

Agile regulations for advanced therapeutic products and clinical trials

Discussion Paper

Health Canada
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1. Context

Protecting the health and safety of Canadians is Health Canada's first priority. Therefore, it is important that Health Canada's product approval regulations allow Canadians access to promising new therapies. New advanced and complex health products, such as those based on artificial intelligence or 3D bioprinting, are leading to new ways to diagnose, treat, and monitor patients and challenging how Health Canada regulates health products. Clinical trials, through which new therapies are tested, are also changing to respond to the demands of increasingly complex products. While Health Canada has strong regulations for drugs and medical devices, some have not kept pace with innovation. Changes are required in order to accommodate highly complex technology while still protecting the health and safety of Canadians.

Health Canada has been working to better understand the evolving health product landscape and identify what regulatory changes might be needed. The Department has been engaging with new partners both domestically and internationally. Following the targeted Health and Biosciences Sector Regulatory Review consultation by the Treasury Board Secretariat in 2018, Health Canada held meetings with key stakeholders, innovators, organizations and thought leaders across the country. These discussions highlighted the need for reform and are summarised in the [Consultation Summary: Health Products Stakeholder Engagement Session June 27, 2018](#) and [What we heard: A summary of scanning and consultations on what's next for health product regulation \(March 2019\)](#).

In [Budget 2019](#), the Government of Canada took a major step towards advancing regulatory modernization to address new technologies in the health and biosciences sector. In particular, it supported the approaches proposed in the [Health and Biosciences Sector Regulatory Review Roadmap](#), including the use of regulatory sandboxes. This ambitious regulatory reform agenda requires the new legislative provisions for the *Food and Drugs Act* provided in the [Budget Implementation Act, 2019](#).

2. How Health Canada proposes to address new and increasingly complex health products

Regulatory Sandboxes

Regulatory sandboxes help industry offer innovative products, services, and applications in Canada. The sandbox protects the health and safety of Canadians while introducing flexibility to the regulatory process to meet the growth and pace of technologies that do not fit within the current regulations.

Moving forward, Health Canada will be focussing its modernization efforts on two key areas:

1. Using a risk-based approach for regulating clinical trials.
2. Creating a flexible approach for authorizing complex and novel health products.

These two areas are crucial to helping Canadians access new health products. The first is necessary for the development and testing of new health products, and the second acts as a new way to bring unique health products to the market.

Using a risk-based approach for regulating clinical trials

Clinical trials are usually the first step in developing new health products. Health Canada has effective clinical trial regulations, but as products evolve so do the trials, creating the need for more flexible clinical trial regulations. In the past, clinical trials were mostly done on a specific drug or device in a select population. The approach was “one-size-fits-all”. This model may be challenging for small-to-medium sized companies. It may also discourage the study of under-represented, very small, or geographically dispersed patient populations. In addition, new trial designs are emerging where multiple therapies from multiple sponsors are studied in parallel for the same disease or condition. These trials benefit patients since the therapies can be adjusted based on their outcomes (Figure 1). The trials may also study both drugs and devices at the same time.

Lower-risk clinical trials are also now being done on approved products to establish new uses. For example, children are often treated with drugs and devices that were only studied in adults. Lower-risk trials could help confirm whether these products also work in kids.

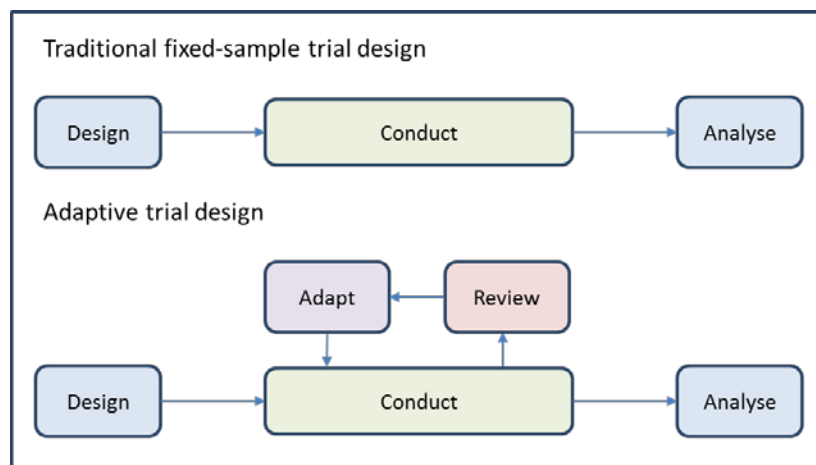


Figure 1. Evolution of Clinical Trial Designs

of all parts of a clinical trial. The new model will also expand the use of evidence gathered through trials. These changes are expected to give patients greater access to more potentially life-saving trials and new therapies. Canadians will also have access to more information on available clinical trials and their results.

Finding the Best Treatment: Platform Trials

Platform trials aim to find the best treatment for a condition by studying different interventions from different companies. They also use specialized statistical tools to increase the number of patients receiving the most promising therapy. This involves multiple trials under a master protocol.

Oversight of the conduct of clinical trials is designed to safely permit unconventional trials designs to better accommodate the needs of patient sub-populations and, where appropriate, adaptive clinical trials design and scientific breakthroughs.

Moving forward, the *Food and Drugs Act* will accommodate new types and designs of trials. It will reduce costs for those conducting low-risk trials, and regulate in proportion to risk. The revised approach will also improve alignment with global partners, and increase Canada’s competitiveness in attracting trials.

The approach is shifting to one that focusses on controlling the conduct

Additionally, foods for special dietary purposes will now be included as products that require clinical trials. Right now, manufacturers are not allowed to conduct clinical trials in Canada on foods for special diets, such as infant formula. This impacts their ability to generate the evidence needed to demonstrate the safety and nutritional characteristics of a new infant formula. The new provision will make those trials possible.

Compliance and enforcement powers in the *Food and Drugs Act* have also been expanded through the recent *Budget Implementation Act, 2019*. New regulations will allow for long-term safety monitoring of higher-risk trials. Legislative provisions will not come into force until a new set of regulations are developed and implemented. Health Canada will consult with stakeholders as it develops this new regulatory approach for clinical trials.

Creating a flexible approach for authorizing complex and novel health products

Most health products will continue to be regulated using existing rules under the *Food and Drugs Act*. Under exceptional circumstances, where current regulations cannot appropriately accommodate a product, a new pathway will be available. This pathway will be reserved exclusively for “Advanced Therapeutic Products,” (ATPs) which are drugs or devices that are so novel, complex, and distinct that current regulations are not equipped to handle them. For example, through gene editing doctors can now diagnose and deliver personalized therapies at a patient’s bedside. This type of individualized medicine does not easily fit within the current regulatory approach, which was designed for more traditional, large-scale therapies.

ATPs can offer tremendous health and economic benefits. As more companies make use of these new technologies, it has become evident that Health Canada needs a risk-based and flexible way to authorize these novel products, while still protecting the health and safety of Canadians. The regulatory pathway proposed is one that can be tailored to the specific product, addressing its unique characteristics while maintaining Health Canada’s high standards for patient safety. Figure 2 provides a more detailed explanation of this new pathway, also known as a regulatory sandbox.

Customization: 3D Bioprinting

3D bioprinting is the creation of an object by building many layers of living cells. The process is highly dependent on software, with a variety of printing techniques being used and continuously updated.

The potential for future uses is staggering: from bioprinting of tissues and organs for transplantation, to pre-clinical testing and personalized drug development.

The ATP pathway could enable the use of customized regulatory requirements. This will allow the agility and flexibility necessary for the appropriate oversight of complex technology, such as the application of 3D bioprinting at the point of care.

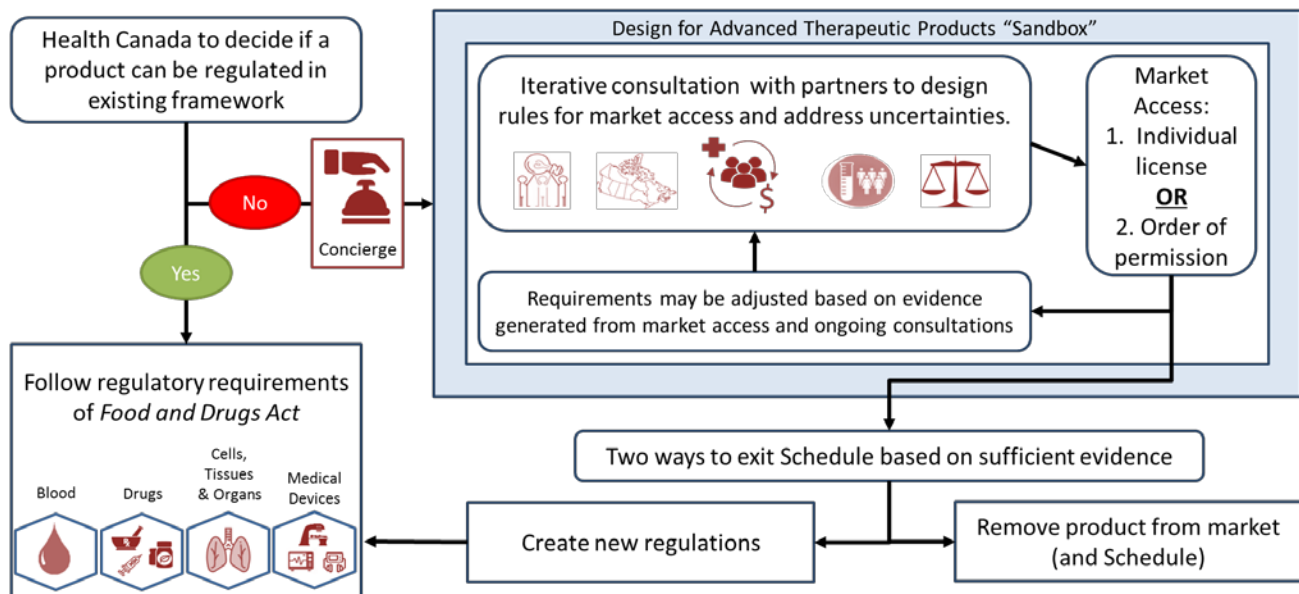


Figure 2. New regulatory pathway for Advanced Therapeutic

This new pathway is only meant for truly unique products. In assessing whether a product may be eligible for the pathway, Health Canada will consult with stakeholders and consider:

- The risks and benefits associated with the product, and steps available to adequately manage and control these risks.
- The extent to which the product is different from already approved drugs or devices.
- The extent to which there are other appropriate controls in place, for example through provincial and territorial legislation.

To sell, import or manufacture ATPs, companies will require one of the following:

- *A licence:* To obtain a licence, those interested would need to submit an application to Health Canada. Once issued, the licence would have terms and conditions associated with it (e.g. quality and safety requirements).
- *An order of permission:* An order could be given as a general permission instead of a licence. This mechanism would be more suitable for lower-risk products, such as wearable medical devices. However, individuals or organizations subject to an order would still need to meet certain requirements, such as reporting safety issues.

In both instances, Health Canada would aim to ensure that ATPs meet both the market licensing and health technology assessment requirements. Health Canada intends to work closely with stakeholders to establish and modify these terms and conditions in response to real-world evidence. In addition, all ATPs would be subject to compliance and enforcement powers under the *Food and Drugs Act*. A product license could be revoked if the product is shown to be unsafe, ineffective, or in violation of terms and conditions.

Health Canada intends to make these changes while keeping in mind the unique challenges of small businesses. Although the issuance of licences is intended to be a cost-recovered service, the costs would be significantly reduced for small businesses. Costing will be conducted in a transparent manner, and stakeholders will be consulted.

Providing a concierge service

Health Canada intends to provide enhanced client service to those with products considered for the ATP pathway. This “concierge service” will help industry to navigate the sometimes complex government system and overcome any hurdles. The service will be particularly important for small to medium sized companies, or those with limited experience interacting with Health Canada. Concierge services generally act as one-stop-shops for interactions with government departments, including access to key information and relevant officials. Several models could be adopted to achieve these goals.

The main objective of the concierge service will be to help sponsors identify whether their product fits under existing regulations, or in exceptional circumstances, whether it should be considered for the ATP pathway. The concierge service will give users a single point of contact for direct, well-informed interactions with a Health Canada representative. In consultations, stakeholders have indicated that they strongly support creating a Health Canada-based concierge service for products looking to be considered for the ATP pathway.

3. Continuing the conversation and seeking further feedback

We are entering new territory in health product regulation. Extensive consultations have helped inform the path forward for regulating complex health products and modern clinical trials. Health Canada will continue the conversation and welcomes other ideas to help ensure our approach supports innovation while protecting citizens.

Specifically, the Department is seeking more feedback on what to consider in developing the clinical trials regulations as well as the pathway for ATPs. The following questions are provided to guide your input:

1. What products would you want to put forward for consideration under the ATP pathway?
2. Can you suggest any good models of an enhanced client “concierge” service that would help companies wishing to be considered for the ATP pathway?
3. What recommendations do you have for creating clinical trials regulations that would attract clinical trials in Canada and be an effective model in the Canadian context?

For more information, please see the [Health and Biosciences Sector Regulatory Review Roadmap](#).

To participate in the consultation, please send feedback to:

hc.hpfb.engagement-mobilisation.dgpsa.sc@canada.ca