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The evolution of Canada's medical device regulatory framework

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The evolution of the medical device regulatory framework in Canada is not as well understood as those of other major jurisdictions such as the US and EU. Canada has been a crucial member of the International Medical Device Regulators Forum (IMDRF) and has been instrumental in laying down the foundational regulatory principles in the global harmonization effort. This article traces the development of Canada's regulatory framework, its role in harmonization, and its current standing.

Keywords – Canadian Medical Devices Regulations, Food and Drugs Act, global harmonization, Health Canada

Introduction

Canada has a well-established, highly diversified medical device industry consisting of mostly small and medium-sized enterprises.[1] The market value is approximately USD$6.5 billion and is expected to grow by 2.1% annually until 2026.[1] However, it is less well understood how Canada regulates medical devices and its role within the global framework. Compared with the US medical device regulatory framework, the modern Canadian regulatory system has had a shorter history. While both Canada and the US can trace the origins of their respective food and drug legislation back to the early 20th century, the modern medical device regulatory paradigm in Canada has been a product of a convergence of international forces and the rapid development of technology. Its evolution has been driven by a proactive approach to regulation informed by a global consensus. This article traces the development of the Canadian medical device regulatory framework to its present day. The aim of the article is to shed light on the evolution of this framework, Canada's role in harmonization, the regulatory nuances in the Canadian regulations, as well as its current approach to emerging technologies.

History of the regulatory system

Canada's Food and Drugs Act[2] was introduced in 1920. The first full medical device regulatory framework was promulgated under the Act in 1975. However, it was not until 1998 that Canada introduced a risk-based classification system, more than 20 years after the enactment of the Medical Device Amendments of 1976, which was a response to a series of incidents in the US, culminating in the Cooper Committee Report.[3] The impetus for medical device legislation in Canada was a regulatory gap exacerbated by the pace of technological innovation.

Under the 1975 regulations, only 5% of medical devices were subject to premarket review.[4] These devices fell within certain categories, which were listed in the regula-

tions. Manufacturers were required to provide labeling containing information on the benefits of the device and instructions for use. The testing methods and results to support the claimed benefit would be provided to the then–Ministry of Health and Welfare (now Health Canada) upon request. Manufacturers may be required to produce evidence of safety and effectiveness under the recommended conditions of use.

Recommendations for Canada's modern regulations called for an approach consistent with the changes in global economy and international reference standards and with evaluative data from other jurisdictions.

There were several challenges to the regulatory framework. The first was the rapid pace of innovation in medical technology combined with a strong demand for new devices. Medical devices were essential in the provision of high-quality healthcare services. Second, in the 1975 framework, only devices that fell into certain categories required premarket review, and that list remained mostly static and did not account for the risk of new medical technology being developed and entering the Canadian market. As a result, the regulatory agency had little insight into what devices were being placed in Canada commercially. Another challenge is that Canada also faced the pressure of international harmonization as a member of the global community.

These challenges then became the impetus for a revised regulatory program in Canada. Between 1991-1992, the government held a series of meetings in consultation with industry stakeholders, health professionals and the public.[4] It was recommended that Canada look to establish a risk-based regulatory system.[4] This became the foundation of the Canadian Medical Devices Regulations (SOR/98-282)[5] or also known as the modern regulations. Notably, the recommendations also called for a regulatory approach that must remain consistent with the changes in global economy and the international reference standards, and evaluative data from other jurisdictions.[4] In a relatively small market, Canadian device manufacturers shared the concern to be competitive international players and therefore wanted to see trade obstacles removed by developing mutually recognized product standards and regulations internationally. Canada recognized that a regulatory system founded on good science must rely on appropriate data from all sources.

Health Canada's organizational structure

Two distinct branches within Health Canada[6] are primarily responsible for regulation and postmarket enforcement and compliance of health products. Respectively, they are the Health Products and Food Branch (HPFB)[7] and Regulatory Operations and Enforcement Branch (ROEB).[8] It is within these branches that roles and responsibilities are subdivided into offices and directorates based on the type of health product or the type of operation. The latter includes such activities as policy planning or resource management.

At a high level, the HPFB's mandate is to manage the health-related risks and benefits of health products and food by minimizing health risks factors while maximizing the safety provided by the regulatory system governing each type of product,[7] whereas the primary role of the ROEB is compliance and enforcement.[8] The medical device arm of the HPFB is the Medical Devices Directorate. Within ROEB, the Medical Devices Compliance Program oversees postmarket compliance and enforcement, recall reporting, inspections, shortage reporting and establishment licensing.[9]

The Medical Devices Directorate[10] is an office within the HPFB and is Canada's regulator of medical devices for human use. It authorizes the sales of medical devices that meet the safety, effectiveness, and quality requirements of the Food and Drugs Act and its implementing regulations. Among its responsibilities are reviewing scientific data to verify the safety, effectiveness, and quality of medical devices, reviewing applications for investigational testing authorization, assessing the poten-

tial benefits and risks of a medical device, authorizing unlicensed medical devices through the Special Access Program channel, and postmarket safety monitoring of devices on the market.

Global harmonization and premarket regulatory landscape

The year 1992 marked the founding of the Global Harmonization Task Force (GHTF) consisting of five jurisdictions (Australia, Canada, EU, Japan, and US). GHTF was the predecessor to the current IMDRF and laid down the foundation for future global harmonization initiatives. The GHTF created a forum for international harmonization of medical device regulatory practices and was an international partnership between major medical device regulatory authorities and the industry. Canada's early involvement in this international task force allowed Canada to pursue a global harmonized approach to pre-market and manufacturing standards. An example of Canada's global alignment was its commitment to incorporating the ISO 9000 series of standards into the drafting of the medical device regulations. Hence, SOR/98-282 incorporated by reference the National Standard of Canada CAN/CSA-ISO 13485:03,[11] Medical devices – Quality management systems – Requirements for regulatory purposes. This version was later superseded by ISO 13485:2016.[12]

In the latter half of the 2010s, Canada was among the five countries, including the US, Australia, Brazil, and Japan, to pave the way for the Medical Device Single Audit Program (MDSAP),[13] an auditing methodology based on the requirements of both ISO 13485 and regional regulations. Since 2019, MDSAP certification has been the foundation of the quality management system for manufacturers selling to the Canadian market.

In 1998, Canada introduced a four-tiered, rule-based risk-based classification scheme after a comparative review of processes used in other jurisdiction such as Australia's Therapeutic Goods Regulations and Europe's then Medical Device Directive. This four-tiered classification system, based on the experience of GHTF, is deemed sufficient to accommodate types of medical devices and allows a system of premarket controls proportionate to risk determined by the framework.[14] Premarket regulatory scrutiny takes a risk-based approach based on the intended purpose and use of the device, potential hazards, and the appropriate controls.

In a global effort to standardize documentation evidence supporting regulatory submissions, Canada was also an adopter of the previous summary technical documentation (STED) structural framework for premarket applications of medium- to high-risk devices (classes III-IV).[15] At the international level, the STED was eventually replaced by IMDRF's table-of-contents format to provide a globally harmonized structure.[16] The adoption of this format demonstrates Canada's consistent support for a global convergence of regulatory standards and best practices.

> *Canada's early involvement with IMDF allowed it to pursue a global harmonized approach to premarket and manufacturing standards.*

Other harmonization initiatives include the Medical Device Single Review Program (MDSRP), which is a project of the Canada-United States Regulatory Cooperation Council. The council is a bilateral forum providing Canadian and US regulators the opportunity to work on reducing unnecessary regulatory burdens on stakeholders while protecting health and safety of citizens and the environment. The MDSRP is one of numerous initiatives between Health Canada and the FDA to work together. Specifically, the MDSRP aims to harmonize premarket technical review requirements for moderate risk medical devices. The FDA and Health Canada will continue this work through the IMDRF's Good Regulatory Review Practices Working Group to develop harmonized premarket requirements to be the foundation for future MDSRP work.[17] The goal is to improve patient access to medical devices, support innovation and strengthen standards development.[17] The work plan is ongoing.

Table. Comparison of medical device regulatory frameworks in Canada and the US

Point of comparison	Health authority	
	Health Canada	**US Food and Drug Administration**
Enabling statute	Food and Drugs Act[2]	Federal Food, Drug, and Cosmetic Act[19]
Regulations	Canadian Medical Devices Regulations SOR/98-282[5]	21 CFR Parts 800-1299
Classification	Class I, II, III, IV	Class I, II, III
Quality system	MDSAP (ISO 13485:2016[12]) SOR/98-282, Part 1	21 CFR Part 820[a,20] (Quality System Regulation)
Clinical investigation and Good Clinical Practice	• SOR/98-282,[5] Part 3 (Medical devices for investigational testing involving human subjects • ISO 14155[21] (Clinical investigation of medical devices for human subjects — good clinical practice)	• 21 CFR Part 812[22] (Investigational Exemption) • 21 CFR Part 50[23] • 21 CFR Part 56[24] • 21 CFR Part 54[25] • 21 CFR Part 820, Subpart C
Premarket licensing, clearance, approval	Medical device license required for Class II, III, IV (Subject to annual renewal)	510(k) – Class II Premarket approval – Class III
Postmarket surveillance	• Mandatory problem reporting • Summary reports (Class II, III, IV) • Issue-related analyses of safety and effectiveness as required • Foreign risk reporting • Section 21.31 and 21.32 of Food and Drugs Act[2]	• Medical device reporting (21 CFR Part 803)[26] • Section 522 of the FD&C Act, 21 USC §360 (FDA's authority to require postmarket surveillance for certain Class II and III devices)[27]

FD&C Act, Federal Food, Drug, and Cosmetic Act; **MDSAP,** Medical Device Single Audit Program; **QSR,** Quality System Regulation.
[a]At the time of writing, the FDA aims to release a final rule in 2023 that will harmonize the Quality System Regulation with the international standard ISO 13485:2016.[20]

Another bilateral collaboration between Canada and the US is the recent joint eSTAR pilot program. The aim is to test the use of a single platform to submit to both regulators. The interactive platform integrates the IMDRF submission structure with automation features to guide the applicant through a comprehensive device submission.[18] The accompanying **Table** provides a comparison of the Canadian and US regulatory frameworks for medical devices.

Emerging technologies

Canada has been a global leader in international harmonization of regulatory standards in emerging technologies. In 2020, Health Canada co-chaired an IMDRF working group on cybersecurity, which published guidance medical device cybersecurity.[28] Another important milestone in the regulation of digital health was in 2021 when a guidance on good machine learning practice for medical device development was published in partnership with the FDA and the UK's Medicines and Healthcare products Regulatory Agency (MHRA).[29] The document outlines 10 principles for promoting safe, effective, high-quality AI- or machine-learning–enabled medical devices. Currently, Health Canada also cochairs IMDRF's Software as a Medical Device (SaMD) Working Group[30] to continue to review previously published technical documents, for example, by taking a product lifecycle approach to regulation of digital health technology.

Advanced therapeutic products framework

One of the main drivers of regulatory innovation is technological advances, which result in ever more complex health products. It is recognized that existing regulatory frameworks may be inadequate to address the nuances of innovative products. In June 2019, Canada amended its Food and Drugs Act to create a new regulatory pathway to address the unique characteristics of designated innovative products, also known as advanced therapeutic products (ATPs).[31] This was a significant step forward in regulatory innovation. An ATP is defined as a therapeutic product or class of therapeutic products representing an emerging or innovative technological, scientific or medical development.[32] These products can be drugs, devices, or any combination of drugs and devices that are "so unique, complex, and distinct that they fundamentally challenge existing regulations and Health Canada's ability to protect people's health."[32] The new framework allows the customization of requirements to provide a flexible regulatory oversight that promotes innovation in product development and reduces barriers to introduce ATPs in Canada, while ensuring rigorous standards of safety and product quality, efficacy, and effectiveness.[31] In addition, Health Canada plans to offer a specialized or "concierge" service to innovators and members of industry to provide guidance as they navigate the ATP framework.[32]

> *Health Canada's shift to stronger oversight of the postmarket phase is consistent with the lifecycle approach taken by other international regulators such as Europe within the current EU MDR framework.*

The identification of potential ATP candidates is a collaborative approach with stakeholders such as product developers, health system partners, and international regulators. Considerations in evaluation of eligibility for ATP designation include risks and benefits of the products and how to manage and control the risks, how different the product is from approved products, and if there are appropriate controls through existing legislation.[33] As of this writing, a public consultation on a draft guidance on the ATP framework had ended in March 2023.[33] A finalized guidance will provide an overview of how Health Canada designates and regulates ATPs under the new statutory authority.

One such ATP candidate that has been identified so far is adaptive machine learning–enabled medical devices (MLMD). Unlike a "locked' algorithm, an "adaptive" algorithm changes its behavior using a defined learning process. The existing regulatory controls do not accommodate such devices that change in response to new inputs in real-world settings in the post-market phase. Within the ATP framework, both premarket and postmarket requirements would be tailored to the specific characteristics of the MLMD.[34] Currently, Health Canada is proposing to add a description of MLMD to Food and Drugs Act to allow this to be regulated as an ATP considering its innovative nature.[34]

Postmarket compliance and data transparency

There has been significant progress in the premarket space through international harmonization, but the postmarket regulatory landscape in Canada had been relatively static since the modern framework was established in 1998. In 2014, there was a fundamental shift toward addressing postmarket regulation, with the enactment of Protecting Canadians from Unsafe Drugs Act (Vanessa's Law). The Act amended Canada's Food and Drugs Act to strengthen Health Canada's ability to collect postmarket safety information.[35] Specifically, the law granted Health Canada the authority to:

- Strengthen safety oversight of therapeutic products throughout their life cycle;
- Improve reporting by specific health care institutions of serious adverse drug reactions and medical device incidents involving therapeutic products; and
- Promote greater confidence in the oversight of therapeutic products by increasing transparency.[36]

In short, the postmarket regulatory space took a turn from a reactive approach to a more proactive approach to regulation, which includes the use of real-world evidence.[37] In this regard, Health Canada's shift to stronger oversight of the postmarket phase is consistent with the lifecycle approach taken by other international regulators such as Europe within the current EU Medical Device Regulation (EU MDR) framework. From 2018 onward, the regulatory agency has issued numerous legislative and regulatory amendments accompanied by policy to operationalize the lifecycle approach to regulation. In parallel with postmarket regulatory changes, additional amendments in the legal framework have been introduced to ensure transparency of clinical data that is accessible by the public.

Regulating from a lifecycle approach

The foundation of the updated framework is a lifecycle approach to regulation. It is well recognized that critical information about the safety and effectiveness of devices can only be learned in the postmarket phase of a product after more users have been exposed to them. Hence, a significant update to the Medical Devices Regulations is the postmarket summary reporting requirement across all Class II-IV products. This new obligation on the manufacturer is consistent with that EU MDR's periodic safety update report (PSUR) so that manufacturers in compliance with the EU MDR would readily be able to modify their PSURs to be Canadian specific. Health Canada has the additional authority to require manufacturers to conduct safety and effectiveness analyses in response to market feedback such as complaints and other safety-related events.

Clinical data transparency

To promote transparency in the oversight of therapeutic products, Health Canada has implemented new regulations to provide public access to specific clinical data in regulatory submissions across therapeutic categories, which include both pharmaceuticals and medical devices. The clinical information subject to public disclosure includes clinical summaries, clinical overview, and relevant documents in clinical study reports such as protocols.[36] This commitment to transparency represents a fundamental shift in the way Health Canada handles clinical trial information, which the regulatory agency had maintained should be kept confidential. The 2014 amendments to the Food and Drugs Act were the culmination of years of reports and advocacy for a more transparent drug review process.[38]

> *Health Canada's clinical data transparency reform is rooted in both legislation and policy, which strengthens the regulator's position should there be a legal challenge to the framework.*

A proactive approach to release regulatory data is also consistent with European Medicines Agency (EMA)'s policies that govern how the agency reactively and proactively disclose data for drugs and biologics.[39] Through the public release of clinical information initiative, Canada goes further than the EMA by proactively releasing data not only for drug submissions, but also Class III and IV medical device applications. This level of transparency currently stands in contrast to the FDA, which rarely proactively releases clinical data, which can be obtained from the FDA by submitting a request under the Freedom of Information Act.[39] It should be noted that Health Canada's transparency reform is rooted in both legislation and policy, which strengthens the regulator's position should there be a legal challenge to the framework.[38] The medtech sector, which has traditionally been subject to a lower level of regulatory scrutiny compared with the pharmaceutical industry, will now be held to a general standard of transparency of regulatory data. This transparency mechanism allows anyone to obtain information. As more clinical data become more accessible to the public, there will be more scrutiny and analysis of regulatory decisions.

Conclusion

The recent shift in the Canadian regulatory framework

can best be attributed to two forces. The first is a shared concern in the global community over the rapid pace of technology and the more linear development of regulatory frameworks. The need for harmonization over regulatory practices and strategies for regulating emerging technologies has brought together global regulators. In the premarket space, there has been significant alignment.

Canada has been an instrumental partner in many IMDRF and GHTF initiatives such as adopting international best practices and spearheading various regulatory initiatives with trusted partners such as the FDA and MHRA. A recent example is the finalization of principles of good machine learning practice for medical devices. Canada's experiment with regulatory innovation with the advanced therapeutic products framework will offer an interesting comparison to the experiences in other jurisdictions when it comes to regulation of highly innovative technologies.

The second force behind the regulatory development has been on the postmarket side. The postmarket development can be attributed to domestic events such as the passage of the Protecting Canadians from Unsafe Drugs Act in 2014,[40] operationalized by both legislative amendments and regulatory policy. One such policy document is the Medical Device Action Plan published in 2018.[41] The additional postmarket requirements compared with the US increases the cost of compliance especially for small manufacturers and will require additional training. Canada's new postmarket framework is closer to that of the EU. The postmarket space remains fluid. Since we are still in the early years after putting this framework to the test, there will likely be new questions as we amass more data. Emerging technologies continue to challenge the regulatory landscape. However, the new postmarket framework creates the transparency that is necessary for probing the safety and effectiveness of the products in the real world.

Abbreviations

ATP, advanced therapeutic product; **FDA**, [US] Food and Drug Administration; **EMA,** European Medicines Agency; **EU MDR,** EU Medical Device Regulation; **GHTF**, Global Harmonization Task Force; **HPFB,** Health Products and Food Branch; **IMDRF**, International Medical Device Regulators Forum; **MDSAP,** Medical Device Single Audit Program; **MDSRP;** Medical Device Single Review Program; **MHRA**, [UK] Medicines and Healthcare products Regulatory Agency; **PSUR,** periodic safety update report; **ROEB,** Regulatory Operations and Enforcement Branch; **SaMD**, software as a medical device; **STED,** summary technical documentation.

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