad-hoc* patient input mechanisms, Health Canada is currently determining the best ways to elicit and consider patient input in a systematic manner in its drug regulatory review process and is exploring the scope and nature of patient input that could be of highest value. A structured framework could aid in transparent decision making about when, on a case-by-case basis, to consider patient perspectives in