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## Class II-IV Medical Device Investigational Testing in Canada

### Canadian Medical Device Classifications

The *Food and Drugs Act* (1) defines a "device" as any article, instrument, apparatus or contrivance, including any component, part of accessory thereof, manufactured, sold or represented for use in the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state. It includes a vast range of equipment, from a simple tongue depressor to robotically assisted surgical machines. In Canada, Medical devices are classified into Class I, II, III, and IV based on the level of invasiveness. The European Union has four classes of medical devices which generally correspond to Canada's four classes, as illustrated in the following table.

| Medical Device Classification System | | | |
|---|---|---|---|
| **Canadian Classification** | **Risk Level** | **Examples** | **European Council Directive 93/42/EEC (MDD)** |
| Class I | Lowest | Reusable surgical scalpel, bandages, culture media | Class I |
| Class II | Low | Contact lenses, epidural catheters, pregnancy test kits, surgical gloves | Class IIa |
| Class III | Moderate | Orthopaedic implants, glucose monitors, dental implants, haemodialysis systems, diagnostic ultrasound systems | Class IIb |
| Class IV | High | HIV test kits, pacemakers, angioplasty catheters | Class III |

### Investigational Testing in Human Clinical Trials

In Canada, Sponsors or Manufacturers should submit an Investigational Testing Application "ITA" to use unapproved Class II, III, and IV devices in clinical trials to the Device Evaluation Division of the Medical Devices office of Health Canada. Clinical trials for medical devices are not classified by phased development as with drugs (i.e., Phase I - IV clinical trials) and as for any standard clinical study in a human, the sponsor should still:

- Protect the rights, safety and well-being of human subjects
- Ensure that the study is conducted with, and that the best interests of the patients are always considered
- Ensure the scientific conduct of the clinical investigation and the credibility of the results

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Devices must be labeled "for investigational use only", and a Class I medical device does not require investigational testing authorization.

The Health Canada application should include:

- A protocol which details the objectives, benefits, risks, methods, and conditions for the trial to function
- Research Ethics Board Attestation (REBA)
- Clinical Trial Site Information Form (CTSI)
- Investigational Testing Application (ITA)
- Qualified Investigator Undertaking (QIU)

In addition, based on the Special Access Program, a medical device that is not yet tested or licensed in Canada can be used in emergency cases where conventional or available treatments have failed. In such a case, health care professionals can apply for authorization to use medical devices through the Therapeutic Products Directorate to assess whether potential risks of using the device outweigh potential benefits.

## Investigational Testing Application "ITA"

When applying for an authorization (to perform a clinical study to assess the safety and performance of a new medical device) to Health Canada, you need to submit an ITA according to the Canadian health program governing the use of Class II, III, and IV medical devices. The requirements for this application are summarized in the table below:

<table>
<tr><th colspan="2">Medical Device</th><th>Health Canada Requirements</th></tr>
<tr><td rowspan="2">Class III and IV</td><td>Class II</td><td>Manufacturer information<br>Device name & identifier<br>Institution name & address<br>Study protocol & Informed Consent Form<br>Labeling (Section 86)</td></tr>
<tr><td></td><td>Device description & materials<br>Description of features<br>Marketing history<br>Risk Assessment (ISO 14971) & Standards list<br>Investigators Agreement & CV<br>Problem reporting requirements- 72 hours<br>IRB Approval<br>Informed consent</td></tr>
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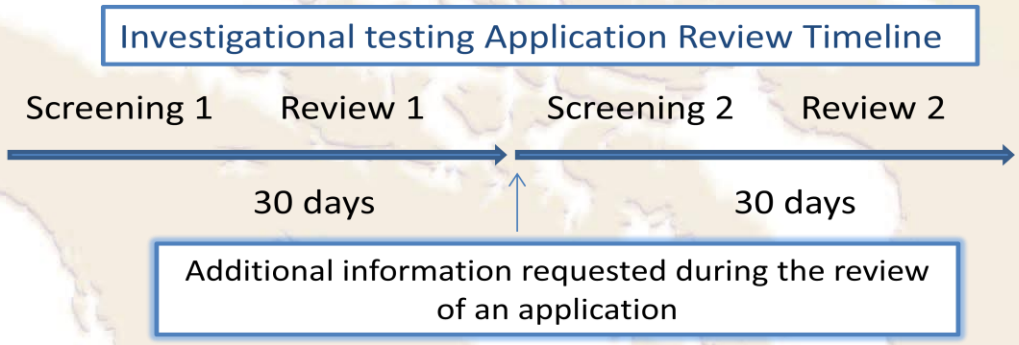
As per the Medical Devices Division of Health Canada, the target review time for a Class II, III, and IV medical device ITA is a total of 30 calendar days. First, the application will go through a screening process, and if it is accepted for review, a screening acceptance letter will be issued.




After approval of an ITA, a "No Objection Letter" (NOL) is sent to the Sponsor indicating Health Canada's agreement on conducting the study. However, Health Canada requires notification of ethics clearance for the study through a Research Ethics Board prior to issuing a No Objection Letter.

If Unlicensed Devices are to be used in conjunction with a Drug in a clinical trial, the Sponsor should sign the application for both an ITA (Devices) and CTA (Drugs) that will be reviewed in parallel.

## Challenges in Medical Device Clinical Development in Canada

The clinical development of a new medical device involves exploratory (pilot) and pivotal clinical studies as well as in vitro and in vivo pre-clinical investigations, if possible. Pilot studies are performed in the early phase of medical device development to capture preliminary safety and effectiveness information on the device before the pivotal study design, and are typically performed at one or two sites with less than 100 patients. Based on pilot study work, Pivotal studies are conducted to determine the safety and effectiveness of a device in a statistically justified number of subjects.

In Canada, there is no equivalent to the FDA 510(k) clearance that allows a medical device company to bypass the expensive and time consuming randomized clinical trial process. FDA 510(k) clearance requires that the sponsor demonstrates that there is a substantial equivalence to products already approved in the US market and that the difference between the “new” and the existing device is acceptable for FDA clearance. Therefore, Health Canada’s requirements for class II, III and IV devices are higher than the standards employed in the US. In addition, over the last five years, the Canadian regulation requirements have become more stringent, which has resulted in significant delays for starting up Clinical studies for a medical device. This,

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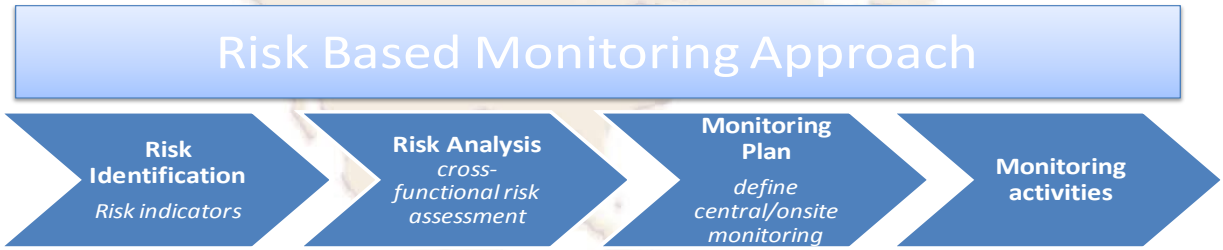
along with the continued increase of clinical research costs has forced Sponsors or Manufacturers to re-evaluate clinical development approaches for medical devices.

## Monitoring Medical Device Trials

Clinical site, investigator, IRB/EC requirements cannot be less stringent than ISO14155-2011, if the standard is part of the requirements for the study. The new ISO14155-2011 "Clinical investigation of medical devices for human subjects - Good clinical practice" is more harmonized with ICH GCP but adapted for medical device trials and has been well received as a global standard for medical device trials than the two earlier versions of the document ISO 14155-1996, and ISO 14155-2003. Other than focusing more on Project Management, GCP requirements and documentation, this complete revised version emphasizes on monitoring activities, and the monitor's role in supporting compliance. Additionally, this version also regulates the electronic data capture systems used in medical device studies that are a critical step in central monitoring activities and part of the new FDA guidelines regarding the Risk-based monitoring approach. This methodology uses adaptive monitoring based on risk assessments that increase Clinical Research Associate (CRA) efficiency and productivity combined to data quality and subject safety.




In conclusion, Vantage BioTrials has a deep understanding of the challenges faced in clinical development for medical devices in Canada. Our team can provide experienced professionals to meet your clinical development needs for both pilot and pivotal studies using efficient study management strategies that can reduce costs and shorten time lines by:

- Developing a well-designed protocol and case report forms (CRFs) to ensure high quality data and efficient monitoring
- Site identification and feasibility analysis
- Support Services to meet ISO 14971-2012 "Application of risk management to medical devices" requirement; management procedures and practices to analyze, evaluate, control, and monitor risk relating to the safety of a medical device throughout the design, development and product lifecycle
- Investigational Testing Application to Health Canada, IRB/EC submission, Labeling assistance, and other global requirements. Efficiently managing study start up, and

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execution in accordance with ICH GCP & ISO 14155-2011, and Canadian Medical device regulations

- Risk analysis/mitigation and risk-based monitoring approach

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*With over 14 years of Pharmaceutical & Academic experience, Ibtissem brings to Vantage BioTrials a wealth of clinical research knowledge. She has a strong understanding and experience with the conduct and implementation of clinical research and medical device studies and in accordance to regulatory and agency requirements.*

**References**:


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## About Vantage BioTrials Inc.

Vantage BioTrials Inc. is a privately owned Clinical Trial Management Organization (CTMO) based in Montréal, Canada, that provides superior trial management services and combines a precise blend of clinical development knowledge, talent and resources that will ensure a clinical study's full potential. By servicing our global Pharmaceutical, Biotech, Medical Device and Generic clients who perform Phase I, II-IV clinical trials, our goal is to exceed their expectations by offering outstanding monitoring, project management and clinical operation services.

To learn more about Vantage BioTrials, please visit us at www.vantagebiotrials.com.