Health Canada Santé Canada

Canada

What we heard: A summary of scanning and consultations on what's next for health product regulation

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YOUR HEALTH AND SAFETY... OUR PRIORITY.

1.0 INTRODUCTION AND CONTEXT

Scientific and technological advances are accelerating the pace of innovation. These advances are increasingly leading to the development of health products that are better able to predict, define, treat, and even cure human diseases. Globally, many factors are driving regulators to think about how to enable health innovation. To this end, Health Canada has been expanding beyond existing partnerships and engaging both domestically and internationally. This expanding landscape of products and services comes with a range of new challenges and opportunities.

In keeping up to date with emerging technologies and working collaboratively through strategic partnerships, Health Canada seeks to position itself as a regulator at the forefront of health innovation. Following the targeted sectoral review of the Health and Biosciences Sector Regulatory Review consultation by the Treasury Board Secretariat, Health Canada held a number of targeted meetings with a broad range of stakeholders.

This report outlines the methodologies used to look ahead at the emerging health technology environment, the potential areas of focus that resulted, and the key findings from consultations.

2.0 METHODOLOGY

To better understand the evolving healthcare landscape, Health Canada conducted an environmental scanning exercise. Methods used to scan the scientific, international, economic, social, environmental, and technological landscapes included:

- Reviewing scientific research, published literature, and reports;
- Scanning relevant media;
- Engaging directly with a range of experts; and,
- Working collaboratively with international regulators.

From this scan, the Department identified the following key drivers that are expected to shape the future of health innovation:

1. **The use of "big data" to inform decision-making:** Health systems are generating more data, and becoming reliant on this data. The increasing accuracy, types, and volume of data available in real time enable automation and machine learning that can forecast activity, behaviour, or trends to support decision-making.
2. **Greater demand for citizen agency:** Canadians increasingly want and have access to more information, resources, options, and platforms to manage their own health (e.g., mobile apps, direct-to-consumer services, decentralization of care).
3. **Increased precision and personalization in health care delivery:** Diagnostic tools and therapies are increasingly able to target individual patients with customized therapies (e.g., individual gene therapy).
4. **Increased product complexity:** Increasingly complex products do not fit well within conventional product classifications and standards (e.g., 3D printing).

5. **Evolving methods for production and distribution:** In some cases, manufacturers and supply chains are becoming more distributed, challenging the current framework governing production and distribution of health products.
6. **The ways in which evidence is collected and used are changing:** The processes around new drug innovation, research and development, and designing clinical trials are evolving in ways that are more flexible and adaptive.

With these key drivers in mind, the Department selected the following six emerging technologies for further investigation to better understand how the health product space is evolving:

1. **Artificial intelligence**, including activities such as machine learning, neural networks, natural language processing, and robotics.
2. **Advanced cell therapies**, such as individualized cell therapies tailor-made to address specific patient needs.
3. **Big data**, from sources such as sensors, genetic information, and social media that are increasingly used to inform patient and health care practitioner decisions.
4. **3D printing** of health products (e.g., implants, prosthetics, cells, tissues).
5. **New ways of delivering drugs** that bring together different product lines and methods (e.g., nano-carriers, implantable devices).
6. **Gene editing**, including individualized gene therapies that can assist in preventing and treating certain diseases.

Next, to test the drivers identified and further investigate emerging technologies, the Department consulted key organizations and thought leaders across the country with expertise in health innovation. To this end, Health Canada held seven workshops with over 140 representatives from industry associations, small-to-medium sized enterprises and start-ups, larger multinational companies, investors, researchers, and clinicians in Ottawa, Toronto, Montreal, and Vancouver. To tap into these groups, Health Canada collaborated with several incubator organizations that support a broad range of health innovations and are working to address the commercialization gap. Discussions focused on challenges with the current system in the context of innovation, as well as the emerging technologies and the issues they are likely to present.

3.0 KEY FINDINGS

Conversations with stakeholders made it clear that advances in science and technology, innovative health products, and health system transformation go hand in hand. Further, the paradigms around the type of care, how, where and when it is delivered, and who delivers it are shifting.

Stakeholders emphasized that innovations in health products – including the new ways the products are designed, manufactured, and used – challenge the existing framework in a number of ways.

3.1 Product classification tools need to evolve to respond to changing environment

In the current regulatory framework, health products are classified as a drug or a device. Within these categories there are further sub-classes and product lines, including recognition that some may be combination products.

Consultations revealed the importance of providing transparency around how classification decisions are made. Stakeholders also noted that new technologies are challenging current product classifications. The increasing convergence of drugs, devices, diagnostics, biologics, artificial intelligence, and other types of advanced technologies is likely to further complicate classification schemes.

Having a transparent classification scheme would provide clarity in terms of which regulatory framework(s) apply, including rules around safety, efficacy, and quality. Such a scheme would enable for a higher level of certainty for developers and investors. Stakeholders also emphasized that having a clear understanding of requirements is essential for the development and testing of products well before seeking market authorization.

In particular, stakeholders identified specific challenges with artificial intelligence-based clinical decision support tools and models that are procedure or service based (i.e., involve providing a subscription service or platform rather than selling a specific product or technology). New service models confirm that it can be the nature of new business models, not necessarily the product itself, that present the most challenges in classifying a new product.

Case Study: New Ways of Delivering Drugs

Novel techniques for the administration of drugs can challenge our traditional classification models because of the ways that they bring together different product lines and methods. Products that use technologies such as nano-carriers, drug delivery augmented with photo-, magnetic-, radio-, or other stimulation or carriers such as exosomes and microbes, are enabling new ways to delivery therapeutic products to specific sites in the body. These innovations are making delivery more precise and less risky to healthy cells.

3.2 A more flexible clinical trials framework would foster innovation and better serve patients

Stakeholders noted that Canada has always had a high calibre framework that guides clinical trial authorizations. They acknowledged the flexibility of the Canadian system and Health Canada's openness and commitment to providing early advice on the design and conduct of clinical trials and product submissions.

Stakeholders also highlighted that science, technology, and research methodologies will continue to advance and that the clinical trials framework will need to evolve to respond to this reality. Having a flexible, enabling clinical trials framework would draw in key companies, investments, and support research and innovation in Canada.

Stakeholders provided a range of suggestions aimed at supporting the evidence needed to determine safety, efficacy, and quality in the context of health product innovation. Namely, they recommended that Health Canada should consider expanding in the following areas:

- Enabling innovative trials designed to simultaneously test a range of therapeutic interventions, companion diagnostics, and/or indications;
- Making it easier to implement multi-sponsor trials as well as multi-site trials and to add additional sponsors or sites to those already started;
- Supporting the use of real-world evidence and real-time collection and analysis of data to rapidly and continually assess and update benefit-harm-uncertainty profiles and ongoing patient care;
- Increasing the use of genomics, biomarkers, and other types of data to better guide and target patient recruitment and treatment;
- Enabling flexibility for clinicians in special circumstances, including those conducting adaptive trials, so they are better able to conduct research while adapting treatments based on patient needs;
- Facilitating the connection and sharing of information so that researchers can build and support each other's work; and
- Supporting the inclusion of under-represented populations in studies and testing of population specific differences, where appropriate.

In addition to supporting innovative trial design and methods, stakeholders emphasized the importance of infrastructure so that trials originate and are delivered in Canada. They noted the value of investing in state-of-the-art centres across the country, which could house trials for various types of advanced technologies. Whether associated with academic or health institutions or acting as standalone sites, stakeholders suggested these centres, if appropriately equipped with the infrastructure and staff to ensure controlled testing and use of advanced technologies, would help to reduce risk and improve access to innovation for all Canadians.

Case Study: Advanced Cell Therapies
While advanced cell therapies are currently regulated as drugs under *the Food and Drug Regulations*, this framework may not be well suited to the increasing number of tailored cell therapy products prepared by physicians at the bedside, and only to be administered to patients for whom they are designed. These products present regulatory challenges because they fall outside of the current health care model in which drugs are manufactured in a factory environment and distributed for broad use by health care professionals, after receiving market authorization based on previous testing of the drug in well-controlled clinical trials.

3.3 Coordination of patient and health data to enable better decision making

Data have the potential to drastically change the health sector. Stakeholders indicated accessibility, privacy, comparability, and interoperability of data are key issues where data are concerned. They noted infrastructure that supports data creation, analysis, sharing, and linkages is also key. They emphasized the need for pan-Canadian strategies to align, integrate,

and make better use of data in decision-making (from clinical to system-based decisions), health product research and development, and market authorization and surveillance.

Stakeholders noted innovators do not always have the resources, knowledge, infrastructure, or capacity to effectively share data or the resources to train employees. This is more pronounced in smaller start-up companies. While cloud-based systems and services offer some hope in this regard, stakeholders indicated that strategies for enabling capacity-building will be important. One such strategy, they suggested, could be the creation of common datasets or platforms, which could be used by various researchers for standardization, validations, and product testing of advanced technologies that use software and artificial intelligence.

Beyond coordination of data, stakeholders emphasized the value in better connecting practitioners and institutions to capture and share information for clinical decision-making. Stakeholders suggested there would be value in a mechanism to share information on the development, use, and outcomes of advanced technologies with individuals with rare diseases, under-represented populations, and specialized communities. While patient registries exist, additional coordination and enhancement would support decision-making and facilitate research and development.

Case Study: Big Data
There is increasing accuracy, variety, and volume of data, which can be used to inform health decisions made by individuals, researchers, health product developers, health practitioners, and healthcare system decision-makers. Data created from sensors, wearables, implants, genomics, clinical trials, self-reporting, and social media are increasingly used to inform health decisions. Domestic and international efforts aimed at collaboration and interoperability are complex and hard to achieve, there may be a role for the regulator in ensuring certain standards are met.

Case Study: Artificial Intelligence
Artificial intelligence through machine learning, neural networks, natural language processing, deep learning, and robotics are helping to unlock the potential of vast stores of health data. These technological advances are aimed at improving development and deployment of health products and services, patient interactions, clinical decision support, research and development, public health surveillance, and health care systems, by more efficiently and effectively using available data and analytics. How this technology makes decisions is not always clear and understandable, posing a challenge for regulators who need to validate how products using this technology will function, as well as creating other challenges related to accountability, privacy, and security.

3.4 Finding the balance between enabling innovation while maintaining patient safety

A common challenge associated with novel technologies is generating the evidence to show the product is safe and effective. Many new technologies simply do not yet have the large-scale, population-based studies required for market authorization. Furthermore, as new technologies are increasingly individualized, they do not necessarily fit the current authorization model. This innovation in manufacturing poses challenges for regulation and patient safety.

While stakeholders supported the need for oversight of these technologies, underscoring the importance of ensuring product safety and efficacy, they emphasized the need for it to be proportional with potential risks, benefits, uncertainties, and with consideration for the realities of providing frontline care. Stakeholders called for a flexible, risk-based approach that permits early or conditional market authorization while simultaneously ensuring robust ongoing product oversight, research, and surveillance. They also suggested a designation be issued earlier on in the process to support product innovation and investment, and indicated that they would value some form of certification from Health Canada (e.g., licence). Such a certification was also suggested to facilitate engagement among manufacturers, health care practitioners, and patients.

Stakeholders raised a number of considerations for authorization and oversight of new innovations:

- Having the needed mechanisms in place to receive stakeholder feedback and make appropriate adaptations post-market as a result;
- Having additional mechanisms in place to identify challenges as they arise post-market so that they can be addressed in a timely manner;
- Clarifying requirements around evidence generation, data sharing, surveillance, and compliance and enforcement, and aligning with the level of risk associated with the product; and,
- Looking to other jurisdictions that have implemented alternative pathways for innovative products (e.g., orphan drugs, digital health products and antimicrobials (USA), regenerative medicines (Japan), priority medicines and advanced therapy investigational medical products (EU)).

These considerations point to the need for a flexible, iterative approach to regulation of new technologies with an emphasis on enabling innovation and information sharing while maintaining appropriate oversight for safety, efficacy, and quality.

Case Study: 3D Printing
Health applications vary from the creation of implants, prosthetics, and anatomical models (as surgical tools and guides); to bioprinting of cells and tissues for pre-clinical testing, drug development, and drug delivery; to the proposed creation of organs for transplantation. The technology uses computer software to program, simulate, and assemble a range of materials to create a single object. Regulation of this technology is particularly challenging because the current framework is designed to regulate a single product from a defined process. 3D printing can be used to create a variety of health products for customised and personalized applications manufactured at the point of care.

3.5 Enabling for alignment and collaboration to foster innovation

Many players are involved in the product lifecycle – product development, market authorization and use, ongoing monitoring, surveillance, and learning – each with specific requirements and rules governing their activities both at the federal and provincial/territorial levels. Stakeholders welcomed efforts to facilitate an understanding of the current frameworks, requirements, and

any associated processes and encouraged Health Canada to improve alignment, where possible.

Stakeholders also recognized collaboration, such as between Health Canada, the Canadian Agency for Drugs and Technologies in Health, the Institut national d'excellence en santé et services sociaux, and other regulators as a meaningful way to address system challenges. They pointed to international efforts, citing the commonalities in safety and efficacy goals across jurisdictions. Efforts related to alignment and collaboration in developing product standards, approvals, and oversight, as appropriate, were welcomed. Stakeholders favoured a "seamless" system with other regulators (e.g., the US Food and Drug Administration and European Medicines Agency).

Case Study: Gene Editing

Gene therapies assist in the prevention and treatment of genetic-based diseases by augmenting a patient's genetic makeup. Gene editing techniques are helping to realize the potential of gene therapy and synthetic biology. This range of tools is making genetic manipulation more exact, efficient and accessible while reducing costs, resource requirements, and time required to make and test genetic changes. Individualization of therapies is a challenge for the health product regulator, who traditionally provides large-scale, population-based market authorizations.

3.6 Dynamic and ongoing stakeholder engagement is necessary for meaningful change

Throughout the consultations, stakeholders expressed the importance of being engaged at all stages – from planning to oversight. Key principles for engagement identified by stakeholders included:

- Engage early and often: Stakeholders felt Health Canada demonstrated a commitment to open, ongoing, and iterative conversations regarding the development of novel approaches to authorizing and overseeing products. Going forward, participants encouraged continued engagement. Participants suggested additional avenues for engagement including convening expert panels and hosting open-to-the-public engagement sessions to provide information to Canadians.
- Inclusive engagement of a wide range of stakeholders: Participants provided suggestions for additional stakeholders that could be included in future discussions including: patients, healthcare professional associations, medical colleges, researchers, environmental stakeholders, health technology assessment and reimbursement bodies, other governments, and health care system planners and decision-makers. Participants emphasized the importance of meeting with stakeholders new to the health landscape, such as mechanical and computer engineers and software developers. They indicated engagement with a wide variety of stakeholders helps identify opportunities for risk mitigation, educate innovators who may not be aware of regulatory requirements, and understand the developing innovation landscape.

- Proactive, targeted outreach with particular patient groups is needed: Stakeholders noted that new innovations may have greater benefits for particular patient groups, such as those with rare diseases, who may have differing needs, concerns, and considerations than the general population. Measures to identify such priority groups as well as their caregivers should be considered going forward.
- Provide appropriate information to help stakeholders effectively navigate the regulatory system: Stakeholders welcomed enhancements to current communications tools, noting it can be challenging to navigate and find all pertinent information. They also identified the need to be able to access subject matter experts to ask questions, or a “single window” to point them in the right direction. Stakeholders also pointed that those unfamiliar with the regulatory system (e.g., start-ups) may have a need for targeted interactions in particular.

4.0 CONCLUSIONS AND NEXT STEPS

The breadth, scope, and accelerating pace of health product innovation demand regulatory attention. Speaking with stakeholders from across Canada underscored that advanced technologies that are being used to create the health products of the future, have reached a critical point in development. Certain scientific and technological advancements, once thought to be a possibility far into the future are increasingly closer to reality. The regulatory and health care systems are beginning to encounter these innovations. There is increasing need to enable innovation in a flexible, risk-based way, with appropriate oversight to ensure safety, quality, and efficacy.

Stakeholders have a critical role in advancements moving forward, and there is recognition that opportunities for enhanced and ongoing collaboration are important. This consultation and ongoing activities with stakeholders are being used to inform regulatory and policy development for emerging health technologies.

Health Canada recognizes the importance of being at the forefront of health innovation and continues to engage stakeholders to help ensure the regulatory system aligns with the evolving health landscape, global realities, and needs of Canadians.