Health Canada Santé Canada

Investigational Testing Application

Huixin Yang, MD & PhD

Medical Devices Bureau, TPD

HPFB, Health Canada

(12th AHWP Meeting)

Chengdu, China, October 23-27/2007

Health Products and Food Branch
Direction générale des produits de santé et des aliments

Investigational Testing

- **Key Activities:** **Application assessments to minimize inherent risks in clinical trials of medical devices**

- **Organizations:** **MDB and OCT (for drug/device combination products) or BGTD (for for drug/device combination products)**

  -MDB: Medical Devices Bureau

  -OCT: Office of Clinical Trial

  -BGTD: Biologics & Genetic Therapies Directerate

Provisions

- **Allow clinical trials of medical devices that do not yet meet all the safety & effectiveness requirements.**
- **Manufacturer must comply with Part 3 of the *Regulations* by*:***
  - **having an investigational testing authorization (ITA) for a Class II, III, and IV devices**

Scope

- **Use of an unlicensed medical device in a clinical investigation**
- **Use of a licensed medical device beyond the conditions of its licence, including**
  - **a new indication;**
  - **a new target population; or**
  - **new conditions of treatment.**

When to Apply

- **All appropriate pre-clinical and animal studies have been completed**
- **The device has been shown to have a reasonable probability of safety & effectiveness**
- **Additional evidence of safety & effectiveness can only be obtained using target populations.**

Pre-Submission Meetings

- **Contacting MDB,HPFB for guidance before submitting an application is recommended for**
  - **new sponsors**
  - **studies of new technologies or new uses of existing technologies**
  - **new device/drug combination products**

How to Apply

- Complete application form
- Append supporting records
- Provide Executive Summary & table of contents
- Send application to the Medical Devices Bureau

Application Requirements

Depend on risk class of the device

- **No Application Required:**
  - **All Class I devices**
- **Abbreviated Application:**
  - **All Class II devices**
- **Full Application:**
  - **All Class III or IV devices**

Format of Abbreviated Application

Application Form

Executive Summary

Table of Contents

1. **Introduction**
   - **1.1 Manufacturer Identification**
   - **1.2 Device Identification, risk** class
2. **Institutional Information**
   - **2.1 Name/Address of Institution(s)**
3. **Protocol**
4. **Device Labelling**

Format of Full Application

- Application Form
- Executive Summary
- Table of Contents
1. Introduction
   - 1.1 Manufacturer Identity
   - 1.2 Device Description
   - 1.3 Design Philosophy
   - 1.4 Marketing History
2. Risk Assessment
   - 2.1 Risk Analysis & 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 REB Approval(s)
4. Protocol
5. Device Labelling
6. Investigator Agreement(s)

Device Description

- **Description of device and materials used in its manufacture and packaging**

- **Including**
  - **colour photographs of the device & its components; and**
  - **engineering diagrams of long-term implanted devices**

- **Engineering diagrams of other devices may be requested if needed to assess safety and potential effectiveness**

Design Philosophy

- Description of features of device that permit it to be used for its intended purpose(s)
- Description of device's design and performance specifications linked to the objectives of the proposed investigational testing
- Table(s) comparing device to previous versions or generations.

Marketing History

- Summary of special access requests & outcomes
- Details of regulatory status in other countries
- Volume of sales to date globally
- Summary of reported problems
- Details of recall in other jurisdictions

Risk Assessment

- **Analysis & evaluation of:**
  - risks inherent in use of the device(s) in the study
  - measures adopted to reduce the risks
  - risks against presumed benefits
  - evidence that risks are reduced to acceptable levels
- **Guidance document:**
  - ISO 14971:2000 Medical Devices -- Application of Risk Management to Medical Devices
- **Who carried out the risk analysis?**

Risk Assessment (cont'd)

- **Results of previous studies**
- **Alternate methods**
  - **Methods currently used to treat or diagnose medical conditions that are the subject of the clinical trial**
- **Precautions**
  - **Cautions, warnings, contraindications, possible adverse effects**

Names of Investigators

- **For all qualified investigators:**
  - **names;**
  - **educational qualifications; and**
  - **relevant research experience.**

- **Identity of principal investigator**

Research Ethics Board Approval

- **Written approval from each institution's Research Ethics Board (REB).**
- **In the absence of an institutional REB, an Ethics Committee must be convened.**
  - **Must conform with the Medical Research Council Policy, "Code of Ethical Conduct for Research Involving Humans."**
- **A conditional ITA *may* be granted pending the receipt of an REB approval.**
- **Testing cannot begin before this approval has been submitted to the TPD.**

Protocol

- **Objective(s)**
- **General study design**
  - **Include number of devices or patients needed to achieve objective(s)**
- **Duration of study & patient follow-up period**
- **Subject selection:**
  - **number of subjects and justification;**
  - **patient characteristics (age, sex, primary and secondary conditions;**
  - **inclusion and exclusion criteria; and**
  - **Diagnostic methods chosen to confirm disease or condition.**

Protocol (cont'd)

- **Methods of assessing the investigational device:**
  - criteria for success or failure;
  - copy of all case report forms;
  - proposed methods of data analysis; and
  - identity of person performing the analysis
- **Control Group**
  - full description; and
  - justification
- **Informed Consent Documentation**
  - accurate description of risks and benefits to patient

Device Label

- **Manufacturer (or sponsor) must submit a copy of the device label.**

- **Includes:**
  - **product monograph;**
  - **all advertising brochures;**
  - **copies of information & instruction for use given to either the qualified investigator or patient.**

Investigator Agreements

- **Manufacturer (or sponsor) must obtain written agreements from each investigator.**
- **Agreement outlines responsibilities of the investigator to**
  - **conduct the testing in accordance with the protocol;**
  - **fully inform each enrolled patient;**
  - **not 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.**

Key Points in Evaluation

- Device can be used safely.
- Not contrary to the best interests of subjects.
- Objectives of the study can be achieved.
- Assuring device safety for this type of use based on an assessment of risk and other safety data.
- Assure the study design will meet the study objectives.

Review Outcomes

1. **Investigational Testing Authorization**
   - Name of investigator(s) and Institution(s)
   - Diagnosis/treatment for which the device may be sold
   - Study protocol identification
   - Number of units to be sold
2. **Request for Additional Information**
3. **Refusal**
   - Device not safe
   - Not in best interests of patients
   - Objective cannot be achieved

Labelling Requirements

- Name of manufacturer
- Name of the device
- “Investigational Device”
- “To Be Used by Qualified Investigators Only”
- For IVDDs: “The performance specifications of this device have not been established”

Advertising

- **Advertiser must hold an authorization**

- **Must clearly indicate:**
  - **that the device is under investigational testing; and**
  - **the purpose for which the device is being tested**

Manufacturer/Sponsor Responsibilities

- **Record Keeping**
  - Records described in Section 81
  - Distribution records
- **Mandatory Problem Reporting**
  - Investigator must report any serious incident to HC within to HC within 72 hours.
- **Other Obligations**
  - Procedures to handle complaints and recalls
  - Implant registration, where appropriate

Cancellation of Authorization/Stop Sale

- **Health Canada may cancel an IT authorization for a Class II, III or IV device or stop the sale of a Class I device if a review of the additional information show that:**
  - **testing endangers the patient, user, or other persons;**
  - **testing is contrary to the best interests of the patients;**
  - **the objective of the testing will not be achieved;**
  - **the investigator is not fulfilling his obligations; or**
  - **false or misleading information supported the IT application.**

Amendment of Authorization

- **The IT regulations do not have a provision for making amendments.**
- **A new authorization must be obtained if changes are made to:**
  - **the study protocol, the identity of the investigators, the institution(s) where the testing is being conducted, and the type of diagnosis or treatment for the device is sold.**
- **A new authorization may be granted after a review of the additional information on the changes.**
- **The new authorization must be obtained before making the changes.**

Performance Target

- Licence:

  -Class II – 15 days

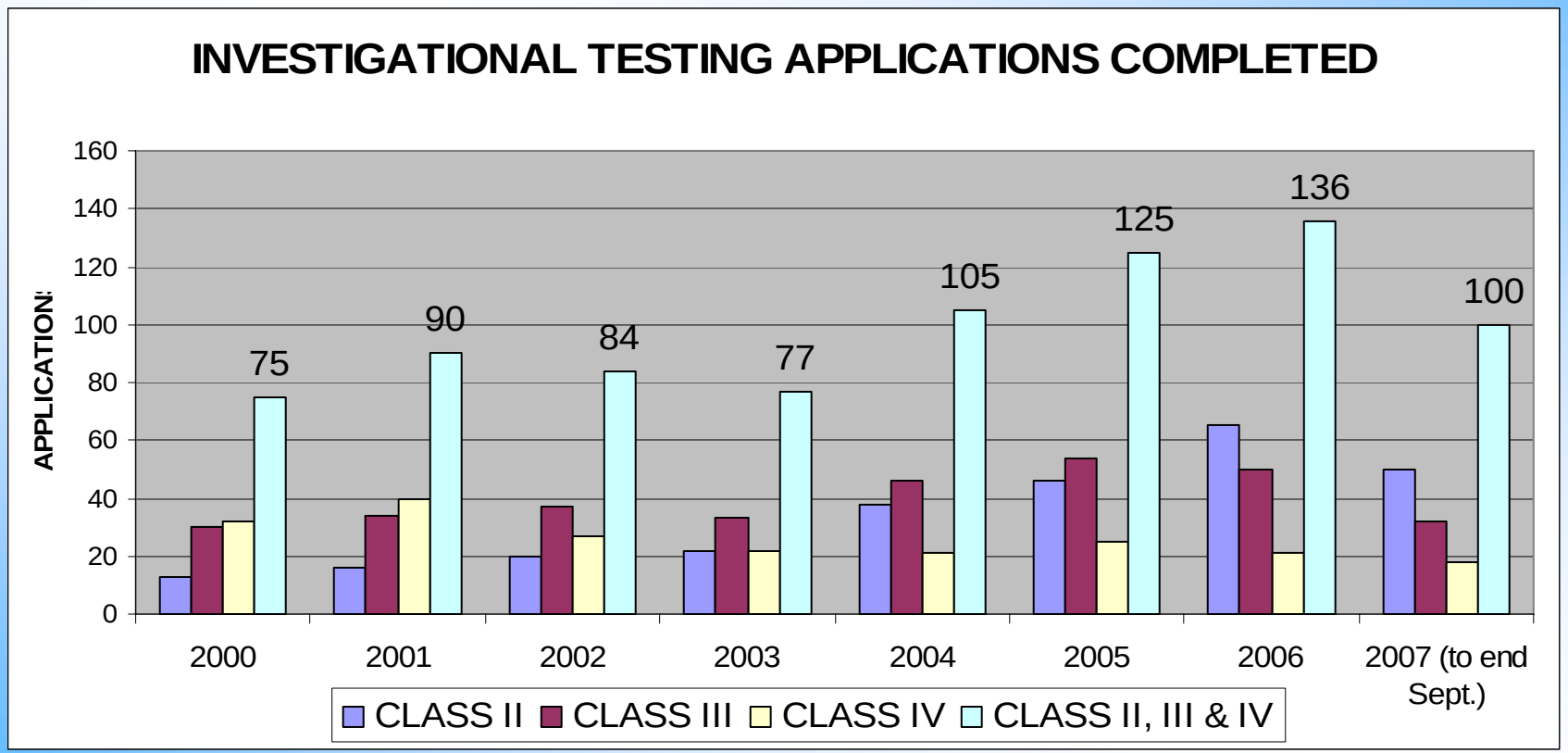
  -Class III 75 days

  -Class IV – 90 days

  -Priority review – 45 days

  -Review of Additional Information – 45 days
- **Investigational Testing – 30 days**
- **Special Access – 3 days**

ITA Completed



Current Considerations

- GCP's (ISO14155).
- Regulatory oversight of study centres.
- Requirement for filing of final study reports.
- Registration of Clinical Trials.
- Harmonization with other regulatory authorities:

GHTF SG-5 –Clinical Safety and Performance.

Further Information

Visit our website at:

http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/index_devices_e.html

Personal Contact:

Huixin Yang, PhD

Tel. (613)954-0373

E-mail: huixin_yang@hc-sc.gc.ca