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APPROVAL PROCESS AND REGISTRATION PROCESS OF MEDICAL DEVICES IN US, CANADA AND INDIA

N.Swetha*,D.Nagarjuna Reddy, M.V.Nagabhushanam, B.Brahmaiah, G.Ramakrishna
Department of Pharmaceutical Regulatory Affairs, Hindu college of Pharmacy, Amaravathi road, Guntur -522002, A.P, India. Email id: brahmaiahmph@gmail.com

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Abstract:
A medical device is any device intended to be used for medical purpose. Thus what differentiates a medical device from an everyday device is its intended use. In the United States, Medical devices are regulated by the FDACenter for Devices and Radiological Health (CDRH). Health Canada, under the authority of the Food and Drugs Act, regulates the sale of drugs and medical devices in Canada. The Central Drug Standards Control Organization (CDSCO) is India's main regulatory body for pharmaceuticals and medical devices. The Drug Controller General of India (DCGI) is the key official within the CDSCO. The approval and registration process and the recent market growth of medical devices is prepared and compared between US (FDA), CANADA (HEALTH CANADA) and INDIA (CDSCO).so my discussion is about approval and registration process of medical devices in US, CANADA AND INDIA.

Keywords: *Medical device approval process, regulatory requirements, registration process, market growth.*

Corresponding author:
N.Swetha,
Department of Pharmaceutical Regulatory Affairs,
Hindu college of Pharmacy, Amaravathi road, Guntur -522002, A.P, India.
Email id: brahmaiahmph@gmail.com

QR code

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INTRODUCTION:

[1]Medical device are an important part of health care, yet they are an extraordinarily heterogeneous class of products. The term ―medical devices includes such technologically simple items as ice bags and tongue depressors on one end of the continuum and very sophisticated items such as cardiac pacemakers and proton therapy devices on the other end.

Medical devices benefit patients by helping health care providers diagnose and treat patients and helping patients overcome sickness or disease, improving their quality of life.

Significant potential for hazards are inherent when using a device for medical purposes and thus medical devices must be proved safe and effective with reasonable assurance before regulating governments allow marketing of the device in their country.

Definition:

'Medical device' means any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of:

- Diagnosis, prevention, monitoring, treatment or alleviation of disease,
- Diagnosis, monitoring, treatment, alleviation of or compensation for an injury,
- Investigation, replacement, modification, or support of the anatomy or of a physiological process,
- Supporting or sustaining life,
- Control of conception,
- Disinfection of medical devices

Providing information by means of in vitro examination of specimens derived from the human body; And does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means.

Note: Products which may be considered to be medical devices in some jurisdictions but not in others include:

- Disinfection substances
- Aids for persons with disabilities
- Devices incorporating animal and/or human tissues
- Devices for in-vitro fertilization or assisted reproduction technologies

Some more examples of Medical Devices:

- Band aids
- ECG
- Heart valves from bovine or porcine tissue
- Knee joints
- Hearing aids
- Bone fillers
- Dental implants
- Defibrillators

CLASSIFICATION OF MEDICAL DEVICES:

	Class A	Class B	Class C	Class D
Risk level	Low Risk	Low-moderate Risk	Moderate-high Risk	High Risk
Example	Thermometers / tongue depressors	Hypodermic Needles / suction equipment	Lung ventilator / bone fixation plate	Heart valves / implantable defibrillator
Certification by Notified body as part of Conformity assessment	Not required. Sole responsibility of manufacturer	Yes, for the manufacturing facility quality management system	Yes, for the design and manufacture of MD	Yes, for the design and manufacture of MD
ICAC marking	Required	Required	Required	Required
Registration with CLAA	Required	Required	Required	Required
Manufacturing Licence	Issued by State FDA	Issued by State FDA	Issued by CLAA	Issued by CLAA post join inspection by CLAA & State licencing authority

UNITED STATES:

REGULATORY BODY:

[2] In the United States, MDs are regulated by the **FDACenter for Devices and Radiological Health (CDRH).**

The establishment (manufacturers, initial importer, specifications developer, contract sterilizer, re-packager and/or re-labeler) must be registered with the FDA as per **FDA 2891- 21 CFR Part 807.**

APPROVAL PROCESS OF MEDICAL DEVICES IN UNITED STATES [3]

1. Classify Medical Device.
2. Implement Quality Management System (GMP Requirements).
3. Submission of Clinical Trial data, If Applicable **Investigational Device Exemption (IDE).**
4. Submission of Marketing Approval Application **510 (k) (Premarket Notification, Premarket Approval Application).**
5. FDA 510 (k) Clearance Letter or PMA Approval Letter.
6. FDA Quality system inspection of Manufacturing Facility.
7. Medical Device Listing in **FURLS** System.
8. Establishment Registration in **FURLS** System.

REGISTRATION PROCESS OF MEDICAL DEVICES IN UNITED STATES [4]

Step 1: Identification of the class of the medical device:

FDA databases are used to determine the class to which medical device belongs based on the Predicate available in the market.

Three-letter Product Code and seven-digit Regulation Number associated with the predicate devices needs to be identified.

If no predicate found, **513(g) or De Novo process** can be used.

Step 2: Quality Management System:

Found in **21 CFR Part 820** should be implemented.

Commonly known as **FDA Good Manufacturing Practice (GMP)** and meets FDA Quality system Regulations.

Assures proper design, supervising and control of manufacturing processes.

Step 3: Pre-Sub feedback:

Pre Submission feedback needs to be obtained for class II and class III from FDA before entering the market to determine whether product require clinical trials or not.

Step 4: IDE (Investigational Device Exemption):

If clinical trials need to be done then, manufacturer needs to apply for IDE.

IDE allows manufacturer to use investigational device for collecting data related to safety and efficacy which are required for **PMA** and in some rear situation in **PMN** submission.

Distribution of the investigational device is limited to the areas mentioned in IDE application and investigation is supervised by IRB (Institution Review Board) comprising health expert and lay

person to assure that ethical principles are followed while conducting the study.
IRB determines the initial risk factors as well as the level of significance of associated risk with the device.
FDA can overrule any risk identified by the IRB.
If IRB determines that a device/clinical study significant risk is associated with the device, the applicant must submit an IDE application to the FDA.

Step 5: PMN and PMA submission;

For class II 510 (k) or PMN (Premarket Notification) application should be submitted and for class III PMA (Premarket Approval) application should be submitted along with the submission fee.

Step 6: Inspection;

For class III FDA conducts facility inspection for all the suppliers that are involved in design and production of the medical device.
All should be compliance with **FDA QSR.**

Step 7: Approval:

For class II FDA issues 510 (k) clearance letter and for class III FDA issues PMN clearance letter.
Clearance letters are posted online.

Step 8: Form 483;

FDA conducts random inspections after issuing registration certificate. If found non-complaint with the regulations FDA can issue form 483

Step 9:Local Representative:

If the manufacturer has no local presence in the US, FDA Agent representative can be applied as a local point of contact with the FDA.

Step 10: Registration:

Devices can be listed and companies can be registered using FURLS system on the FDA website in accordance with 21 CFR Part 807.
The appointed US Agent must be specified.
The FDA Establishment Registration and Listing must be renewed on a yearly basis.

Step 11: Authorization:

The FDA listing on their website will serve as authorization to commercialize the device in the US.
Device can now be sold in US
This authorization will continue until and unless some major changes are done for example design, intended to use etc.

MARKET GROWTH:

[5] The **United States** remains the largest **medical device market** in the world, with a market size of around $156 billion, and it represented about 40 percent of the global **medical device market** in 2017.The industry is responsible for almost 2 million jobs in the **United States**, including both direct and indirect employment.

The medical technology industry employs people in all 50 states. U.S. medical device companies are highly regarded globally for their innovative and high technology products.

R&D spending continues to represent a high percentage of medical device industry expenditures, averaging 7 percent of revenue.

Compared to several other industries including automotive, defense, and telecommunications, the medical device industry invests a higher percentage of yearly revenues into product innovation, reflecting the competitive nature of the industry and constant innovation and improvement of existing technologies.

CANADA:

REGULATORY BODY:

[6] Health Canada, under the authority of the **Food and Drugs Act**, regulates the sale of drugs and medical devices in Canada. Health Canada is divided into two parts;

Health Products and Food, and Therapeutic Products Directorate.

Medical Devices Bureau is under **Therapeutic Products Directorate** which is divided into:

Device Evaluation, Licensing Services and Research and Surveillance.

Medical Devices in Canada are subject to the Medical Devices Regulations (referred to as the Regulations) under the Food and Drugs Act.
The Regulations set out the requirements governing the sale, importation and advertisement of medical devices.

APPROVAL PROCESS OF MEDICAL DEVICES [7]:

Step1:

Determine the classification of your medical device according to Schedule 1, Part 1 of the **Canadian Medical Devices Regulations (CMDR) SOR/98-282**as published by **Health Canada.**
Devices fall into Class I, Class II, Class III or Class IV.

Step 2:

For all devices except Class I, implement an **ISO 13485:2003 quality management system** which includes the additional specific requirements of the CMDR.
ISO 13485 certification, used to demonstrate compliance with European regulations, does not meet Canadian requirements. Updates to the existing procedures, or new procedures, must be

implemented.

Step 3:

For all devices except Class I, have **ISO 13485 quality system** (re)audited by a Registrar accredited by Health Canada under the Canadian Medical Devices Conformity Assessment System (CMDCAS).

Several large European Notified Bodies also act as Registrars recognized by Health Canada. Your new ISO 13485 certificate will be issued upon successful completion of the audit.

Step4:

For Class I devices apply for a **Medical Device Establishment License (MDEL),**

For Class II, III, and IV devices, apply for a **Canadian Medical Device License (MDL)** application for your device.

Compared to a US 510(k) application, MDL applications are simpler for Class II devices and about the same for Class III devices.

Class IV MDL applications are comparable to a US PMA application. Note that an MDL application is for the device itself whereas an MDEL is a permit for the distributor/importer, or a manufacturer of Class I devices.

Documents must be submitted in English or French.

Step5:

For Class I devices, submit **MDEL** application, prepare mandatory procedures and pay Health Canada fees.

For Class II devices, Submit **MDL** application, Fee Form, labeling (IFU), Declaration of Conformity and ISO 13485 (CMDCAS) certificate. Pay Health Canada fees.

Step6:

Health Canada reviews MDL application (Class II, III and IV) and Premarket Review Document (Class III and IV only).

Step7:

For Class I devices, approved applications will be posted on the Health Canada website and your MDEL certificate will be emailed to you.

For Class II, III, and IV devices, issued licenses will be posted on the Health Canada website, and copies of your MDL will be emailed to you.

Note: For Class IV MDLs Health Canada will post a summary of their decision on their website.

Step8:

You may now begin marketing your device in Canada.

Licenses do not expire as long as you renew your registration and pay the annual fees to Health Canada.

Failure to file your renewal and pay fees by the annual deadlines will result in your license(s) being revoked.

REGISTRATION PROCESS OF MEDICAL DEVICES IN CANADA:

[8]To register a product the device must be classified as a class I, II, III or IV product.

Quality management systems must be applied for all medical devices except class I products. Canada has adopted **ISO 13485:2003** as a Canadian National Standard and labeled it **CAN/CSA-ISO 13485:2003.**

For class II devices the quality system must satisfy the requirements for CAN/CSA-ISO 13485:2003, excluding design.

For class III and IV devices the quality system must satisfy the requirements for CAN/CSA-ISO 13485:2003, including design. The manufacturer shall

Identify the risks inherent in the device. In the Device License Application for class IV devices a risk assessment is required.

It is recommended to work according to the standard **ISO 14971**.

Distributors and importers of medical devices need to obtain an establishment license exempt for custom-made devices and devices imported or sold for special access.

This is also required for manufacturers of medical devices class I.

Manufacturers of class I products selling solely through a licensed establishment do not need an establishment license.

To sell or advertise a class II, III or IV product in Canada manufacturers need a device licensing but not an establishment license although distributors and importers do.

Manufacturers also need a declaration of conformity.

Custom-made devices class III and IV requires authorization from the Ministry of Health for importation into Canada.

MARKET GROWTH:

[9]In 2017, total **healthcare** expenditures were valued at approximately CDN$242 billion. **Healthcare** spending in **Canada** is projected to increase from 4.4 percent to 7.5 percent by 2020. ... The **Canadian medical device market** is sophisticated and mature, with a strong demand for high-quality **medical** technologies.

Overview of medical device industry:

Canada has one of the largest economies in the world and the eighth largest medical device market. It was valued at US$6.2 billion in 2015 and is projected to grow steadily, but modestly, increasing to approximately US $8.6 billion by 2020.

The Canadian medical device market is sophisticated and mature, with a strong demand for high-quality medical technologies. The majority of medical

devices used in the Canadian healthcare system are imported. But, medical device exports are on the rise. Canada is home to a robust manufacturing industry with hubs in Ontario and Quebec.

Opportunities in the Canadian market:

Medical device imports account for 80% of the medical device market, so there is plenty of opportunity in Canada for foreign manufacturers. Diagnostic equipment is in greatest demand, as well as patient monitoring equipment, consumables, patient aids, orthopedics/prosthetics, and dental products. The Canadian regulatory process is also well established. Manufacturers with FDA clearance in the US may have an easier time transitioning into the Canadian market.

Industry challenges in Canada:

Medical device manufacturers based outside North America will encounter fierce competition from US companies in the Canadian market. The United States controls more than half of the Canadian market mostly due to geographic proximity and similarities in safety and quality standards between the two countries. Exporters from China, Mexico, and Germany also have solid footing in the Canadian market.

INDIA:

REGULATORY BODY:

[10] The **Central Drug Standards Control Organization (CDSCO)** is India's main regulatory body for pharmaceuticals and medical devices.

The Drug Controller General of India (DCGI) is the key official within the CDSCO.

The DCGI is responsible for the approval of the manufacturing of certain drugs (vaccines, large volume parenteral, blood products, r-DNA derived), specific medical devices, and new drugs.

In India, the manufacturing, import, sale, and distribution of medical devices are regulated under **India's Drugs & Cosmetic Act and Rules (DCA**).

APPROVAL PROCESS OF MEDICAL DEVICES IN INDIA [11]

Step 1:

Medical devices and IVDs are regulated by the Drug Controller General of India (DCGI) within the Central Drugs Standard Control Organization (CDSCO), part of the Ministry of Health and Family Welfare.

The regulatory framework for medical devices is based on the **Medical Device Rules, 2017.**

Only a limited number of medical devices and IVDs require registration in India.

A full list can be found in the CDSCO's **List of Medical Devices and In Vitro Diagnostics Along with their Risk Class.**

Step 2:

Appoint an India Authorized Agent to interact with the CDSCO on your behalf.

Your Agent must have a valid wholesale license (Forms 20B and 21B/21C), and be granted Power of Attorney to manage your registration and device importation in India.

Step 3:

Some IVDs require in-country performance testing through the **National Institute of Biological (NIB).**

Step 4:

Compile device application (Form MD-15), including manufacturing facility information, device technical information, ISO 13485 certificate, IFU, testing results (if applicable), clinical data (if applicable), proof of approval in the US, EU, Australia, Canada, or Japan, plus proof of approval in your home country (satisfied by CFS/CFG).

Step 5:

File registration applications with the **CDSCO** and pay fees.

All documents must be in English.

Step 6:

The CDSCO reviews applications and may require a Technical Presentation.

Novel devices will also undergo a **Subject Expert Committee (SEC) review.**

Step 7:

The CDSCO will issue a Registration Certificate.

The Certificate does not expire; however, registration maintenance fees are due every five years.

Step 8:

Once approved, only your India Authorized Agent may import products.

However, you can obtain multiple registrations for the same device through different Authorized Agents.

REGISTRATION PROCESS OF MEDICAL DEVICES IN INDIA:

[12] Medical devices defined as drugs must be registered with the Ministry of Health and have an import license to be sold in India.

Other devices are not subject to this yet but will be under the new legislation.

Medical devices not defined as drugs only require an import license.

Medical devices defined as drugs are subject to the current legislation the Drug and Cosmetics Act and the Guidelines for Import and Manufacture of Medical Devices.

Quality systems for medical devices do not exist, although CE-marked or FDA approved products are preferred because of their quality and performance.

Manufacturers of medical devices defined as drugs must apply **Good Manufacturing Practices (GMP)**

and conduct suitable tests to prove the product quality.
The quality systems shall concern design, development and manufacture. This kind of devices also requires risk management in form of ISO 14971.
The registration shall be done according to Rule 24A of the Drugs and Cosmetic Act and Form 40 shall be filed.
The applicant can be the manufacturer, the importer or the responsible agent in India.
The Drugs Controller General India (DCG (I)) wants applicant details such as name, address and contact number of the applicant.
The department also wants name and addresses of the manufacturer and the manufacturing premises, the importer, the local authorized representative and the local manufacturer if there is one.

A copy of the Plant Master File shall be submitted with the application.
The information required in the Plant Master File is described in the Clarifications on Guidelines for Import and Manufacture of Medical Devices.
Information on approval in other countries such as US clearance, CE certificate or approval in Australia, Canada or Japan shall be documented and copies of ISO or EN certificates submitted.

A list of countries where the product is sold and a list of countries where the product has been withdrawn from the market and the reasons for the withdrawal are required.
Product information, a GMP certificate and a master file are necessary.
The master file shall have a description of components and materials used and information on the manufacturing process including flow charts, quality assurance procedures and process controls, risk management according to ISO 14971 and test protocols and reports for stability, biocompatibility, toxicology and validation/verification of sterilization where these tests are applicable.
Labeling of devices according to **GHTF** guidelines or ISO specifications is accepted.
Manufacturers of medical devices shall have documented procedures for distribution records, complaint handling, adverse incident reporting and product recall.
A registration of a medical device defined as a drug is valid for five years.

MARKET GROWTH:

[13] The Indian healthcare sector is one of the country's most lucrative sector with reference to the number of employment generated as well as revenue for the country.
Advancement in the medical field has yielded huge success in the treatment and eradication of some illnesses and diseases in **India.**

The healthcare industry has over the years developed several medical devices to aid both the patients and the medical professionals for efficient health care services.
Some of these devices are segmented into diagnostic imaging, consumables, I-V diagnostics, patient aid, orthos and prosthetics. There are different devices with varying applications in the healthcare sector.

COMPARISION OF MEDICAL DEVICE REGISTRATION AND APPROVAL PROCESS IN US, CANADA & INDIA

S. No	Point of Comparison	USA	CANADA	INDIA
1	Regulation Authority (s)	USFDA	MDL and MDEL	CDSCO
2	Classification Categories	Class I	Class I	Class A
		Class II	Class II	Class B
		Class III	Class III	Class C
			Class IV	Class D
3	Regulatory Pathway	510 (K) application	CLASS I – medical device establishment license (MDEL)	Market Authorization application to Competent Authority
		Premarket Approval (PMA)	CLASS II, III,IV – Canadian medical device license (MDL)	

S. No	Point of Comparison	USA	CANADA	INDIA
4	Fees for available pathways	MIDUFA FY2017	For Class I devices, submit MDEL $7,641.	Manufacturing License:
		510 (K) $ 4,690		Rs 6,000/- License Fee
		PMA $ 234, 495	For Class II devices, Submit MDL, Pay Health Canada fees.	Rs 1,500/- Registration Fee
				Import License:
				$ 1,000/- Registration Fee
				$ 5,000/- Inspection of Premises
5	Quality Management Systems requirement	21 CFR Part 820	Canadian National Standard CAN/CSA ISO 13485:2003-except class I	BIS 15575 or ISO 13485
6	Assessment of Technical Data performed by	USFDA	HEALTH CANADA	CDSCO
7	Establishment Registration Requirement	Establishment Registration	Medical device establishment license	Premises Registration
8	Medical Device Regulations	21 CFR Part 800	Medical Devices Regulations (SOR/98-282)	Drugs and Cosmetics Act, 1940
		21 CFR Part 801		
		21 CFR Part 803		
		21 CFR Part 806		
		21 CFR Part 807		
		21 CFR Part 808		
		21 CFR Part 809		
		21 CFR Part 810		
		21 CFR Part 812		
		21 CFR Part 814		
		21 CFR Part 820		
		21 CFR Part 821		
		21 CFR Part 822		
		21 CFR Part 830		
		21 CFR Part 860		
		21 CFR Part 861		
9	Validity of License	Indefinite, unless revoked or product recalled	Licenses do not expire as long as you renew your registration and pay the annual fees to Health Canada.	3 years from the date of approval, for Notified Devices

S. No	Point of Comparison	USA	CANADA	INDIA
		Annual Establishment Registration is required		
10	Labelling Requirements	As per 21 CFR Part 801	Section 21(1), (a) to (j) of the Regulations.	As per Drugs & Cosmetics Act, 1940
				GSR 703
11.	Timelines for Approval(months)	Class I (1)	Class I (1)	6-12 months for Notified Devices
		Class II (3-6)	Class II (3-6)	
		Class III (18-30)	Class III (9-15)	

CONCLUSION:

The overall study concludes that there are interesting comparisons and differences between medical devices regulatory systems across US, CANADA and INDIA. In the process of medical device development lot of research work has to be carried out during the development phase .But the research related activities has to be in accordance to the procedures adopted by the health agency.

REFERENCES:

1.www.centropiaggio.unipi.it/sites/default/files/course/material/ravizza1.pdf
2.https://www.omicsonline.org/.../medical-devices-regulation-in-united-states-of-america-e.
3.https://www.emergobyul.com/resources/usa-process-chart
4.https://www.emergobyul.com/resources/usa-process-chart
5.https://www.grandviewresearch.com/industry.../us-medical-device-manufacturers-market
6.https://2016.trade.gov/td/health/canadamdprofile.pdf
7.https://www.emergobyul.com/resources/canada-process-chart
8.https://www.emergobyul.com/services/canada/canada-device-license
9.https://www.emergobyul.com/resources/market-canada
10.https://www.pacificbridgemedical.com/regulatory-services/medical-device/.../india
11.https://www.emergobyul.com/resources/india-process-chart
12.https://morulaa.com/medical-device/step-by-step-process-to-register-your-medical-devic. www.makeinindia.com/article/-/v/sector-survey-medical-devices