JOURNAL OF PHARMACEUTICAL SCIENCE AND BIOSCIENTIFIC RESEARCH (JPSBR)

(An International Peer Reviewed Pharmaceutical Journal that Encourages Innovation and Creativities)

Comparison of Regulatory Framework for Registration of Medical Device in CANADA and MALAYSIA

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ABSTRACT:

The knowledge and compliance with regulatory requirements is a key to success in development and marketing of medical devices. As the use of medical devices has increased, stringent regulatory standards are required to ensure safety, efficacy and performance of medical devices with least adverse effects. Recently introduced guidelines help to provide adequate guidance for effective registration by competent authorities, manufacturers and importers. The Malaysian medical devices regulatory framework is based on the global harmonization trends as promoted by "the Global Harmonization Task Force (GHTF)" and Canada follows well developed and specific guidelines "Medical Devices Regulations (SOR/98-282)". The present article overviews the detailed regulation framework for registration of medical devices in Canada and Malaysia.

Keywords: Global Harmonisation Task force **(**GHTF), Common Submission Dossier Template, Quality management systems, Filing of medical device licence application, Regulation of medical devices.

Article history:
Received 18 Feb 2014
Accepted 10 March 2014
Available online 13 April 2014

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INTRODUCTION [1]:

Medical devices are becoming more important in the health care sector. Medical devices increase the demand for better regulatory frameworks to ensure that products entering the market are safe and efficient. One of the major issues for companies is to be updated on the regulatory requirements and implement them in the process. A company that does not succeed with this may lose thousands of dollars in the delay of marketing the product.

GENERAL DEFINITION[2] :

The term "Medical Devices" includes everything from highly sophisticated computerized medical equipment down to simple wooden tongue depressors. The intended primary mode of action of a medical device on the human body, in contrast with that of medicinal products, is not metabolic, immunological, or pharmacological.

MEDICAL DEVICES REGULATORY FRAMEWORK IN CANADA[3]:

New medical device regulations came into force in Canada on July 1, 1998,. The introduction of these regulations represents a substantial change for the medical device regulatory environment in Canada, while simultaneously introducing a risk-based classification system, and imposing on both manufacturers and importers new licensing, reporting, and fee requirements.

Risk-Based Classification System

The new regulations establish a risk-based classification system for medical devices, with Class I being the lowest risk and Class IV being the highest.

Device Licenses

Device licenses are the basis of the new system, and confer a right on the manufacturer or importer to sell the device. Devices that are Class II, III and IV are required to have a device license. Class I devices are not so required.

Establishment Licenses

Under the regulations, importers, distributors and manufacturers of Class I devices only, need an establishment license, while manufacturers of Class II, III and IV devices do not. For manufacturers of Class I devices only the establishment license requirement replaces the need to hold a device license.

Quality System Requirements

The regulation eventually requires that Class II devices be manufactured in accordance with ISO 9002 (ISO 13488 for medical devices), and that Class III and IV devices be manufactured in accordance with ISO 9001 (ISO 13485 for medical devices). Proof of compliance will be in the form of an attestation from an officer of the manufacturer.

Classification [4]: Total of 16 rules for medical Devices excluding in-vitro diagnostic devices and 7 rules for in-vitro diagnostic devices.

Table: 1Classification of Medical Device as per Canadian regulation

Classification	Risk level	EXAMPLES
Class I	Lowest risk	Tongue Depressor
Class II	Lowest to moderate risk	Surgical gloves, needles
Class III	Moderate to high risk	Ultrasound diagnostic imaging equipment
Class IV	Highest risk	Pacemakers

An application for a medical device licence shall be submitted following detail[3]:

a) The name of the device;

b) The class of the device;

c) The identifier of the device, including the identifier of any medical device that is part of a system, test kit, medical device group, medical device family or medical device group family;

d) The name and address of the manufacturer as it appears on the device label; and

e) The name and address of the establishment where the device is being manufactured, if different from the one referred to in paragraph (d)

An application for a Class II medical device licence shall contain additional information:

a) A description of the medical conditions, purposes and uses

b) A list of the standards complied

c) An attestation by a senior official of the manufacturer that the device meets the safety and effectiveness requirements;

- The device label meets the applicable labelling requirements of these regulations;
- In the case of a near patient in vitro diagnostic device, investigational testing has been conducted on the device using human subjects similar to the conditions of use; and

d) A copy of the quality management system certificate

An application for a Class III medical device licence shall contain, in addition:

a) A description of the device and of the materials used in its manufacture and packaging;

b) A description of the features of the device

c) A list of the countries other than canadawhere the device has been sold,

d) A list of the standards complied with in the design and manufacture of the device to satisfy the safety and effectiveness requirements;

e) In the case of a device to be sold in a sterile condition, a description of the sterilization method used;

f) summary of all studies to ensure that the device meets the safety and effectiveness requirements

g) In the case of a near patient in vitro diagnostic device, a summary of investigational testing conducted on the device using human subjects

h) A bibliography of all published reports dealing with the use, safety and effectiveness of the device; and

i) A copy of the quality management system certificate

An application for a Class IV medical device licence shall contain, in additional

a) Description of the device and of the materials used in its manufacture and packaging;

b) A description of the features of the device that permit it to be used for the medical conditions, purposes and uses

c) A list of the countries other than canada where the device has been sold,

d) A risk assessment comprising an analysis and evaluation of the risks, and the risk reduction measures

e) A quality plan setting out the specific quality practices

f) The specifications of the materials used

g) The manufacturing process of the device;

h) A list of the standards complied with in the design and manufacture

i) Process validation studies,

j) If appropriate, software validation studies, and

k) Literature studies;

FILING OF MEDICAL DEVICE LICENCE APPLICATIONS[3]:

- Manufacturers are requested to send all original applications, application amendments and responses to Additional Information Letters to:
- Information Dissemination Unit Licensing Services Division Medical Devices Bureau, Room 1605, Main Statistics Building #3 Postal Locator 0301H1, Ottawa, Ontario KIA OL2

Review Process for registration of Medical Device in Canada[3]:

1 Administrative Processing

All application types will be examined for administrative completeness e.g., fee form, appropriate fee. The Bureau will target to complete this examination within four (4) calendar days of receipt in the Bureau.

2 Application Validation Process

All applications will be subject to an examination for validity of regulatory information for the type of application in question e.g., risk class, application type, catalogue detail, device purpose, as defined in the Medical Devices Regulations and as described in various guidance documents.

3 Screening

All Class III, IV, and Class III, IV Licence Amendment (for significant changes) applications will be screened for technical completeness to ensure that the requisite information for the type of application in question, as defined in the Medical Devices Regulations and as described in various guidance documents, has been submitted.

4 Review

Upon issuance of a Screening Acceptance Letter, applications will enter the review queue of each Section in Device Evaluation Division. The review target for Class III Licence Applications and Class III Licence Amendments (for significant changes) is sixty (60) calendar days from the date of the Screening Acceptance Letter.The review target for Class IV Licence Applications and Class IV Licence Amendments (for significant changes) is seventy-five (75) calendar days from the date of the Screening Acceptance Letter.

5 Registration: Registration of Medical Devices for 1 year.

- **FEES[5]:**
  - **Fee for Review of Medical Devices Registration:**
  - **For Class II:** $365
  - **For Class III:** $5,255
  - **For Class IV:** $12,225

MEDICAL DEVICES REGULATORY FRAMEWORK IN MALAYSIA[6,7]: The Medical Device Act 2012 has been gazetted on 9th February, 2012 by the Malaysian Government. The Medical Device Regulations 2012, the subsidiary legislations under the Medical Device Act 2012, has been approved by the Minister of Health and has been published in the Gazette on 31st December 2012.The Malaysian medical devices regulatory framework is based on the global harmonization trend as promoted by the Global Harmonization Task Force (GHTF), Asian Harmonization Working Party (AHWP) and Medical Device Product Working Group (MDPWG) of the ASEAN Consultative Committee for Standards and Quality (ACCSQ) and supported by the World Health Organization (WHO).International standards shall be widely used to demonstrate conformance to essential principles of safety and performance of a medical device.

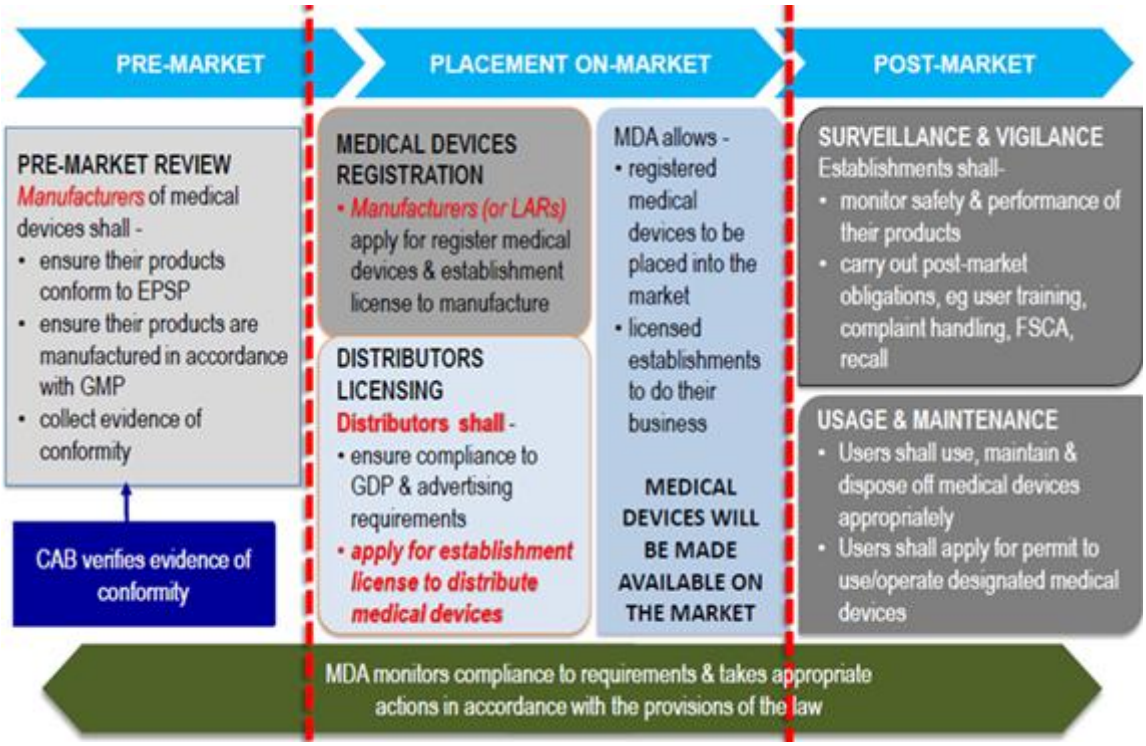

Figure 1: MEDICAL DEVICES REGULATORY FRAMEWORK IN MALAYSIA

- **Classification**[7]**:**Total of 16 rules for medical Devices excluding in-vitro diagnostic devices and 9 rules for in-vitro diagnostic devices.

Table: 2 Classification of Medical Device as per Malaysian regulation

Classification	Risk Level	Examples
Class A	Low risk	Surgical retractors/tongue depressors
Class B	Low to moderate risk	Hypodermic needle / suction equipment
Class C	Moderate to high risk	Lung ventilator / orthopaedic implants
Class D	High risk	Heart valves/implantable defibrillator

- **PLACEMENT OF MEDICAL DEVICES ON THE MALAYSIAN MARKET**[8]

  - Elements of conformity assessment
    - The elements of a conformity assessment system.
    - Conformity of the quality management system (QMS)
      - Quality management system (QMS)
      - System for post-market surveillance (PMS)
    - Conformity assessment of medical device safety and performance
      - Summary technical documentation i.e. Common Submission Dossier template (CSDT)
      - Declaration of conformity (DoC)
    - Registration
      - Registration of medical devices and establishments

  - **Essential Elements of conformity assessment system:**
    - Executive summary
    - Description of medical device
    - Summary of design verification and validation documents
    - Pre-clinical studies
    - Software validation studies
    - Clinical evidence
    - Medical device labeling

- Manufacturer information
- Special requirement for medical device used in clinical investigation

- **Conformity of the quality management system (QMS)**

Table: 3 Conformity of the quality management system (QMS) and System for post-market surveillance (PMS)

Quality management system (QMS)	System for post-market surveillance (PMS)
• In manufacturing process good management is the important • Poor management may bring about inconsistency in products quality • QMS provides a preventive approach to assuring medical device quality. • A manufacturer needs to demonstrate the ability to produce medical devices having consistent quality. • For Class B, C and D medical devices, the manufacturer should put an effective and appropriate QMS in place. • Manufacturers of Class C and D devices shall have a full QMS that includes design and development. • The QMS is subject to periodic audits and reviews by the CAB and/or RA.	• Prior to placing a medical device on the market, the manufacturer shall put in place, as part of its QMS, a system for PMS. • PMS is a mixture of pro-active and reactive activities to ensure continued conformity of a medical device. • It includes pro-active collection and assessment of information on quality, safety or performance of medical devices after they have been placed on the market. • Reporting and investigation of adverse events and corrective and preventive actions are compulsory.

- **Conformity assessment of medical device safety and performance**

For the placement of medical device technical document is necessary. Technical documentation provides the evidence to demonstrate that a medical device conforms to Essential Principles for Safety and Performance (EPSP). For the purposes of conformity assessment, the manufacturer shall establish a subset of technical documentation to be submitted to Regulatory Authority or Conformity Assessment Body, in the format of Common Submission Dossier Template (CSDT).

- **Common Submission Dossier Template (CSDT):**

CSDT is a format to be used for submitting the required information for the purpose of registration of medical devices. Essentially, the CSDT contains elements of the GHTF document "Summary Technical Documentation for demonstrating conformity to EPSP".

❖ **The main sections of CSDT are;**

- **Executive summary**
  - Introductory descriptive information
  - Marketing history
  - Intended use
  - List of Regulatory approval
  - Status of any pending application
  - Safety and performance related information
  - Relevant Essential Principles for Safety and Performance (EPSP) and method used to demonstrate conformity
- **Device description**
  - Complete description
  - Principle of Operation
  - Risk class and Applicable rule
  - Description of accessories
  - Novel futures
  - Drawings and Diagrams
  - Intended use
  - Instruction for use
  - Contraindication
  - Warning
  - Precautions
  - Potential Adverse effect or side effects
- **Summary of design verification and validation documents**
  - **Reports of tests:**
    - Performance Testing
    - engineering tests;
    - laboratory tests;
    - biocompatibility tests;
    - animal tests;
    - simulated use;

- **Pre-clinical studies**
  - The CSDT shall contain documentation on pre-clinical studies conducted for the medical device.
  - The documentation shall include the report and/or certification and/or declaration of—
  - biocompatibility tests conducted on materials used in a medical device,
  - pre-clinical physical tests conducted on the medical device,
  - Pre-clinical animal studies to support the probability of effectiveness in humans.
  - The report shall contain information on the objectives, methodology, results, discussion and conclusions of the testing.
- **Medical device labeling**
- **Risk analysis**
- **Manufacturer information**

➢ **Review Process for registration of Medical Device in Malaysia includes several steps:**

1. **Determination of Medical Device according to Definition**

2. **Device classification send to authority:** Manufacturer has to classify medical devices according to classification rules. If having any dispute between manufacturer and Conformity assessment body, manufacturers have to inform authority. Authority notified within 90 days.

3. **Conformity assessment and placement on the market:** Essentially, prior to placing a medical device into the market, conformity assessment is conducted to provide objective evidence of safety, performance and benefits and risks to maintain public confidence. Conformity assessment is the technical term given to the process of evaluation and approval. The elements of a Conformity of the quality managementsystem are Quality management system (QMS) and System for post-market surveillance (PMS). Also includes Conformity assessment of medical device safety and performanceSummary technical documentation and Declaration of conformity (DoC).

4. **Application for Registration:** After conformity assessment manufacturer have to apply for registration via Medc@St.Application for establishment licence shall only be made via MeDC@St at MDA website www.mdb.gov.my/ and an applicant shall open an account to access MeDC@St. After opening account applicant have to log in to upload application.Application must be as per Common Submission Dossier Template.

5. **Review of application:** If authority satisfied, authority notified to applicant in writing.

6. **Registration** by authority for 5 years

➢ **Fees[9]:**

Table: 4 Fees according to Malaysian Medical device regulation

Description of fees	Fee payable (RM)
(1) MEDICAL DEVICE REGISTRATION	
a) Application fee	
(i) a Class A medical device	100
(ii) a Class B medical device	250
(iii) a Class C medical device	500
(iv) a Class D medical device	750
(b) Registration fee	
(i) a Class A medical device	-
(ii) a Class B medical device	1000
(iii) a Class C medical device	2000
(iv) a Class D medical device	3000

COMPARISON OF MEDICAL DEVICE REGULATION IN CANADA AND MALAYSIA:

Table No 5

Conclusion: The Canadian Medical device regulation is pre-established as compared with Malaysian regulation. Malaysian Medical Device regulation follows Global Harmonisation task force guidelines. But both countries have its own guidelines for the registration process, classification rules and conformity assessment procedure. Time duration limit for review of medical device registration fixed in Canadadivergence to Malaysian regulation. Medical device registeredfor fiveas per Malaysian regulationyearswhereas in Canada only for one year. Canadian application fees for registration seen costly as compared with Malaysian application fees.On comparing both countries, it has been seen that they have specific advantages on own specification of regulations.

Acknowledgement: We are acknowledging Dr. K. Pundarikashudu, Director of L.J Institute of Pharmacy for providing us facilities and guidance.

Table: 5Comparison of Medical Device Regulation in Canada and Malaysia

		Malaysia	Canada
Authority		Medical Device Authority	Health Canada Authority
Process of registration		Simple	Complex
Classification Rules			
Medical Device excluding In-vitro Medical devices		16 Rules	16 Rules
In-vitro Medical devices		7 Rules	9 Rules
Conformity Assessment		Done by Private bodies	Done by HCA
Steps for Registration			
	Step:1	Determination of Medical Device according to Definition	Administrative Processing
	Step:2	Device classification send to authority	Application Validation Process
	Step:3	Conformity assessment and placement on the market	Screening
	Step:4	Application for Registration	Review
	Step:5	Review of application	Registration
	Step:6	Registration	-
CSDT Format		Compulsory	Own specification
Time of registration Process		Not Mention	Max. 75 days for class IV
Fees For application		Applicable	-
QMS Certificate		Compulsory	Compulsory
Registration For		5 years	1 year
Fees		Class A - 100RM Class B -250RM Class C -500RM Class D -750RM	Class I- - Class II-$365 Class III-$5,255 Class IV-$12,225

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