

February 22, 1999

To: Medical Devices Stakeholders

Subject: Preparation of an Application for Investigational Testing - *In Vitro* Diagnostic Devices (IVDD)

The *Medical Devices Regulations* set out the requirements governing the sale, importation and advertisement of medical devices. The goal of the Regulations is to ensure that medical devices distributed in Canada are safe, effective, and meet quality standards. The Therapeutic Products Programme published these new Regulations in *Canada Gazette II* in May 1998 and began implementation on July 1, 1998.

This document, titled Preparation of an Application for Investigational Testing - *in vitro* Diagnostics Devices, sets out the Programme's guidance on the above.

The purpose of this guidance document is to assist manufacturers and/or device sponsors in their preparation of the necessary documentation that is required to obtain an authorization for the sale of an *in vitro* diagnostic device for investigational testing, under the *Medical Devices Regulations*.

For more information on how to prepare an application for investigational testing for IVDD medical devices please contact:

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Attachments



Therapeutic Products Programme

OUR MISSION: To ensure that the drugs, medical devices, and other therapeutic products available in Canada are safe, effective and of high quality.

Programme des produits thérapeutiques

NOTRE MISSION: Faire en sorte que les médicaments, les matériels médicaux et les autres produits thérapeutiques disponibles au Canada soient sûrs, efficaces et de haute qualité.

Therapeutic Products Programme
GUIDANCE DOCUMENT

Preparation of an Application for Investigational Testing - *in vitro* Diagnostics Devices

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1	Page 14, Section 7.2, first paragraph : <i>Mandatory Problem Report</i>	<p>Paragraph rewritten.</p> <p>Old paragraph: “Sections 59 to 62 of the <i>Medical Devices Regulations</i> with respect to mandatory problem reporting apply to devices undergoing investigational testing. The investigator and/or the manufacturer are responsible to notify the Therapeutic Products Programme within 72 hours of any incident that meets the criteria as defined in Subsection 59(1) of the <i>Medical Devices Regulations</i>.”</p> <p>New paragraph: “Sections 59 to 62 of the <i>Medical Devices Regulations</i> with respect to mandatory problem reporting apply to devices undergoing investigational testing. The investigator <u>is</u> responsible to notify the Therapeutic Products Programme <u>and the manufacturer</u> within 72 hours of any incident that meets the criteria as defined in Subsection 59(1) of the <i>Medical Devices Regulations</i>.”</p>

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1.0 Introduction

1.1 Purpose

This guidance document is intended to provide assistance to manufacturers and/or device sponsors in preparing the documentation necessary to obtain an authorization for the sale of an *in vitro* diagnostic device (IVDD) for investigational testing under the *Medical Devices Regulations*.

All medical devices sold in Canada must meet the safety and effectiveness requirements set out in Sections 10 to 20 of the *Medical Devices Regulations*. The only exceptions to these requirements are devices sold under Part 2 of the Regulations for custom or special access purposes and devices sold under Part 3 for investigational testing purposes. For additional information on the special access programs available under Part 2 of the Regulations, refer to the guidance document “How to Apply for Authorization to Obtain Custom-Made or Special Access Devices (GD004).”

1.2 Background

Section 9 of the *Medical Devices Regulations* states that all devices sold or offered for sale in Canada must meet the safety and effectiveness requirements of the regulations. There are exceptions for medical devices sold under Parts 2 and 3 of the Regulations.

Part 3 of the regulations will allow for the investigational testing of medical devices in Canada which do not yet meet the safety and effectiveness requirements listed in Sections 10 to 20 of the Regulations. An Authorization for Investigational Testing will not be issued until a manufacturer and/or device sponsor has complied with the requirements of Sections 79 to 88 of the Regulations.

1.3 Scope

This guidance document is intended to aid manufacturers and/or device sponsors in organizing and submitting an application for Investigational Testing Authorization for Class II, III and IV IVDDs. It also provides details on the manufacturers’ responsibilities when conducting investigational testing using Class I devices.

This document will also assist investigators and institutions involved in the investigational testing of IVDDs in Canada to understand their roles and responsibilities in this process. This document is not applicable to the investigational testing of non-IVDDs in Canada. For more information manufacturers and/or device sponsors are referred to the draft guidance document titled “Preparation of an Application for Investigational Testing - Medical Devices, (http://hc-sc.gc.ca/dhp-mps/md-im/applic-demande/guide-ld/md_gd_ita_im_ld_aee-eng.php)

1.4 Definitions

ADDITIONAL INFORMATION - A written request made under Section 84 for additional information necessary to determine whether the conditions set out in subsection 83(1) have been met.

DEVICE IDENTIFIER - means a unique series of letters or numbers or any combination of these or a bar code that is assigned to a medical device by the manufacturer and that identifies it as different from similar devices.

DEVICE NAME - in respect of a medical device, includes any information necessary for the user to identify the device and to distinguish it from similar devices.

IN VITRO DIAGNOSTIC DEVICE (IVDD) - a medical device or a product subject to Section 3 of the *Medical Devices Regulations*, that is to be used *in vitro* for the examination of specimens derived from the human body.

Section 3

(1) These regulations apply to an *in vitro* diagnostic product that is a drug or that contains a drug as if the product were a medical device.

(2) Subsection (1) does not apply to *in vitro* diagnostic products that are or contain drugs listed in Schedule E or F to the *Food and Drugs Act* or in the Schedule to Part G or Part J of the *Food and Drug Regulations*.

NEAR PATIENT IVDD - is defined as an IVDD for use outside a laboratory environment for home testing or point-of-care testing, such as in a pharmacy, a health care professional's office or at the bedside.

2.0 How to Apply for an Investigational Testing Authorization

2.1 The Application

To apply for an authorization to conduct investigational testing on human subjects in Canada, a manufacturer and/or device sponsor must use the application form in Appendix 1. Appended to this application form will be the necessary supporting records as detailed in Section 81 paragraphs (a) to (k). To facilitate the timely evaluation of these applications it is recommended that the manufacturer provide an executive summary, a table of contents and the discrete chapters appropriate for each type of medical device. The presentation and structure of the investigational testing authorization application should be organized into sections as outlined in Appendix 2.

Applications are to be sent to:

Medical Devices Bureau
Therapeutic Products Programme
Health Canada
11 Holland Avenue, Address Locator: 3403A
Ottawa, Ontario K1A 0K9

Telephone: 613-954-0297
Facsimile: 613-957-6345
Email: DED_Manager@hc-sc.gc.ca

2.2 Review and Authorization

Following the review of the application, the Minister may issue an authorization to conduct the proposed investigational testing, provided the device can be used without seriously endangering the life or health of patients, users or other persons, the testing is not contrary to the best interests of the patients and the objective of the testing is achievable. All investigational testing carried out in Canada must conform to the principles of the Declaration of Helsinki and the Medical Research Council's "Code of Ethical Conduct for Research Involving Humans - May 1997."

If the documentation provided with the application is not sufficient to enable a determination under Subsection 83(1), then ADDITIONAL INFORMATION may be requested under Section 84.

An investigational testing authorization will specify the information listed in Section 83 subsection (2) of the *Medical Devices Regulations*.

The authorization will remain valid provided no changes are made to the investigational protocol, the identity of the qualified investigators and the institution where the testing is being conducted and the type of diagnosis or treatment for which the device is sold.

2.3 Changes Made During an Investigational Testing Authorization

If changes are made to the investigational protocol, the identity of the qualified investigators and the institution where the testing is being conducted and the type of diagnosis or treatment for which the device is sold, a new authorization must be obtained from TPP. This authorization may be granted after a review of ADDITIONAL INFORMATION related to the proposed change. This authorization must be obtained in advance of implementing the changes.

2.4 Rejection or Refusal of an Application

An investigational testing application may be rejected if the manufacturer and/or device sponsor fails to provide the records described in Section 81. The authorization may be refused if it is determined that:

- the device cannot be used safely for investigational testing;
- the investigational testing is not in the best interests of patients; or
- the objective of the testing cannot be achieved.

In the case of a refusal to issue an investigational testing authorization, the manufacturer and/or device sponsor may appeal the decision.

2.5 Additional Guidance

This guidance document, "Preparation of an Application for Investigational Testing - *in vitro* Diagnostic Devices" provides information for devices in general, if a manufacturer has specific questions or concerns they are urged to contact the Manager, Device Evaluation Division, Medical Devices Bureau.

3.0 Access to Information Act and the Confidentiality of Authorization Applications

Information provided to the Programme by manufacturers and/or device sponsors is subject to the provisions of the Access to Information Act. Authorization application information containing trade secrets, scientific, technical, commercial or financial information that is confidential is protected from disclosure by this Act. It is also the Programme's current policy to keep confidential, information regarding investigational testing authorization applications that have been received or granted.

4.0 When to Apply for an Authorization for Investigational Testing

4.1 General directions

Investigational Testing (IT) is a study aimed at supporting the determination of safety and effectiveness of an investigational IVDD prior to general marketing. The intent of IT for an IVDD is to minimize the risk of obtaining inaccurate results by addressing the factors that may adversely affect the performance of the device. After obtaining pre-clinical data, the investigational device is to be tested in the target population in Canada by the investigators (including self-administered tests) to validate the performance of the device under the conditions in which the test is intended to be used. The data gathered during IT is reviewed by Medical Devices Bureau as evidence of safety and effectiveness for consideration of issuing a licence for the device.

4.2 Indications for obtaining authorization for IT

An investigational testing application is indicated when the following conditions are met: (a) pre-clinical analytical studies have been completed, (b) proposed cut-off between positive and negative results have been established, (c) the evidence for the safety and effectiveness of the device has not been adequately established for clinical use, (d) additional evidence for safety and effectiveness can be obtained only by trials with target populations.

5.0 Presentation of the Investigational Testing Authorization Document

Manufacturers and/or device sponsors are requested to follow the structure presented in Appendix 2 when applying for an investigational testing authorization. Sections that are not applicable should be clearly indicated. In certain instances, it may be necessary to follow a special or unique format. In such cases, the concurrence of the Manager, Device Evaluation Division should be obtained in advance.

Information in the document should be recorded in either French or English. Material in a foreign language must be accompanied by an English or French translation.

All documents should be legible and the page size, including tables should be uniform. The submission should be bound for easy access, for example in three-ring binders. Each volume must be clearly labelled and numbered both on the spine and on its front cover.

The pagination may be sequential for the entire submission or by volume. In the executive summary and table of contents, individual sections of text should be identified both by the assigned decimal number and by the correct title as suggested in this guideline, Appendix 2. Cross references should include both volume and page number.

6.0 The Requirements of an Application for Investigational Testing Authorization

The requirements of an investigational testing authorization application are presented below. These requirements differ depending on the risk based classification of the device in question.

6.1 Class I IVDDs

Section 80(3) of the *Medical Devices Regulations* permits a manufacturer or importer of a Class I medical device to sell the device to a qualified investigator for the purpose of conducting an investigational test provided the seller possesses all the records and information detailed in Section 81 of the regulations.

There is no need to make an application to the Therapeutic Products Programme to conduct investigational testing of Class I IVDDs in Canada.

6.2 Class II IVDDs

An application for an investigational testing authorization of a Class II device must contain the following information in four distinct chapters, Introduction, Institutional Information, Protocol and Labelling.

6.2.1 Introduction

6.2.1.1 Section 81(a) - Manufacturer Identification

The complete name and address of the device manufacturer and importer (if applicable) including contacts and telephone number must be provided. This information should agree with the information provided on the application form.

6.2.1.2 Section 81(b) - Device Identification

The manufacturer and/or device sponsor must provide the name of the device and the DEVICE IDENTIFIERS, as they appear on the label. This includes any component, part or accessory that is part of the device.

The risk classification of the device as determined by the manufacturer for the purpose of the investigational testing must be provided. This risk classification may differ from that of the device in general sale, if for example a new indication is being investigated.

6.2.2 Institutional Information

6.2.2.1 Section 81(h) - Name of the Institutions

For a Class II investigational testing authorization application, the name and address of each institution at which the testing is proposed to be conducted is required. These

institutions will be listed as part of the Authorization provided under Section 83(2).

6.2.3 Protocol

6.2.3.1 Section 81(i) - Protocol

The protocol of the proposed investigational testing should follow the Clinical Protocol outlined in Appendix 4.

6.2.4 Device Label

6.2.4.1 Section 81(j) - Device Label

Section 81(j) requires the manufacturer and/or device sponsor to submit a copy of the device label. This will include the product monograph and all advertising brochures intended to be used with the device. It will also include copies of information and instruction for use given to either the qualified investigator or patient.

Device labels must be provided with the application for investigational testing. Section 86 of the *Medical Devices Regulations* sets out the requirements of a label on a device sold for investigational testing. In addition to the name of the device and the name of the manufacturer, Subsections 86(c) and 86 (d) and 86(e) require that the statements “Investigational Device”, “To be Used by Qualified Investigators Only”, and “The performance specifications of this product have not been established” and “Instrument de recherche”, “Réservé uniquement à l’usage de chercheurs compétents” and “Les spécifications de rendement de l’instrument n’ont pas été établies” be present in English and French. An alternate wording may be used, provided the above meaning is conveyed.

6.3 Class III or IV IVDD That Is Not Used for Patient Management, and Not Including A Near-Patient IVDD

These IVDDs must conform to the following conditions:

- 1) The investigational IVDD will not be used for diagnostic purposes without confirmation by another medically established diagnostic procedure, and thus the investigational test results will not impact on patient management decisions.
- 2) The investigational IVDD will not be conducted outside of a laboratory environment, and thus will not be used as a near-patient IVDD.

The application must contain the following information in four distinct chapters: Introduction, Institutional Information, Protocol, and Labelling.

6.3.1 Introduction

6.3.1.1 Section 81(a) - Manufacturer Identification

The complete name and address of the device manufacturer and importer (if applicable) including contacts and telephone number must be provided. This information should agree with the information provided on the application form.

6.3.1.2 Section 81(b) - Device Identification

The manufacturer and/or device sponsor must provide the name of the device and the DEVICE IDENTIFIERS, as they appear on the label. This includes any component, part or accessory that is part of the device.

The risk classification of the device as determined by the manufacturer for the purpose of the investigational testing must be provided. This risk classification may differ from that of the device in general sale, if for example a new indication is being investigated.

6.3.2 Institutional Information

6.3.2.1 Section 81(h) - Name of the Institutions

For a Class II investigational testing authorization application, the name and address of each institution at which the testing is proposed to be conducted is required. These institutions will be listed as part of the Authorization provided under Section 83(2).

6.3.2.2 Section 81(h) Research Ethics Board Approval

If the investigational testing includes procedures that are considered to pose high risk to the test subject, written approval from the institution's Research Ethics Board will be required indicating that the investigational testing may be carried out there.

The procedures considered to pose risk are:

- 1) The testing is invasive.
- 2) There is a requirement of sampling presenting significant risk.
- 3) The persons providing the tissues are individually identifiable (see Code of Ethical Conduct for Research Involving Humans, Tri-council Working Group of Canada, 1997). In the absence of an institutional Research Ethics Board, an Ethics Committee must be convened that conforms with the Canadian Institutes of Health Research (CIHR) Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans, (<http://www.rcr.ethics.gc.ca/eng/index>). This Policy is available on the CIHR website at www.cihr-irsc.gc.ca or by contacting the CIHR.

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Ottawa, ON K1A 1H5

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A conditional investigational testing authorization may be granted by the TPP pending the

receipt of a Research Ethics Board approval. However the investigational testing cannot begin, until this approval has been obtained and submitted to the TPP.

6.3.3 Protocol

6.3.3.1 Section 81(i) - Protocol

The protocol of the proposed investigational testing should follow the Clinical Protocol outlined in Appendix 4.

6.3.4 Device Label

6.3.4.1 Section 81(j) - Device Label

Section 81(j) requires the manufacturer and/or device sponsor to submit a copy of the device label. This will include the product monograph and all advertising brochures intended to be used with the device. It will also include copies of information and instruction for use given to either the qualified investigator or patient.

Device labels must be provided with the application for investigational testing. Section 86 of the *Medical Devices Regulations* sets out the requirements of a label on a device sold for investigational testing. In addition to the name of the device and the name of the manufacturer, Subsections 86(c) and 86 (d) and 86(e) require that the statements “Investigational Device”, “To be Used by Qualified Investigators Only”, and “The performance specifications of this product have not been established” and “Instrument de recherche”, “Réservé uniquement à l’usage de chercheurs compétents” and “Les spécifications de rendement de l’instrument n’ont pas été établies” must be present in English and French. An alternate phrase may be used, provided the above meaning is conveyed.

6.4 Class III Or IV IVDD That Is Used for Patient Management Decision and All Class III and IV Near-Patient IVDDs

These IVDDs are characterized in the following way:

- 1) The investigational IVDD may be used for diagnostic purposes without confirmation by another medically established diagnostic procedure, and thus the test results may impact on patient management decisions. An example of this will be a new category of IVDD for which there is no corresponding medically established diagnostic procedure to confirm/compare with.
- 2) The investigational IVDD is a Near-patient IVDD. Tests on the Near-Patient IVDDs are performed by individuals not professionally trained for laboratory testing and may result in a great degree of variability in the clinical outcomes measured. Thus safety and performance of such devices may be quite different from those used by professionally trained staff, unless the direction provided for their use, interpretation and follow-up have been properly adapted to, and validated in, the target population of intended users whose language may be English or French.

The application must contain the following information in six distinct chapters: Introduction, Risk Analysis, Institutional Information, Protocol, Labelling, and Investigator Agreements.

6.4.1 Introduction

6.4.1.1 Section 81(a) - Manufacturer Identification

The complete name and address of the device manufacturer and importer (if applicable) including contacts and telephone number must be provided. This information should agree with the information provided on the application form.

6.4.1.2 Section 81(b) - Device Identification

The manufacturer and/or device sponsor must provide the name of the device and the DEVICE IDENTIFIERS, as they appear on the label. This includes any component, part or accessory that is part of the device.

The risk classification of the device as determined by the manufacturer for the purpose of the investigational testing must be provided. This risk classification may differ from that of the device in general sale, if for example a new indication is being investigated.

6.4.1.3 Section 81(c) - Device Description

This section of the regulations requires a description of the device and of the materials used in its construction and packaging. This description should include good quality colour photographs of the device, its components, parts and accessories and engineering diagrams, where appropriate.

A complete list of all the device constituent components is required.

6.4.1.4 Section 81(d) Design Philosophy

This paragraph requests a description of the features of the device that permit it to be used for the medical conditions, purposes and uses for which it is manufactured, sold or represented by the manufacturer. To satisfy this requirement, a brief description of the device's design philosophy and performance specifications should be provided and linked to the objectives of the proposed investigational testing. References and comparisons with appropriate previous versions or generations of the device should be presented. A tabular format is preferred for this comparison.

This section should include an overview of the purposes and principles of operation for the device and should include a summary of the method of use and operation of the device.

6.4.1.5 Section 81(e) Marketing History

In this paragraph a summary of the marketing history of the device is requested. Include a

summary of special access requests made to the Programme and the outcome of these requests. In addition the manufacturer and/or device sponsor is requested to provide details of the regulatory status of the device in other major world markets, and the volume of sales to date globally. A summary of reported problems with the device and details of any recalls in other jurisdictions is also required.

6.4.2 Risk Assessment and Risk Reduction

Subsection (f) Section 81 requires a risk assessment, comprised of a risk analysis and risk evaluation of the risks inherent in the use of the device and the risk reduction measures adopted for the purposes of conducting the investigational testing. For further guidance in this area the reader is referred to the current draft of ISO/DIS 14971-1 "Medical Devices - risk management Part 1: Application of risk analysis".

This first element to be considered is a risk analysis. This will include the complete description and identification of the devices and accessories under consideration. A list of possible hazards must be prepared for these devices. Secondly, these risks must be evaluated against the presumed benefits of the device. And thirdly, an indication of the way by which the risks has been reduced to acceptable levels must be provided.

The identity of who has carried out the risk analysis must be provided. There are several techniques that can be used for the analysis of risk, the choice of method must be appropriate for the device and the risk involved.

6.4.2.1 Section 81(f)(i) - Previous Studies

The results of any previous research, testing and studies conducted with the device must be provided. These results provide a background to the investigational testing authorization application.

6.4.2.2 Section 81(f)(ii) - Alternate Treatments

A description of currently available alternate treatments should be presented. This may include the methods currently used to diagnose or treat the medical conditions that are the subject of the current investigational testing authorization request.

6.4.2.3 Section 81(f)(iii) - Precautions

All known information respecting any cautions, warnings, contraindications and possible adverse effects associated with the use of the device must be presented.

6.4.3 Institutional Information

6.4.3.1 Section 81(g) - Names of Investigators

The names of all qualified investigators to whom the device is proposed to be sold must be submitted to TPP, including their qualifications and experience. Often there are many investigators involved in an investigational test at a particular site. In this case, the

principle investigator should be identified. An abbreviated *curriculum vitae*, detailing the educational qualifications of the investigator and their relevant research experience (in a related area), should be submitted.

6.4.3.2 Section 81(h) - Name of the Institutions

The name and address of each institution at which the testing is proposed to be conducted is required. These institutions will be listed as part of the Authorization provided under Section 80(2).

6.4.3.3 Section 81(h) - Research Ethics Board Approval

Written approval must be received from each institution proposed to carry out the testing. This approval may be in the form of an Research Ethics Board decision.

A conditional investigational testing authorization may be granted by the TPP pending the receipt of a Research Ethics Board approval. However the investigational testing cannot begin, until this approval has been obtained and submitted to the TPP.

6.4.4 Protocol

6.4.4.1 Section 81(i) - Protocol

The protocol of the proposed investigational testing should follow the Clinical Protocol outlined in Appendix IV.

6.4.5 Device Label

Section 81(j) requires the manufacturer and/or device sponsor to submit a copy of the device label. This will include the product monograph and all advertising brochures intended to be used with the device. It will also include copies of information and instruction for use given to either the qualified investigator or patient.

Device labels must be provided with the application for investigational testing. Section 86 of the *Medical Devices Regulations* sets out the requirements of a label on a device sold for investigational testing. In addition to the name of the device and the name of the manufacturer, Subsections 86(c) and 86 (d) and 86(e) require that the statements “Investigational Device”, “To be Used by Qualified Investigators Only”, and “The performance specifications of this product have not been established” and “Instrument de recherche”, “Réservé uniquement à l’usage de chercheurs compétents” and “Les spécifications de rendement de l’instrument n’ont pas été établies” must be present in English and French. An alternate phrase may be used, provided the above meaning is conveyed.

6.4.6 Investigator Agreements

6.4.6.1 Subsection 81(k) - Investigator Agreements

The manufacturer and/or device sponsor are required to obtain investigator agreements from each investigator enrolled in the investigational testing. This agreement outlines the responsibilities of the investigator to:

- conduct the testing in accordance with the protocol;
- fully inform each enrolled patient;
- not to permit the device to be used outside the agreed protocol;
- supervise the use of the device; and
- report all incidents under Section 59 of the regulations to the Minister within 72 hours.

A copy of an investigator agreement form is provided in Appendix 3. An alternate format is acceptable provided the five (5) conditions described in subsection 81(k) are adequately addressed.

7.0 Manufacturer and/or Device Sponsor Responsibilities

7.1 Record Keeping

The manufacturer and/or device sponsor of a medical device undergoing investigational testing in humans in Canada must maintain the records described in Section 81 of the *Medical Devices Regulations*. For Class II, III and IV devices a portion of these records are submitted to the Therapeutic Products Programme in order to obtain the authorization detailed in Sections 82 and 83.

The requirement to maintain distribution records described in Section 52 to 56 apply to devices sold for the purpose of investigational testing.

7.2 Mandatory Problem Reporting

Sections 59 to 62 of the *Medical Devices Regulations* with respect to mandatory problem reporting apply to devices undergoing investigational testing. The investigator is responsible to notify the Therapeutic Products Programme and the manufacturer within 72 hours of any incident that meets the criteria as defined in Subsection 59(1) of the *Medical Devices Regulations*.

Subsection 59(1) defines two types of device related incidents. The first is related to a failure or a deterioration in the effectiveness of the device or any inadequacy in its labelling or in the directions for use accompanying it. The second involves an incident that has led to the death or a serious deterioration in the health of a patient, user or other person or, where it is reasonable to believe that such an incident were it to recur, could lead to the death or a serious deterioration of the state of health of a patient, user or other person.

For additional information and guidance, the reader should consult the guidance document "*Mandatory and Voluntary Problem Reporting for Medical Devices*", http://www.hc-sc.gc.ca/dhp-mps/pubs/medeff/_guide/2011-devices-materiaux/index-eng.php

7.3 Other Obligations

Sections 57 and 58 and 63 to 65 of the *Medical Devices Regulations* apply to devices authorized for investigational testing. The manufacturer and/or device sponsor is required to have documented procedures in place to handle product complaints and recalls. In addition, the appropriate records of these activities must be maintained. For additional information, the guidance document "*Guidance on Complaint Handling and Recall*", http://www.hc-sc.gc.ca/dhp-mps/compli-conform/prob-report-rapport/gui-0054_recall-retrait-doc-eng.php, should be consulted. Sections 66 to 68 describing the manufacturer's responsibilities with regard to implant registration are also applicable (as appropriate) to devices authorized for investigational testing.

Section 87 of the regulations describes the limitations placed on the advertisement of devices undergoing investigational testing in Canada. Only devices which have been authorized under subsection 83(1) can be advertised. The advertisement must clearly state the device is the subject of investigational testing and the proposed purpose of the testing.

8.0 Additional Information - Cancellation of an Authorization

Section 85 of the *Medical Devices Regulations* allows for the cancellation of an investigational testing authorization for Class II, III or IV devices and the stop sale of a Class I device for investigational purposes. The conditions for stopping an investigation test are outlined in subsection 83(1) paragraphs (a) to (e).

Prior to cancelling an authorization, TPP may request information from the manufacturer and/or device sponsor to substantiate that the conditions set out in subsection 83(1) are still applicable. If this information is not received, the authorization will be cancelled.

Appendix 1:
Application Form for Investigational Testing Authorization



APPLICATION FOR INVESTIGATIONAL TESTING AUTHORIZATION

(disponible en français)

1. DEVICE CLASSIFICATION

- Class II Class III Class IV

2. DEVICE NAME (as it appears on label)

[Note: this is the device name for which the Authorization will be issued]

--

3. PROTOCOL IDENTIFICATION:

Include the type of diagnosis or treatment for which the device will be sold.

--

4. NAME AND ADDRESS OF MANUFACTURER (as it appears on the label)

[Note: this is the name and address to which the Authorization will be issued]

Company Name		
Street Address/P.O. Box		
City		
Province/State		
Postal/Zip Code		
Country		
Contact Name and Title:		
Telephone No.:		Fax No.:
E-Mail Address:		



APPLICATION FOR INVESTIGATIONAL TESTING AUTHORIZATION (disponible en français)

5. MAILING ADDRESS FOR REGULATORY CORRESPONDENCE (if different from 4)

Note: (i) The authorization will be issued to Company named in Item 4 but will be sent to the Company shown below if different. (ii) The Company named below must be authorized by the manufacturer named in Item 4 to submit an authorization application on their behalf. See the Authorization of Contact form for details.

Company Name:	
Street Address/P.O. Box	
City	
Province/State	
Postal/Zip Code	
Country	
Contact Name and Title:	
Telephone No.:	Fax No.:
E-Mail Address:	

6. DEVICE TYPE (check one only)

Single Device	
Medical Device Group	
Medical Device Family	
Medical Device Group Family	
Test Kit	
System	

7. PREFERRED NAME CODE: (xxAAA) optional

--

8. IS THIS DEVICE A NEAR PATIENT *IN VITRO* DIAGNOSTIC (IVDD)? Yes No

IS THIS DEVICE INTENDED TO BE SOLD FOR HOME USE Yes No



APPLICATION FOR INVESTIGATIONAL TESTING AUTHORIZATION

(disponible en français)

9. DEVICE USAGE CATEGORY

(73) Anaesthesiology	
(74) Cardiovascular	
(76) Dental	
(77) Ear, Nose & Throat	
(78) Gastroenterology & Urology	
(79) General & Plastic Surgery	
(80) General Hospital	

(84) Neurology	
(85) Obstetrics & Gynaecology	
(86) Ophthalmology	
(87) Orthopaedics	
(89) Physical Medicine	
(90) Radiology/Imaging	

FOR IVDDs ONLY

(75) Chemistry	
(81) Haematology	
(82) Immunology	

(83) Microbiology	
(88) Pathology	
(91) Clinical Toxicology	

10. DOES THIS DEVICE CONTAIN A DRUG?

Yes No

(Note: this question does not apply to IVDDs)

If yes

Brand /Trade Name of Drug:
Active Ingredient:
Drug Manufacturer:
Applicable Drug Identification Number (if any):



APPLICATION FOR INVESTIGATIONAL TESTING AUTHORIZATION

(disponible en français)

11. DEVICE DETAIL

Please provide the following information, where applicable for each component device, part or accessory.

Name of Device, Components, Parts and/or Accessories as per product label	Device Identification Number if previously assigned	Model or catalogue number



APPLICATION FOR INVESTIGATIONAL TESTING AUTHORIZATION *(disponible en français)*

12. ATTACHMENTS

In addition to items 1 to 11, of the Application for investigational testing, please indicate (✓) which of the relevant information requirements listed below, are included as attachments to this application, or will be provided at a later date. For details regarding content and format, please refer to the guidance documents “Preparation of an Application for Investigational Testing - Medical Devices” and “Preparation of an Application for Investigational Testing - *In Vitro* Diagnostic Devices”

	Attached	To Come
Background Information		
Risk Assessment		
Ethics Committee or IRB Approval(s)		
Protocol		
Device Label		
Investigator Agreements		

13. If this Device contains a drug and it does **not** have a Drug Identification Number, **I the Manufacturer of this device attest** that the (**drug meets**) (**drug does not meet**) acceptable standards of safety, efficacy and quality.

I hereby certify that the information provided on this application and in any attached documentation is correct, complete and in accordance with all relevant sections of the *Medical Devices Regulations*.

Name of Signing Official: _____

Signed: _____ **Date:** _____



AUTHORIZATION OF CONTACT

(disponible en français)

(✓ application type)

This form authorizes the person named in **Section B** to submit this application for : a new device licence; an amended device licence; investigational testing; on behalf of the company identified in **Section A**.

Section A

I hereby authorize the person named in **Section B** to submit this application for: a new device licence; an amended device licence; investigational testing; to the Minister on my behalf. The Medical Devices Bureau will accept either this form or a signed letter of authorization on company letterhead.

Name: _____

Title: _____

Company: _____

Telephone Number: _____ Fax Number: _____

Signature: _____ Date: _____

Section B

I hereby accept the responsibility to submit this application for: a new device licence; an amended device licence; investigational testing; to the Minister by the person named in **Section A**. The Medical Devices Bureau will accept either this form or a signed letter of authorization on company letterhead.

Name: _____

Title: _____

Company: _____

Telephone Number: _____ Fax Number: _____

Signature: _____ Date: _____

Medical Devices Bureau
Therapeutic Products Directorate
Health Canada
11 Holland Avenue, Address Locator: 3002A
Ottawa, Ontario K1A 0K9

Telephone: 613-954-0297
Facsimile: 613-957-6345
Email: DED_Manager@hc-sc.gc.ca

Appendix 2 - Proposed Format for an Investigational Testing Application

The following is the suggested format for an investigational testing application, some of the sections are not applicable to Class II applications.

Application Form
Executive Summary
Table of Contents
1 Background Information
1.1 Device Description
1.2 Design Philosophy
1.3 Marketing History
2 Risk Assessment
2.1 Risk Analysis and Evaluation
2.2 Previous Studies
2.3 Alternate Treatments
2.4 Precautions
3 Institutional Information
3.1 Investigator(s)
3.2 Name of Institution(s)
3.3 Research Ethics Board Approval(s)
4 Protocol
5 Device Label
6 Investigator Agreement(s)

Appendix 3 - Investigator's Agreement

INVESTIGATOR'S AGREEMENT IN ACCORDANCE WITH SUBSECTION 81(k) OF THE *MEDICAL DEVICES REGULATIONS*

Device Name/Nom de l'instrument: _____

Protocol Number/N^o du Protocole: _____

I, _____
, undertake, in accordance with Subsection 81(k) of
the *Medical Devices Regulations*, as outlined below,
to:

(i) conduct the investigational testing in accordance
with the protocol:

(ii) inform a patient who is to be diagnosed or treated
with the device of the risks and benefits associated
with its use and obtain the written consent of the
patient,

(iii) not use the device or permit it to be used for any
purpose other than the investigational testing specified
in the protocol,

(iv) not permit the device to be used by any person
other than myself, except under my direction,

(v) in the event of an incident that is related to a failure
of the device or a deterioration in its effectiveness, or
any inadequacy in its labelling or in its directions for
use and has lead to the death or a serious deterioration
in the state of health of a patient, user or other person,
or could do so were it to recur, report the incident and
the circumstances surrounding it to the Director and
the manufacturer or importer of the device, within 72
hours after its discovery.

(Tel: (613) 957-4587 Fax: (613) 957-6345)

Je, _____
, m'engage conformément à la section 81(k) du
Règlement sur les instruments médicaux, comme
décrits ci-bas, à :

(i) effectuer l'essai expérimental conformément
au protocole:

(ii) informer le patient qui fera l'objet du
diagnostic ou du traitement au moyen de
l'instrument des risques et des avantages que
comporte son utilisation et obtiendra son
consentement écrit,

(iii) ne pas utiliser l'instrument ni n'en permettre
l'utilisation à des fins autres que l'essai
expérimental décrit dans le protocole,

(iv) ne pas permettra que l'instrument soit utilisé
par une personne autre que moi, sauf sous ma
direction,

(v) advenant un incident qui d'une part, est lié à
une défaillance de l'instrument, une dégradation
de son efficacité ou un étiquetage ou mode
d'emploi défectueux; d'autre part a entraîné la
mort ou une détérioration grave de l'état de santé
d'un patient, utilisateur ou autre personne, ou
serait susceptible de le faire s'il se reproduisait,
rapporter l'incident en question de même que les
circonstances s'y rapportant, au Directeur et au
fabriquant, ou à l'importateur de l'instrument, et
ce, en deçà de 72 heures après la découverte de
l'incident.

(Tél: (613) 957-4587 Téléc: (613) 957-634

Signature

Date

Appendix 4 - Clinical Protocol

CLINICAL PROTOCOL

This section is aimed at assisting the manufacturer in developing an investigational plan that would assess, in clinical settings, performance characteristics of an IVDD assay, that would lead to the evaluation of the clinical significance of the IVDD.

1 Introduction

- 1.1 Intended use (the detection of an analyte/marker by the assay).
- 1.2 Indications for use (clinical settings in which the assay will be used).
- 1.3 A brief description of the biological principle of the test.
- 1.4 The methodology intended to be used.

2 Objective

The objective will be to establish the performance characteristics of the assay in the population it is targeted to be used, and thus substantiate the proposed labelling claims .

As applicable, the specific objectives will specify the particular characteristics (sensitivity, specificity, reproducibility etc.) that are proposed to be evaluated, and show how well the investigational IVDD correlates with the comparator assay/procedure.

3 Study Design

The study should be designed to establish the performance characteristics of the IVDD. The investigational device should be tested in parallel with an approved method used to determine the presence or absence of the disease in the subject whose specimen is tested. The comparator may be a clinical diagnostic criteria or an approved laboratory test, preferably a test of reference.

Supported with rationale the study design should include:

- 3.1 An overview of the study design, delineating which characteristic(s) of the assay performance is to be assessed.
- 3.2 Description of the method with which the investigational assay will be correlated with a comparator assay or a medical procedure.
- 3.3 If two or more test procedures are possible for the assay (e.g., automated/manual; different incubation modes/temperatures/times) performance values for the different methods should be collected for submission to MDP.
- 3.4. Subject/specimen specifications

3.4.1 Subject/patient eligibility

Statements should be made with respect to : (a) the ultimate population for which the device is intended, (b) inclusion and exclusion criteria, (c) participants' age, sex, (d) the medical diagnosis of the participant, including the method used for the diagnosis.

3.4.2 The number of subjects and specimens

Statements should be made with respect to: (a) statistical basis proposed to be used, (b) availability/feasibility of obtaining the required numbers.

3.5 Clinical sites

3.5.1 The selection should aim at choosing varied geographical sites to show the applicability of the assay in populations differing in the prevalence of the disease tested.

3.5.2 The names and addresses of the clinical sites and the name and telephone number of the principal investigator for each testing site.

3.5.3 A certificate of accreditation or equivalent for the laboratories attesting that the laboratory is capable of high volume clinical investigation and that it meets the requirements of Good Laboratory Practice or equivalent.

4 Laboratory Testing Procedures

This section should contain information on:

4.1 The type of specimen, whether it is retrospective, prospective, established panel.

4.2 Sample collection, processing storage and transport methods

4.3 Outcomes/features measured: the calculations and interpretation of the test results

4.4 What procedures to follow, if it is to be the procedures set out in the package insert, or a different one. The procedure should be given in a step-by-step fashion.

4.5 How quality control is to be implemented for all devices/procedures.

5 Data collection and analysis

5.1 Report forms: samples of all the forms used in the study to record observations should be appended. The forms should be designed to ensure that the necessary data will be recorded and reported.

5.2 Raw data: proposed provisions for collections for submission to MDP line data and photographs of gels

5.3 Data inclusion and exclusion criteria for calculations and analysis: this should be adhered to for the entire duration of the IT.

5.4 Statistical analysis methods, describing the rationale for their selection

5.5 Definitions of true positive, true negative, and possibly equivocal results should be given for the purpose of establishing sensitivity and specificity of the device.

6 Interpretation of the results

The summary data should be interpreted to demonstrate the clinical significance of the IVDD.

7 Data presentation

7.1 Raw line data of the performance should be presented, and where applicable, results should be expressed as the number initially reactive, repeat reactive, and agreement with the test of record. Attempts of resolution of any discordant or discrepant results should be presented as well.

7.2 Pictures, rather than photocopies of blots, gels etc. should be supplied.

7.3 Analyses, conclusions and summary of results including explanations of discrepant results are required.

7.4 A copy of the laboratory evaluation report signed and dated by the principal investigator should be submitted.

8 Regulatory and Administrative Information

Statements addressing the following should be included:

8.1 Expected commencement and completion dates

8.2 Conditions for disclosure of data

8.3 Training and monitoring of the personnel of the study site by the manufacturer for conformance with protocol

8.4 Documentation and handling of deviations from the protocol by the clinical site

8.5 Documentation and handling of protocol changes.

9 Bibliography

A list of publications consulted for writing the protocol should be appended.

10 Additional Requirements for Near-Patient IVDDs

Apart from the laboratory evaluations of the performance of the assay, a consumer field evaluation would also be required to determine the device's performance when used by lay users, unassisted, following instructions provided in the labelling. The lay users should be representative of the target users for which the test is intended.

Additional or alternate steps to be followed for NPT-IVDDs are:

10.1 Objective of the IT: In addition to the study objectives stated above, the objective should be to assess how well the package insert is comprehended by the performer of the test. In the case of a home-test IVDD, the study should assess also how well the subject is able to understand the interpretations and implications of the test results.

The specific objectives will be to determine if the users understand the purpose of the test, the conditions for its use, the tests' limitations, the meaning the results (positive, negative or indeterminate) and the appropriate follow up.

10.2 Study design : The additional objectives should be taken into account in the study design.

10.3 Clinical sites: the requirements stated in this document, in item 3.5, will not be applicable for NPT-IVDDs. The studies will be conducted in physician's offices, hospital emergency rooms, STD clinics, residential houses (home test).

10.4 Qualified investigator: For purposes of IT a qualified investigator should take on the responsibility of overseeing the study.

10.5 Test procedures: all the requirements described in item 4, "Laboratory Testing Procedures" will be applicable even though the tests will be carried out outside a laboratory.

10.6 Training of testing personnel: Contrary to the statement in item 8.3 of this document, there will not be any formal training of the individuals performing the tests. However, the overall activity of the IT should be monitored by the manufacturer.