|  |
| --- |
| **Consultation on Medical Device Investigational Testing Authorizations (ITAs)**  Health Canada is exploring how best to address longstanding stakeholder concerns regarding the current regulatory framework for medical devices and how it may be unintentionally limiting investigational testing activity in Canada. |

**PURPOSE**

Canada has become a country of choice for developing and testing innovative health products. However, in order to remain competitive in the clinical trial landscape and continue to be responsive to the health needs of patients and interests of investigators, Health Canada is studying how to address longstanding concerns and increase research, while protecting patient safety. This issue was prioritized in Health Canada’s Action Plan on Medical Devices, which was published in December 2018. The Action Plan identified the need to better align the regulatory frameworks for device investigational testing (IT) and drug clinical trials, and to adopt international best practices, where appropriate.

To advance these objectives, Health Canada is now seeking feedback from stakeholders on five key issues regarding the application requirements and processes for medical devices used in investigational testing.

**BACKGROUND**

**Investigational Testing Regulatory Framework**

Investigational testing refers to the clinical study of a medical device, intended to demonstrate clinical safety and/or effectiveness. Studies could also involve medical devices already on the market that are being evaluated for new intended uses, new populations, new materials or design changes. In Canada, about 400 investigational testing authorizations (ITAs) are issued annually.

Manufacturers and importers must meet the regulatory requirements under Part 3 of the *Medical Devices Regulations* (MDR) in order to receive an ITA from Health Canada to sell a Class II, III or IV device to a qualified investigator for the purpose of conducting investigational testing. There is no requirement to obtain an ITA for a Class I medical device; however, some requirements still apply, as outlined below.

|  |  |
| --- | --- |
| **Requirements under Part 3 of the MDR** | |
| **Class I Medical Devices** | **Class II, III and IV Medical Devices** |
| * Records and documentation requirements under section 81 of MDR * Labelling of investigational medical device * Advertising of investigational medical device * Post-authorization requirements (distribution records, complaint handling, mandatory problem reporting, recalls) | * Records and documentation requirements under section 81 of MDR * Application for authorization * Labelling of investigational medical device * Advertising of investigational medical device * Post-authorization requirements (distribution records, complaint handling, mandatory problem reporting, recalls, registration of implantable devices) |

Part 3 of the MDR also provides authority for Health Canada to request additional information either prior to authorization or during the study and to intervene in the study, if necessary.

**ISSUES FOR DISCUSSION**

There are some differences in the regulatory requirements for device IT and drug clinical trials. For example, the *Food and Drug Regulations* incorporate Good Clinical Practices (GCPs) for drug clinical trials, provide sponsors with the ability to file amendments and notifications, and ease administrative burden by permitting parallel applications for clinical trials and Research Ethics Board (REB) approvals. More consistent regulatory approaches across the product lines would provide comparable patient protection while encouraging research in Canada. In 2018, the *Applications for Medical Device Investigational Testing Authorizations* guidance document was updated to incorporate by policy some best practices from the drug clinical trial framework. Health Canada is now evaluating the success of these changes and assessing whether additional reforms might be appropriate.

Health Canada is also considering international best practices that could make the Canadian investigational testing environment more competitive. The issues outlined in this discussion document exemplify key areas where Canada’s device IT framework is inconsistent with those of other jurisdictions. Further study needs to be conducted to determine the appropriate approach for Canada.

Health Canada invites your feedback on the following issues:

**1. Expanding the scope of who can apply for an ITA**

Under the MDR, only manufacturers may apply to conduct investigational studies on medical devices. Although a delegation mechanism exists in the *Guidance Document: Applications for Medical Device Investigational Testing Authorizations* to allow an investigator (such as a clinician or health care facility) authorized by the manufacturer to become the regulatory correspondent, the investigator cannot file the ITA application and is not legally responsible for the investigational testing.

In the United States and the European Union, a study on an investigational medical device may be carried out by either a manufacturer or an independent investigator.

|  |
| --- |
| **QUESTIONS:**  a. What has been your experience with this delegation mechanism?  b. Is there a need to enable an investigator, independent of the device manufacturer, to pursue the investigational testing of a medical device? Please explain.  c. What challenges would you anticipate when an independent investigator undertakes investigational testing of an unlicensed medical device, or a new use for a licensed medical device? |

**2. Revisions to an ITA**

Under the current regulatory framework, there are no provisions that allow Health Canada to authorize revisions to an investigational testing authorization (ITA). Part 3 of the MDR only outlines the requirements for a new ITA. As such, the Regulations require that any changes must be submitted in a new ITA application.

A policy approach was recently implemented in the 2018 guidance document, *Applications for Medical Device Investigational Testing Authorizations,* to allow manufacturers to submit revisions to previously authorized ITAs in an abbreviated manner. The guidance document provides examples of changes that require the submission of a revised ITA. The current interpretation of a significant change to an ITA pertains to revisions to clinical trial sites, investigators, the number of patients, the protocol, the informed consent form, and the device itself. The guidance, however, does not provide a further mechanism by which certain minor changes could be submitted to Health Canada through a notification process (which would not require authorization).

A provision to allow modifications and notifications of an ITA would better align the frameworks for Canada and its international partners, including the United States and the European Union.

|  |
| --- |
| **QUESTIONS:**  a. What has been your experience with the policy approach to ITA revisions outlined in the 2018 guidance document that allows manufacturers to submit revisions to previously authorized ITAs in an abbreviated manner?  b. Is there a need to create a pathway that allows manufacturers to simply notify Health Canada of minor changes to an ITA? If so, what changes do you think should fall under this category? Please explain. |

**3. Research Ethics Board (REB) approval of investigational testing of Class III and IV devices**

The MDR requires REB approval prior to issuance of an ITA involving Class III and IV medical devices.[[1]](#footnote-1) However, recent changes to the *Guidance Document: Applications for Medical Device Investigational Testing Authorizations* allow for an authorization letter to be issued prior to the receipt of REB approval, provided that this approval is provided to Health Canada before the study is initiated.

Allowing regulatory approvals and ethics approvals to be done in parallel, rather than sequentially, would bring Canada in line with its international partners (United States and the European Union).

|  |
| --- |
| **QUESTIONS:**  a. What has been your experience with the policy approach outlined in the 2018 guidance document that allows issuance of an ITA prior to REB approval?  b. Would it be helpful to have a notification process (with no requirement for authorization) to address minor changes to an ITA resulting from REB approval? |

**4. Inclusion of Good Clinical Practice (GCP) standard in regulations**

It is internationally recognized that research in humans should be conducted according to generally accepted principles of GCP, as stated in the ISO 14155 standard - *Clinical investigation of medical devices for human subjects*. These clinical practices provide assurance that the data and reported results are credible and accurate, and that the rights, integrity, and privacy of research subjects are protected.

The MDR do not currently set out GCP standards to strengthen patient protection during investigational studies. However, the *Guidance Document: Applications for Medical Device Investigational Testing Authorizations* recommends that manufacturers conform to the GCP standard of ISO 14155.

Inclusion of this GCP standard in regulation would better align Canada with its international partners. The United States and the European Union regulatory authorities both have GCP requirements for medical device investigational testing.

|  |
| --- |
| **QUESTIONS:**  Is there a need to require compliance with the ISO standard on *Clinical investigation of medical devices for human subjects - Good clinical practice* (ISO 14155)? Please explain. |

**5. Exemption of certain ‘research use only’ devices from the ITA requirements**

“Research use only” devices typically do not involve patients and therefore present no risk to patient safety (e.g., studies involving validation of in-vitro devices using remnant samples). For this reason, the current requirement to have these devices authorized under Part 3 of the MDR causes administrative delays and disincentives for researchers. The MDR do not define “research use only” device, nor do they identify the conditions under which their use in investigational testing would not require Health Canada authorization. One exception is with respect to magnetic resonance imaging pulse sequences, where Health Canada decided that investigators were no longer required to obtain authorization prior to starting a trial using a “work-in-progress” pulse sequence (when certain conditions were met).

In the United States and the European Union, manufacturers of research use only devices are exempted from certain regulatory requirements.

|  |
| --- |
| **QUESTIONS:**   1. Should certain “research use only” devices be exempted from the authorization requirements under Part 3 of the MDR? Please explain. 2. If you responded yes to question 5a, what products should be considered for exemption? Please explain. |

1. There is no requirement to obtain an ITA for a Class I medical device but REB approval is still required for investigational testing involving Class I devices. With regard to investigational testing of Class II medical devices, evidence of REB approval is required, but does not need to be submitted to Health Canada prior to receiving an ITA. [↑](#footnote-ref-1)