Health Canada Santé Canada

November 2, 2011

Notice

Our file number: 11-120116-490

Re: Guidance Document: Preparation of Summary Technical Documentation (STED)-based Class III and Class IV Premarket Medical Device Licence Applications, not including *In Vitro* Diagnostic Devices (IVDDs)

Health Canada is pleased to announce the release of the *Guidance Document: Preparation of STED-based Class III and Class IV Premarket Medical Device Licence Applications, not including In Vitro Diagnostic Devices (IVDDs)*. It will replace the 2003 *Guidance for Manufacturers preparing a Premarket Application Using the Summary Technical Documentation (STED) for Demonstrating Conformity to the Essential Principles of Safety and Performance of Medical Devices.* A draft version of this guidance was first released for consultation in October 2010. Comments from stakeholders have been considered in producing this final version.

The STED was developed by the Global Harmonization Task Force (GHTF) to encourage and support convergence of regulatory systems for medical devices among jurisdictions. Health Canada has adopted use of the STED for premarket licence applications and licence amendment applications for Class III and Class IV medical devices. Although the use of the STED is not mandatory, Health Canada strongly encourages manufacturers to follow this guidance when submitting Class III and IV medical device licence applications and amendment applications.

This guidance document integrates the STED within the Canadian medical device licensing framework by detailing both Canadian specific requirements and STED-based filing requirements for device licence applications. This document is intended to aid manufacturers in the preparation of STED-based licence applications and licence amendment applications for Class III and Class IV non-*in vitro* diagnostic devices filed pursuant to the Canadian *Medical Devices Regulations*.

The implementation date is November 1, 2011. Once implemented, all premarket device licence applications for the above-noted medical devices are expected to be prepared as specified herein.

For more information on this guidance document, please contact:

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Health Canada Santé Canada

GUIDANCE DOCUMENT

Preparation of Summary Technical Documentation (STED)-based Class III and Class IV Premarket Medical Device Licence Applications, not including *In Vitro* Diagnostic Devices (IVDDs)

Published by authority of the
Minister of Health

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Health Products and Food Branch

Canada

Our mission is to help the people of Canada maintain and improve their health. *Health Canada*	The Health Products and Food Branch's mandate is to take an integrated approach to the management of the risks and benefits to health related products and food by: • Minimizing health risk factors to Canadians while maximizing the safety provided by the regulatory system for health products and food; and • Promoting conditions that enable Canadians to make healthy choices and providing information so that they can make informed decisions about their health. *Health Products and Food Branch*

Également disponible en français sous le titre : Ligne directrice : Préparation de demandes précommercialisation d'homologation de matériels médicaux de classes III et IV fondées sur la Summary Technical Documentation (STED)

FOREWORD

Guidance documents are meant to provide assistance to industry and health care professionals on **how** to comply with the policies and governing statutes and regulations. They also serve to provide review and compliance guidance to staff, thereby ensuring that mandates are implemented in a fair, consistent and effective manner.

Guidance documents are administrative instruments not having force of law and, as such, allow for flexibility in approach. Alternate approaches to the principles and practices described in this document ***may be*** acceptable provided they are supported by adequate scientific justification. Alternate approaches should be discussed in advance with the relevant program area to avoid the possible finding that applicable statutory or regulatory requirements have not been met.

As a corollary to the above, it is equally important to note that Health Canada reserves the right to request information or material, or define conditions not specifically described in this guidance, in order to allow the Department to adequately assess the safety, efficacy or quality of a therapeutic product. Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

This document should be read in conjunction with the accompanying notice and the relevant sections of other applicable guidances.

TABLE OF CONTENTS

1.0 INTRODUCTION

The *Summary Technical Documentation* (STED) *for Demonstrating Conformity to the Essential Principles of Safety and Performance of Medical Devices* was developed by the Global Harmonization Task Force (GHTF) and has been adopted by Health Canada for use in Class III and Class IV premarket device licence applications and licence amendment applications. The STED is intended to provide a globally harmonized content document for medical device applications and has been integrated in this guidance document, which includes both Canadian specific and STED-based submission requirements for device licence applications filed pursuant to the Canadian *Medical Devices Regulations.* It is believed that use of the STED will reduce time and costs for both industry and the regulator, and will ultimately result in timely access to medical devices for Canadians.

All Class III and Class IV medical devices undergo a review of submitted evidence of safety and effectiveness as part of the licensing process in Canada. The evidence to be submitted in support of a Class III or Class IV medical device licence application is set out in sections 32(3) or 32(4) of the *Medical Devices Regulations*, respectively. Amended licence applications for Class III and Class IV medical devices must contain a full description of the device, a statement of the intended use (or indication for use), and information relevant to the change set out in section 32 of the *Medical Devices Regulations*.

The *Essential Principles of Safety and Performance of Medical Devices* are a GHTF-derived list of both general and specific safety and performance recommendations for medical devices, similar to the general Safety and Effectiveness Requirements set out in sections 10 to 20 of the Canadian *Medical Devices Regulations*. Canadian regulatory requirements in support of Class III and Class IV medical device licence applications not covered by the STED are identified and addressed in this guidance document.

This guidance document is meant to be read in conjunction with the STED published February 21, 2008 (http://www.ghtf.org/documents/sg1/sg1final-n11.pdf). The document entitled *Essential Principles of Safety and Performance of Medical Devices* dated May 20, 2005 (http://www.ghtf.org/documents/sg1/sg1n41r92005.pdf) should also be consulted. For additional information on requirements to support a Class III or Class IV device licence application, please refer to the Canadian *Medical Devices Regulations* (MDR) (http://laws.justice.gc.ca/en/f-27/sor-98-282/252292.html).

1.1 Policy Objective

To facilitate the submission to Health Canada of STED-based device licence applications and licence amendment applications for Class III and Class IV medical devices filed pursuant to section 32 of the *Medical Devices Regulations*.

1.2 Policy Statement

This guidance document is to be used in the preparation of Class III and Class IV medical device licence applications and medical device licence amendment applications.

1.3 Scope

The scope of this guidance document is Class III and Class IV premarket device licence applications and device licence amendment applications for non-*in vitro* diagnostic medical devices.

This guidance document should be used to the extent possible in the preparation of licence applications for combination products involving medical devices.

This document is not applicable to Class II medical devices or *in vitro* diagnostic devices (IVDD). It does not specifically address issues relating to the determination of significant change amendments or administrative amendments. This document does not replace, but rather complements, the device specific premarket guidance documents listed in Appendix C.

1.4 Definitions

***In vitro* diagnostic device (IVDD)** means a medical device that is intended to be used *in vitro* for the examination of specimens taken from the body (refer to MDR).

Proprietary Information Submission refers to a document provided by a subcontractor or manufacturer that contains specific objective evidence, for example material characterization or sterilization processing characteristics. This data is often independent of final device processing and can be referenced by many different device licence applications. If the document has been submitted by someone other than the manufacturer, permission must be granted by the submission owner for each licence application using the information contained in the **Proprietary Information Submission**.

2.0 GUIDANCE FOR IMPLEMENTATION

2.1 Format of Summary Technical Documentation (STED)-based Applications

This section outlines the format of STED-based licence applications for Class III and Class IV non-*in vitro* diagnostic medical devices.

Health Canada's STED-based application consists of two Modules: Module 1 specifies the Health Canada specific requirements; Module 2 specifies the STED-based requirements. The

format of Module 2 may be at the discretion of the manufacturer as long as its contents are clearly and explicitly linked to the corresponding sections of the STED.

Where similar content is requested for both Modules 1 and 2, information should be provided in full in Module 1, with clear references from Module 2 to the relevant sections of Module 1.

The application's **Table of Contents** should use the headings provided in Tables 1 and 2, with clear references to the corresponding page numbers that contain the relevant information. If no information is available or required under a specific heading, that section of the application should be marked "not applicable" or "not relevant" and justification for the absence of such information should be provided.

As per the Table of Contents, the Cover Letter should be placed within the Additional Class III/IV Premarket Information section for Health Canada's processing needs. The Administrative Information will be detached from the application and/or amendment application prior to being reviewed.

For medical device licence amendment applications, a full device description and the intended use (or indication for use) statement are required in addition to those sections that are relevant to the change. When information under a specific heading remains unchanged, that section/subsection of the application should be marked "not changed" and cross-reference made to the previously filed application(s) containing that information. The cross-reference should include the Canadian licence number, application ID, device name and manufacturer's name of the previously filed application.

2.2 Electronic Applications

Health Canada is developing a phased migration plan from the current paper-based application to an electronic-based application for medical devices. To facilitate this transition, applicants are encouraged to submit premarket review documents for Class III and IV medical device licence applications and amendment applications in electronic format, as well as the required paper copy.

Electronic documents should be provided on compact discs (CDs) or digital video discs (DVDs). Please refer to the current Health Canada Notice regarding *Guidance for Industry: Preparation of a Premarket Review Document in Electronic Format for a Class III and Class IV Medical Device Licence Application* for additional details. The electronic-based application must also include a Letter of Attestation confirming that the content of the electronic application is identical to that of the accompanying paper copy. The Letter of Attestation should be on the manufacturer's letterhead and signed and dated by a senior official of the manufacturer. Applicants should consult the updated notice on the preparation of a premarket review document in electronic format for a sample Letter of Attestation and electronic file requirements.

3.0 SUMMARY TECHNICAL DOCUMENTATION (STED)-BASED CLASS III PREMARKET LICENCE APPLICATION CONTENT

An application for a Class III medical device licence must contain the information and documents set out in section 32(3) of the *Medical Devices Regulations*. Table 1 provides an overview of the format for a Class III medical device premarket application.

Table 1: Table of Contents Format for a Class III Device Premarket Application (non-*in vitro* diagnostic)

Section/ Sub-section	Main Heading	Application Location		
		tab or section	pages	volume
Module 1	**Health Canada Requirements**			
1.0	**Table of Contents**			
2.0	**Administrative Information**			
2.1	Application Form and Fee Form			
2.2	Quality Management System Certificate			
3.0	**Pre-Submission Correspondence**			
4.0	**Additional Class III Premarket Information**			
4.1	Cover Letter			
4.2	Executive Summary			
4.3	Submission Traceability Table for Class III Applications			
4.4	Licence Amendments			
4.5	Design Philosophy			
4.6	Indications and/or Intended Use and Contraindications			
4.7	Marketing History/Regulatory Status			
4.7.1	Canadian			
4.7.2	International			
4.7.3	Incident Reports and Recalls			
4.8	Standards (Health Canada Declaration of Conformity)			
4.9	Shelf Life Validation for Product			
4.10	Summaries			
4.11	Bibliography			
Module 2	**Summary Technical Document (STED)-based Requirements**			
5.0	**Device Description and Product Specification, Including Variants and Accessories**			
5.1	Device Description			
5.2	Product Specification			
5.3	Reference to Similar and Previous Generations of the Device			
6.0	**Labelling**			

7.0	**Design and Manufacturing Information**			
7.1	Device Design			
7.2	Manufacturing Process			
7.3	Design and Manufacturing Sites			
8.0	**Essential Principles (EP) Checklist**			
9.0	**Product Verification and Validation**			
9.1	General			
9.2	Biocompatibility			
9.3	Medicinal Substances			
9.4	Biological Safety			
9.5	Sterilization			
9.6	Software Verification and Validation			
9.7	Animal Studies			
9.8	Clinical Evidence			

MODULE 1 Health Canada Requirements

(3)1.0 Table of Contents

This section is a placeholder for the Table of Contents for the entire application. The Table of Contents should list all documents included in the application and should follow the structure found in Table 1 above. The last two columns are to be completed by the manufacturer and identify both the section number as well as page numbers. Sections that are not applicable should be clearly denoted "N/A".

(3)2.0 Administrative Information

(3)2.1 Application Form and Fee Form

A completed and signed application form and fee form should be presented in this subsection.

(3)2.2 Quality Management System Certificate

This subsection includes a copy of the quality management system certificate certifying that the quality management system under which the device is designed and manufactured satisfies CAN/CSA ISO 13485:2003, Medical devices - Quality management systems - Requirements for regulatory purposes. Health Canada will only accept quality system certificates that have been issued by special third party auditing organizations called Canadian Medical Devices Conformity Assessment System (CMDCAS) recognized registrars. A list of Health Canada recognized registrars is available at http://www.hc-sc.gc.ca/dhp-mps/md-im/qualsys/cmdcas_scecim_accep_cert13485_gd207-eng.php.

(3)3.0 Pre-Submission Correspondence

During the product lifecycle, pre-submission correspondence, including teleconference meetings, may be held between Health Canada and the applicant. This subsection is a placeholder for any pre-submission-related information. This includes the information package that is required to be submitted prior to pre-submission meetings. Examples of documents that are to be placed in this subsection include the meeting agenda, presentation slides, final meeting minutes, and any email correspondence related to specific aspects of the application.

(3)4.0 Additional Class III Premarket Information

The following headings do not appear in the GHTF STED Guidance document but these sections must be included in the application to Health Canada for a Class III medical device application.

(3)4.1 Cover Letter

Any information submitted to Health Canada should be accompanied by a cover letter. The cover letter should include the purpose of the application and a brief description of the package being submitted. It may also include information pertaining to Proprietary Information Submission. The cover letter should not contain any detailed scientific information.

(3)4.2 Executive Summary

An Executive Summary of the scientific content being submitted in support of the Class III device licence (or amendment) application should be provided and include the device name, its general purpose, as well as a high level summary of key supporting documentation. Every effort should be made to provide introductory text or narratives to help connect the submitted documents. Any exceptions or unusual circumstance which the manufacturer wishes to highlight, specific to the device or application, should be mentioned in the Executive Summary.

(3)4.3 Submission Traceability Table for Class III Applications

To facilitate the review process, complete and submit the Submission Traceability Table for Class III application located in **Appendix A**. Omission of this table from the application may result in screening deficiencies.

(3)4.4 Licence Amendments

If the application is an amendment to a licensed device, a detailed description of the amended device and a description of the modifications are required, including changes in

design, performance, and indications. A comparison table to device(s) currently licensed in Canada may be used. The reasons for the modifications should be stated.

(3)4.5 Design Philosophy

This subsection should include a brief description of the principles and theories that enable the device to be used for the medical conditions and purposes for which it is manufactured, sold or represented by the manufacturer. This information should be linked to the claimed indications for use or performance. Unique or novel design features should be highlighted and related literature may be provided.

If the application is based on a modification of a licensed device, a detailed description of the device and a description of the modifications are required, including changes in design, performance, and indications. A comparison table to a device licensed in Canada may be used. The reasons for the modifications should be stated.

(3)4.6 Indication and/or Intended Use and Contraindications

The claimed indication for use and/or intended use statement, as it appears on the label, must be stated in this subsection. Contraindications for the device should also be listed as they appear on the label.

(3)4.7 Marketing History/Regulatory Status

(3)4.7.1 Canadian

This subsection should include requests made to Health Canada's Special Access Program (SAP) and the outcome of these requests.

If predicate devices manufactured by the applicant are licensed in Canada and have identical features or specifications as the subject device, provision of this information may be used towards the demonstration of safety and effectiveness for this device and therefore should be provided. This subsection may also state the name of that predicate, its Canadian medical device licence number and the number of units sold in Canada.

(3)4.7.2 International

A list of countries or regions other than Canada where the device has been sold and the total number of units sold in those countries should be provided in this subsection.

If predicate devices manufactured by the applicant are marketed internationally and have identical features or specifications as the subject device, provision of this information may be used towards the demonstration of safety and effectiveness for this device and therefore should be provided. This subsection should also state the name of that predicate, countries marketed in, its approval reference number (if applicable), and the number of units sold.

(3)4.7.3 Incident Reports and Recalls

This subsection should include a summary of each reported incident respecting the device and details of any recalls of the device in countries where the device has been sold. Sufficient information should be provided such that estimated rates of occurrence of reported incidents can be determined.

If predicate devices are presented in the sections above, this subsection should summarize reported incidents and recalls for those predicates and the outcome or corrective action taken at the time of application.

(3)4.8 Standards

Please refer to a), b) and c) of the third paragraph of subsection 11.1 (General) of the GHTF STED guidance document for general content information.

In accordance with Health Canada's *Guidance Document: Recognition and Use of Standards* under the *Medical Devices Regulations* (http://www.hc-sc.gc.ca/dhp-mps/md-im/applic-demande/guide-ld/md_gd_standards_im_ld_normes-eng.php), the safety and effectiveness of a medical device can be established through the use of Canadian recognized standards. Where the applicant chooses to demonstrate conformity to a recognized standard, the Health Canada Declaration of Conformity form should be provided in this section. The full title, version or identifying number, date and responsible agency of each standard must be provided in the tabular format provided. If the publication year is different from what appears on the list recognized by Health Canada, an explanation of the differences between the two versions of the standard must be provided along with justification for why these differences will not have a detrimental impact on the safety and effectiveness of the medical device. Applicants should consult the *List of Recognized Standards* by Health Canada at the following location: http://www.hc-sc.gc.ca/dhp-mps/md-im/standards-normes/index-eng.php.

If the Health Canada form is not used, evidence that the device meets an equivalent or better standard, or alternative evidence of safety and effectiveness, must be provided. Certificates of compliance created by the manufacturer or a third party are not sufficient.

(3)4.9 Shelf Life Validation for Product

Shelf life tests that validate the stability and continued functionality of the product, including chemical and physical properties, and critical performance characteristics under the storage conditions specified by the manufacturer over the stated shelf-life (until the expiration date is reached), should be included in this section.

(3)4.10 Summaries

Where detailed test reports are provided in Module 2 of the application, a summary of each test conducted and the conclusions drawn from those tests should be provided in this section. Also to be provided with the test summaries is context relating to why the tests are being presented and the risks they address.

(3)4.11 Bibliography

To facilitate the review process, the manufacturer and/or device sponsor is requested to provide a bibliography of all relevant published literature dealing with the use, safety and effectiveness and the indications for use of the specific device in question. If information within the article is being provided as key evidence of safety or effectiveness, a summary of the relevant sections, including data upon which the conclusions are drawn, should be provided. Copies of the articles should also be provided. If relevant information is being provided under Clinical Evidence in Module 2 of the application, a statement to that effect should be included in this subsection.

MODULE 2 STED-based Requirements

Some sections of the STED are not required pursuant to Section 32(3) of the *Medical Devices Regulations*. They may be excluded at the discretion of the manufacturer.

(3)5.0 Device Description and Product Specification, Including Variants and Accessories

(3)5.1 Device Description

Please refer to section 6.1 of the GHTF STED guidance document for content information.

Firms that manufacture or process the device under contract to the manufacturer and/or device sponsor may elect to submit all or a portion of the material specifications applicable to their facility directly to the Therapeutic Products Directorate (TPD) in the form of a Proprietary Information Submission. The manufacturer or device sponsor should inform these firms of the need to provide detailed information on the device.

Manufacturers and/or device sponsors referencing information held in a Proprietary Information Submission submitted by another company must obtain permission from the owner of the submission each time the submission is accessed. The letter of permission should indicate the extent of information to be considered for each application.

(3)5.2 Product Specification

Please refer to section 6.2 of the GHTF STED guidance document for content information.

(3)5.3 Reference to Similar and Previous Generations of the Device

Please refer to section 6.3 of the GHTF STED guidance document for content information.

(3)6.0 Labelling

Please refer to section 7.0 of the GHTF STED guidance document for content information.

Applicants should also consult the Health Canada document entitled *Guidance for the Labelling of Medical Devices under Section 21 to 23 of the Medical Devices Regulations* (http://www.hc-sc.gc.ca/dhp-mps/md-im/applic-demande/guide-ld/labl_etiq_dv10-eng.php) for guidance on the labelling requirements for medical devices in Canada.

(3)7.0 Design and Manufacturing Information

(3)7.1 Device Design

This section is generally not required for Class III medical device applications.

(3)7.2 Manufacturing Process

This section is generally not required for Class III medical device applications.

(3)7.3 Design and Manufacturing Sites

Please refer to section 8.3 of the GHTF STED guidance document for content information.

(3)8.0 Essential Principles (EP) Checklist

Please refer to section 9.0 of the GHTF STED guidance document for content information.

(3)9.0 Product Verification and Validation

For a Class III premarket medical device licence application, only a summary of each test conducted and the conclusions drawn from those tests are required in the original application. Where detailed reports are provided in this section, summaries should be added to section 3.4.9.1 of Module 1, along with context relating to why the tests are being presented and the risks they address.

(3)9.1 General

Please refer to section 11.1 of the GHTF STED guidance document for content information.

(3)9.2 Biocompatibility

Please refer to section 11.2 of the GHTF STED guidance document for content information.

Biocompatibility testing should be carried out in conformance to ISO 10993 standards. Alternative testing may be acceptable if a rationale is provided. A Declaration of Conformity can be used (see section 4.8 above) to support the method, but results obtained must be also summarized and pass fail criteria indicated along with conclusions drawn [for example is (e.g.), slight cytotoxicity was observed (average=1), the device is deemed biocompatible]. Where multiple methods are outlined in the standard, an indication of which method was chosen should be stated.

(3)9.3 Medicinal Substances

Please refer to section 11.3 of the GHTF STED guidance document for content information.

(3)9.4 Biological Safety

This section is generally not required for Class III medical device applications.

If the device contains heparin or tallow derivatives (e.g., glycerol) of animal origin, the information outlined in section 11.4 of the GHTF STED guidance document is required. If the device contains other materials of animal origin, classification of the device should be confirmed with the Medical Devices Bureau.

(3)9.5 Sterilization

Please refer to section 11.5 of the GHTF STED guidance document for content information.

(3)9.6 Software Verification and Validation

Please refer to section 11.6 of the GHTF STED guidance document for content information.

Please note that forward looking statements regarding the evaluation and testing are not accepted. Final verification and validation results must be summarized and the release version of the software clearly identified.

(3)9.7 Animal Studies

Please refer to section 11.7 of the GHTF STED guidance document for content information.

(3)9.8 Clinical Evidence

Please refer to section 11.8 of the GHTF STED guidance document for content information.

4.0 SUMMARY TECHNICAL DOCUMENT (STED)-BASED CLASS IV PREMARKET APPLICATION CONTENT

An application for a Class IV medical device licence application must contain the review information and documents set out in section 32(4) of the *Medical Devices Regulations*. Table 2 provides an overview of the format for a Class IV medical device premarket application. Applicants are expected to follow the content and format as set out in this subsection when preparing a Class IV premarket medical device licence application.

Table 2: Table of Contents Format for a Class IV non-*in vitro* diagnostic device premarket application

Section/ Sub-section	Main Heading	Application Location		
		tab or section	pages	volume
Module 1	**Health Canada Requirements**			
1.0	**Table of Contents**			
2.0	**Administrative Information**			
2.1	Application Form and Fee Form			

2.2	Quality Management System Certificate			
3.0	**Pre-Submission Correspondence**			
4.0	**Additional Class IV Premarket Information**			
4.1	Cover Letter			
4.2	Executive Summary			
4.3	Submission Traceability Table for Class IV Applications			
4.4	Licence Amendments			
4.5	Design Philosophy			
4.6	Indications and/or Intended Use and Contraindications			
4.7	Marketing History/Regulatory Status			
4.7.1	Canadian			
4.7.2	International			
4.7.3	Incident Reports and Recalls			
4.8	Implant Registration			
5.0	**Supplemental Manufacturing and Quality Control**			
5.1	Device Specific Quality Plan			
5.2	Process Validation			
6.0	**Supplemental Safety and Effectiveness**			
6.1	Summaries			
6.2	Standards			
6.3	Shelf Life Validation for Product			
6.4	Bibliography/ Literature Studies			
Module 2	**Summary Technical Document (STED)-based Requirements**			
7.0	**Device Description and Product Specification, Including Variants and Accessories**			
7.1	Device Description			
7.2	Product Specification			
7.3	Reference to Similar and Previous Generations of the Device			
8.0	**Labelling**			
9.0	**Design and Manufacturing Information**			
9.1	Device Design			
9.2	Manufacturing Process			
9.3	Design and Manufacturing Sites			
10.0	**Essential Principles (EP) Checklist**			
11.0	**Risk Analysis and Control Summary**			
12.0	**Product Verification and Validation**			
12.1	General			
12.2	Biocompatibility			
12.3	Medicinal Substances			
12.4	Biological Safety			

12.5	Sterilization			
12.6	Software Verification and Validation			
12.7	Animal Studies			
12.8	Clinical Evidence			

MODULE 1 Health Canada Requirements

(4)1.0 Table of Contents

This section is a placeholder for the Table of Contents for the entire application. The Table of Contents should list all documents included in the application and should follow the structure found in Table 2 above. The last two columns are to be completed by the manufacturer and identify both the section number as well as page numbers. Sections that are not applicable should be clearly denoted "N/A".

(4)2.0 Administrative Information

(4)2.1 Application Form and Fee Form

A completed and signed application form and fee form should be presented in this subsection.

(4)2.2 Quality Management System Certificate

This subsection should include a copy of the quality management system certificate certifying that the quality management system under which the device is designed and manufactured satisfies CAN/CSA ISO 13485:2003, *Medical devices - Quality management systems - Requirements for regulatory purposes*. Health Canada will only accept quality system certificates that have been issued by special third party auditing organizations called Canadian Medical Devices Conformity Assessment System (CMDCAS) recognized registrars. A list of Health Canada recognized registrars is available at http://www.hc-sc.gc.ca/dhp-mps/md-im/qualsys/cmdcas_scecim_accep_cert13485_gd207-eng.php

(4)3.0 Pre-Submission Correspondence

During the product lifecycle, pre-submission correspondence, including teleconference meetings, may be held between Health Canada and the applicant. This subsection is a placeholder for any pre-submission-related information. This includes the information package that is required to be submitted prior to the pre-submission meeting. Examples of documents that are to be placed in this subsection include the meeting agenda, presentation slides and final meeting minutes, and any email correspondence related to specific aspects of the application.

(4)4.0 Additional Class IV Premarket Information

The following headings do not appear in the GHTF STED Guidance document but content regarding these topics are to be included in the application to Health Canada for a Class IV medical device application.

(4)4.1 Cover Letter

Any information submitted to Health Canada should be accompanied by a cover letter. The cover letter should include the purpose of the application and a brief description of the package being submitted. The cover letter should not contain any detailed scientific information.

(4)4.2 Executive Summary

An Executive Summary of the scientific content being submitted in support of the Class IV device licence (or amendment) application should be provided and include the device name, its general purpose, as well as a high level summary of key supporting documentation. Every effort should be made to provide introductory text or narratives to help connect the submitted documents. Any exceptions or unusual circumstance which the manufacturer wishes to highlight, specific to the device or application should be mentioned in the Executive Summary

(4)4.3 Submission Traceability Table for Class IV Applications

To facilitate the review process, complete and submit the Submissions Traceability Table for Class IV application located in **Appendix B**. Omission of this table from the application may result in a screening deficiency.

(4)4.4 Licence Amendments

If the application is an amendment to a licensed device, a detailed description of the amended device and a description of the modifications are required, including changes in design, performance, and indications. A comparison table to device(s) currently licensed in Canada may be used. The reasons for the modifications should be stated.

(4)4.5 Design Philosophy

This subsection should include a brief description of the principles and theories that enable the device to be used for the medical conditions and purposes for which it is manufactured, sold or represented by the manufacturer. This information should be

linked to the claimed indications for use or performance. Unique or novel design features should be highlighted.

If the application is based on a modification of a licensed device, a detailed description of the device and a description of the modifications are required, including changes in design, performance, and indications. A comparison table to a device licensed in Canada may be used. The reasons for the modifications should be stated.

(4)4.6 Indication and/or Intended Use and Contraindications

The claimed indication for use and/or intended use statement as it appears on the label must be stated in this subsection. Contraindications for the device should also be listed as they appear on the label.

(4)4.7 Marketing History/Regulatory Status

(4)4.7.1 Canadian

This subsection should include requests made to Health Canada's Special Access Program (SAP) and the outcome of these requests

If predicate devices manufactured by the applicant are licensed in Canada and have identical features or specifications as the subject device, provision of this information may be used towards the demonstration of safety and effectiveness for this device and therefore should be provided. This subsection should also state the name of that predicate, its Canadian medical device licence number and the number of units sold in Canada.

(4)4.7.2 International

A list of countries or regions other than Canada where the device has been sold and the total number of units sold in those countries should be provided in this subsection.

If predicate devices manufactured by the applicant are marketed internationally and have identical features or specifications as the subject device, provision of this information may be used towards the demonstration of safety and effectiveness for this device and therefore should be provided. This subsection should also state the name of that predicate, countries marketed in, its approval reference number (if applicable), and the number of units sold.

(4)4.7.3 Incident Reports and Recalls

This subsection should include a summary of each reported incident respecting the device and details of any recalls of the device in countries where the device has been sold. Sufficient information should be provided such that estimated rates of occurrence of reported incidents can be determined.

If predicate devices are presented in the sections above, this subsection should summarize reportable problems and recalls for those predicates and the outcome or corrective action taken at the time of application.

(4)4.8 Implant Registration

Applications for devices listed in Schedule 2 to the *Medical Devices Regulations* (Regulations) should include samples of the implant registration cards as outlined in Section 66 of the Regulations.

(4)5.0 Supplemental Manufacturing and Quality Control

(4)5.1 Device Specific Quality Plan

This subsection should include a quality plan that sets out the specific quality practices, resources and sequence of activities that are relevant to the device.

The quality plan as described in ISO 10005 provides a mechanism to link specific requirements of the product, project or contract to existing generic quality system procedures. A diagram may be used to outline how the quality system requirements will be met.

(4)5.2 Process Validation Studies

If process results could not be verified in full during routine production by inspection or testing, the results of process validation studies must be presented. Process validation data should include test data and methods, information on controls, number of samples examined, frequency of testing, and why process validation was used (e.g., routine end product tests have insufficient sensitivity, or reliability of a changed process is unknown). The procedures for monitoring and controlling the process parameters of a validated process must also be fully described. Process validation related to sterilization or shelf life, captured in subsection 6.2, need not be included in this subsection.

(4)6.0 Supplemental Safety and Effectiveness

(4)6.1 Summaries

Where detailed test reports are provided in Module 2 of the application, a summary of each test conducted and the conclusions drawn from those tests should be provided in this section. Also to be provided with the test summaries is context relating to why the tests are being presented and the risks they address.

(4)6.2 Standards

Please refer to a), b) and c) of the third paragraph of subsection 11.1 (General) of the GHTF STED guidance document for general content information.

In accordance with Health Canada's *Guidance Document: Recognition and Use of Standards under the Medical Devices Regulations* (http://www.hc-sc.gc.ca/dhp-mps/md-im/applic-demande/guide-ld/md_gd_standards_im_ld_normes-eng.php), the safety and effectiveness of a medical device can be established through the use of Canadian recognized standards. Where the applicant chooses to demonstrate conformity to a recognized standard, the Health Canada *Declaration of Conformity form* should be used and provided in this section. The full title, version or identifying number, date and responsible agency of each standard must be provided in the tabular format provided. If the publication year is different from what appears on the list recognized by Health Canada, an explanation of the differences between the two versions of the standard must be provided along with justification for why these differences will not have a detrimental impact on the safety and effectiveness of the medical device. Applicants should consult the *List of Recognized Standards* by Health Canada at the following website: http://www.hc-sc.gc.ca/dhp-mps/md-im/standards-normes/index-eng.php.

If the Health Canada form is not used, evidence that the device meets an equivalent or better standard or alternative evidence of safety and effectiveness must be provided. Certificates of compliance created by the manufacturer or a third party are not sufficient.

(4)6.3 Shelf Life Validation for Product

Shelf life tests that validate the stability and continued functionality of the product, including chemical and physical properties, and critical performance characteristics under the storage conditions specified by the manufacturer over the stated shelf-life (until the expiration date is reached) should be included in this section. This is separate from section 11.5 of the GHTF STED guidance in which package validation is discussed.

(4)6.4 Bibliography/ Literature Studies

To facilitate the review process, the manufacturer and/or device sponsor is requested to provide a bibliography of all relevant published literature dealing with the use, safety and effectiveness and the indications for use of the specific device in question. If information within the article is being provided as key evidence of safety or effectiveness, a summary of the relevant sections, including data upon which the conclusions are drawn, should be provided. Copies of the articles should also be provided. If relevant information is being provided under Clinical Evidence in Module 2 of the application, a statement to that effect should be included in this subsection.

MODULE 2 Summary Technical Documentation (STED)-based Requirements

(4)7.0 Device Description and Product Specification, Including Variants and Accessories

(4)7.1 Device Description

Please refer to section 6.1 of the GHTF STED guidance document for content information.

Firms that manufacture or process the device under contract to the manufacturer and/or device sponsor may elect to submit all or a portion of the material specifications applicable to their facility directly to the Medical Devices Bureau in the form of a Proprietary Information Submission. The manufacturer or device sponsor should inform these firms of the need to provide detailed information on the device. Manufacturers and/or device sponsors referencing information held in a Proprietary Information Submission filed by another company must obtain permission from the owner of the submission each time that submission is accessed. The letter of permission should indicate the extent of information to be considered for each application.

(4)7.2 Product Specification

Please refer to section 6.2 of the GHTF STED guidance document for content information.

(4)7.3 Reference to Similar and Previous Generations of the Device

Please refer to section 6.3 of the GHTF STED guidance document for content information.

(4)8.0 Labelling

Please refer to section 7.0 of the GHTF STED guidance document for content information.

Applicants should also consult the Health Canada document entitled *Guidance for the Labelling of Medical Devices under Section 21 to 23 of the Medical Devices Regulations* (http://www.hc-sc.gc.ca/dhp-mps/md-im/applic-demande/guide-ld/labl_etiq_dv10-eng.php).

(4)9.0 Design and Manufacturing Information

(4)9.1 Device Design

Please refer to section 8.1 of the GHTF STED guidance document for content information.

(4)9.2 Manufacturing Process

Quality control steps should be identified in the information provided to obtain a general understanding of the manufacturing process (including but not limited to an overview of production, assembly, any final product test and packaging of the finished medical device).

Please refer to subsection 8.2 (Manufacturing Processes) of the GHTF STED guidance document for general content information.

(4)9.3 Design and Manufacturing Sites

Please refer to section 8.3 of the GHTF STED guidance document for content information.

(4)10.0 Essential Principles (EP) Checklist

Please refer to section 9.0 of the GHTF STED guidance document for content information.

(4)11.0 Risk Analysis and Control Summary

Please refer to section 10.0 of the GHTF STED guidance document for content information.

(4)12.0 Product Verification and Validation

Detailed information [that is (i.e.), test design, test protocol, results, methods of data analysis, conclusion and discussion] on all preclinical studies (i.e., physical, mechanical and bench tests,

as well as animal studies) are required in this section. Summaries may also be provided along with the full reports.

(4)12.1 General

Please refer to section 11.1 of the GHTF STED guidance document for content information.

(4)12.2 Biocompatibility

Please refer to section 11.2 of the GHTF STED guidance document for content information.

Biocompatibility testing should be carried out in conformance to ISO 10993. Alternative testing may be acceptable if a rationale is provided. A Declaration of Conformity can be used (see section 4.6 above) to support the method. Results obtained must be summarized, and pass fail criteria indicated along with the conclusions drawn (e.g., slight cytotoxicity was observed (average 1/ 3), the device is deemed biocompatible). Where multiple methods are outlined in the standard, an indication of which method was chosen should be provided.

(4)12.3 Medicinal Substances

Please refer to section 11.3 of the GHTF STED guidance document for content information.

(4)12.4 Biological Safety

Please refer to section 11.4 of the GHTF STED guidance document for content information.

(4)12.5 Sterilization

Please refer to section 11.5 of the GHTF STED guidance document for content information.

(4)12.6 Software Verification and Validation

Forward looking statements are not accepted by Health Canada. The release version of software implemented on the subject device should be stated (if applicable), and summaries of the release version's verification and validation results should be provided if these are not already included in the section 4.12.

Please refer to subsection 11.6 of the GHTF STED guidance document for content information.

(4)12.7 Animal Studies

Please refer to section 11.7 of the GHTF STED guidance document for content information.

(4)12.8 Clinical Evidence

Please refer to section 11.8 of the GHTF STED guidance document for content information.

5.0 PRESENTATION OF APPLICATIONS

This section describes the physical specifications for STED-based paper applications. A paper application will serve as the official copy until such time as Health Canada is prepared to accept applications solely in electronic format. Only one copy of an application is required. Manufacturers and/or device sponsors should follow the format outlined below.

5.1 Organization and Identification of Application Volumes

Paper applications should be bound for easy access of information. Three-ring binders of four inches or less should be used for all application volumes. The Administrative Information may be submitted in a separate docket or document protector and placed before the Pre-Submission Correspondence; however no other sections should be submitted within separate dockets or document protectors. Each binder should be identified with the device name, manufacturer's name, and licence number (if applicable). Each binder should be sequentially numbered, starting with Volume 1. Also to be specified on the binder label are the volume number out of the total number of volumes, the section(s) contained within the volume, and the date of the application (month, day and year). Below is an example of a binder label.

Device Name: "ABC"
Manufacturer's Name: "XYZ"
Licence Number: "12345"
Volume: 1 of 3
Sections: 1-6
Submission Date: January 01, 2010

The above information should appear on the spine as well as on the front cover of the binder.

5.2 Organization and Identification of Information within Applications

Information within an application should be organized into a series of sections and subsections. Tables 1 and 2 provide an overview of the structure that applicants are expected to follow for Class III and Class IV premarket medical device licence applications, respectively. In the Table of Contents, sections and subsections should be identified both by the assigned decimal number and heading. The pagination may be sequential for the entire application, by volume or by section.

As per the Table of Contents, the Cover Letter should be placed within the Additional Class III/IV Premarket Information section for Health Canada's processing needs. The Administrative Information will be detached from the application and/or amendment application prior to being reviewed.

If cross-references are made within an application, both the volume and page numbers should be clearly identified. Acronyms or abbreviations should be defined the first time they are used in each volume. Alternately, an abbreviation/acronym key may be provided at the beginning of each volume. Tabs should be used to identify the start of new sections and appendices.

5.3 Language

Information in an application should be recorded in either English or French. Any material in a language other than English or French must be accompanied by an English or French translation.

5.4 Margins and Font

Text, tables and figures should be prepared using margins that allow the document to be printed on 8.5 x 11 inch paper. The left-hand margin should be sufficiently large such that information is not obscured by the method of binding. The font for narrative text and text within tables and figures should be of a style and size that can be easily read, even after photocopying. Times New Roman, 12-point font is recommended for narrative text.

APPENDIX A: SUBMISSION TRACEABILITY TEMPLATE FOR A CLASS III DEVICE PREMARKET APPLICATION

Health Canada Section / Subsection (For internal use Only)	Review Areas	Application Location		Corresponding Summary Technical Document (STED) Section/ Subsection
		tab or section	pages	
1	**Background Information**			
1.1	Device Description			
1.1.1	General Device Description			6.1, 6.2, 11.3
1.1.2	Licence Amendments			**Not Applicable (N/A)**
1.2	**Design Philosophy**			6.1 c) 6.3
1.3*	**Indications and/or Intended Use**			**N/A**
2	**Device Labels, Package Labelling and Documentation**			7
3.0*	**Marketing History/Regulatory Status**			N/A
3.1	Canadian			
3.2	International			
3.3	Incident Reports and Recalls			
4	**Safety and Effectiveness Studies**			
4.1	Standards			11.1 a) b) 3rd para.
4.2	Preclinical Studies			
4.2.1	Physical/Mechanical/Bench Tests			11.1 a)b)c) 2nd Para
4.2.2*	Shelf Life Studies of Product			**N/A**
4.2.3	Software Verification and Validation			11.6
4.2.4	Biocompatibility Tests			6.1f), 11.2
4.2.5	Animal Studies			11.1, 11.7
4.3	Clinical Evidence			11.8, GHTF/SG5/N2
4.4	Sterilization			11.5
4.5	Literature Studies and Bibliography			11.1 e) 2nd para.

* These sections are Health Canada specific and not covered in the Summary Technical Document (STED).
** N/A = Not applicable.

APPENDIX B: SUBMISSION TRACEABILITY TEMPLATE FOR A CLASS IV DEVICE PREMARKET APPLICATION

Health Canada Section/ Subsection (For internal Use Only)	Review Areas	Application Location		Corresponding Summary Technical Document (STED) Section/ Subsection
		tab or section	pages	
1	**Background Information**			
1.1	Device Description			
1.1.1	General Device Description			6.1, 6.2, 11.3
1.1.2	Licence Amendments			**Not Applicable (N/A)**
1.2	**Design Philosophy**			6.1 c), 6.3
1.3*	**Indications and/or Intended Use**			**N/A**
1.4*	**Implant Registration System**			**N/A**
2	**Device Labels, Package Labelling and Documentation**			**7**
3.0*	**Marketing History/Regulatory Status**			**N/A**
3.1	Canadian			
3.2	International			
3.3	Incident Reports and Recalls			
4	**Manufacturing and Quality Control**			
4.1	Material Specifications			6.1 i)
4.2	Devices Containing Animal/Human Material			11.4
4.3*	Device Specific Quality Plan			**N/A**
4.4	Manufacturing Process and Quality Control Activities			8.1, 8.2
4.5*	Process Validation Studies			**N/A**
4.6	Sterilization, Packaging and Shelf-life Validation Studies			11.5

***** These sections are Health Canada specific and not covered in the Summary Technical Document (STED).
****** N/A = Not applicable.

Appendix B: Submission Traceability Template for a Class IV device premarket application (Con't)

Health Canada Section/ Subsection (For internal Use Only)	Review Areas	Application Location		Corresponding Summary Technical Document (STED) Section/ Subsection
		tab or section	pages	
5	**Safety and Effectiveness Studies**			
5.1	Standards			11.1 a) 3rd para.
5.2	Preclinical Studies			
5.2.1	Physical/Mechanical/Bench Tests			11.1 a)b)c) 2nd Para
5.2.2*	Shelf Life Studies of Product			**N/A**
5.2.3	Software Verification and Validation			11.6
5.2.4	Biocompatibility Tests			11.2
5.2.5	Animal Studies			11.1, 11.7
5.3	Clinical Evidence			11.8, GHTF/SG5/N2
5.4	Literature Studies and Bibliography			11.1 e) 2nd para.
6	**Risk Assessment**			10

* These sections are Health Canada specific and not covered in the STED
** N/A = Not applicable.

APPENDIX C: DEVICE SPECIFIC PREMARKET GUIDANCE DOCUMENTS

- *Device Licence Applications for Ultrasound Diagnostic Systems and Transducers* (http://www.hc-sc.gc.ca/dhp-mps/md-im/applic-demande/guide-ld/ultrasound_ultrasons-eng.php).

- *Guidance Document on the Regulation of Medical Devices Manufactured From or Incorporating Viable or Non-Viable Animal Tissue or their Derivative(s)* (http://www.hc-sc.gc.ca/dhp-mps/md-im/applic-demande/guide-ld/anim_tiss-eng.php).

- *Pre-Market Guidance on Bare Cardiovascular Stents* (http://www.hc-sc.gc.ca/dhp-mps/md-im/applic-demande/guide-ld/stents_nues-eng.php).

- *Preparation of a Premarket Review Document for Breast Implant and Tissue Expander Device Licence Applications* (http://www.hc-sc.gc.ca/dhp-mps/md-im/applic-demande/guide-ld/breast_impl_mammaires-eng.php).

- *Consultation on the Release of Draft Guidance Document-Medical Device Applications for Implantable Cardiac Leads* (http://www.hc-sc.gc.ca/dhp-mps/consultation/md-im/consult-draft_ebauche_cardi_lead_sondes-eng.php)

Additional Premarket Guidance Documents:

For up to date listings of Health Canada Guidance Documents related to medical devices see http://hc-sc.gc.ca/dhp-mps/md-im/index-eng.php