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Comparative Study of Medical Devices in USA, Europe and India

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Abstract

Any medical equipment must get a marketing authorisation from a regulatory authority before it can be sold. Obtaining authorization is a lengthy, multi-step process that requires relevant authorities to review material. After analyzing the information given by the Manufacturer, the concerned Regulatory authority provides marketing authorization. Manufacturers in the United States must apply to the US Food and Drug Administration for Marketing Authorization (USFDA). There are two types of applications in the United States: 510(k) and Pre-Market Application (PMA). The marketing of medical devices is permitted by national authorities in the EU. Notified Bodies (Third Parties) ensure Quality Assurance both before and after approval via third-party compliance. The sale and import of medical devices are approved by India's Central Drugs Standard Control Organization (CDSCO). The CLAA scheme regulates medical devices. The central licensing authority for medical devices in India is the Drug Controller General of India (DCGI). This study aims to collect information on medical device regulations in three regions: the United States, the European Union, and India, and compare market authorization provisions in each region, as well as make this complex subject easier to understand for the readers. The medical device sector is made up of several different sorts of items that are used for a variety of purposes. Medical devices must be governed by tight rules according to the different risk categories since their safety and effectiveness are critical to human health. A common framework for medical device regulations is a comprehensive product life cycle regulatory system that includes product design, manufacture, premarket gatekeeping, and post market monitoring. Medical gadgets, on the other hand, are diverse and inventive, putting current regulatory systems to the test. As a result, competent authorities in charge of medical devices around the world are constantly updating their regulatory systems to ensure that medical devices are safe and effective. The goal of this study is to provide an overview of the regulatory regimes for medical devices in the United States.

Keywords: Medical Devices; Marketing Authorization; Classifications; Case Studies; Warning Letter, Effectiveness; Harmonisation

Abbreviations: USFDA: US Food and Drug Administration for Marketing Authorization; PMA: Pre-Market Application; CDSCO: Central Drugs Standard Control Organization; DCGI: Drug Controller General of India; DOC: Declaration of Conformity; PMA: Premarket Approval; IFU: Instructions for Usage; IDE: Investigational Device Exemption; FIH: First in Human; CGMP: Current Good Manufacturing Practices; MDR: Medical Device Reporting CLAA: Central Licensing Approval Authority; HVAD: Heartware continuous-flow ventricular assist device; PMA: Positive mental attitude.

Introduction

A medical device is any such device used in the treatment, diagnosis and therapy of patients Table 1.

USA	Europe	India
Class I	Class I	Class A
Class II	Class IIa	Class B
Class III	Class IIb	Class C
	Class III	Class D

Table1: Classification of Medical devices.

The Regulations of Medical Devices is sizeable and quickly developing discipline. Different Regulatory Authorities under remote regulatory assessment (RRA) is a voluntary program for medical device facilities under FDA have given us strategies every now and then. Obtaining authorization can be a lengthy and complex process, requiring the assessment of material by relevant authorities [1]. After evaluating the information provided by the Manufacturer, the concerned Regulatory authority grants marketing authorization. Obtaining authorization is a lengthy, multi-step process that necessitates the assessment of material by relevant authorities [1]. The concerned Regulatory authority grants marketing authorization after evaluating the information provided by the Manufacturer. Routine medical treatments such as bandaging a sprained joint, diagnosing numerous diseases, or implanting a prosthetic hip would be impossible without medical gadgets. The medical device industry in India is growing rapidly, at a rate of 15.8% over the past five years [1]. This compares favorably with the global medical device industry, which is growing at a rate of 4.1%. Medical technology is increasingly important in the modern world. The prevalence of diseases treated with medical devices has increased significantly in recent years [2].

Materials and Methods

This is a descriptive observational study; it has been provided with various guidelines for the regulations of medical devices in various countries. The guidelines are ICH GCP E6 which addresses the elements of Good Clinical Practice in the design, conduct and reporting of human subjects' research related to medical devices. Not only has this it also included ISO Guidelines too. For regulation of medical devices in USA it follows the guidelines of USFDA where regulations related to medical devices are in Title 21.

In case of India the guidelines of Central Drug Standard Control Organizations are followed where the regulations of medical devices are in the Drug and Cosmetics Act. For Europe, Medical Device Directive Commission is there. The member states observes the directives of EU which changes as in keeping with guidelines and obligations [2,3].

A marketing authorization from a regulatory authority is required to commercialize any medical equipment. The concerned Regulatory authority grants marketing authorization after evaluating the information provided by the Manufacturer [2]. Medical devices are used in many different settings by people of all levels of expertise. Even by laypersons at home, paramedics, clinicians and opticians, dental professionals and healthcare professionals in highly specialized facilities use medical devices. Today, there are 500,000 different types of medical devices [3]. Rationale Medical devices are used in many different settings by people of all levels of expertise. Even by laypersons at home, paramedics, clinicians and opticians, dental professionals and healthcare professionals in highly specialized facilities use medical devices. Today, there are 500,000 different types of medical devices [3]. To market any scientific device, regulatory authorization is required. The authorization process is complicated and involves a series of steps, with the goal of assessing records via means of authorized authorities. The records provided by the Manufacturer show that the advertising authorization for this product is valid.

Despite being one of the top twenty markets for medical devices in the world and Asia's fourth largest market behind Japan, China, and South Korea, India's medical devices sector is relatively modest in comparison to the rest of the manufacturing industry. Although precise data and figures on the subject are unavailable, an educated assessment would put the sector's worth at around Rs. 30,900 crores in output terms. The Indian medical device industry is primarily driven by imports, accounting for about 65 percent of the overall market [2,3].

Results

S. No	Country	Definition	Legal Framework	Approval Process
1	USA	Any medical device or related article, including a component part, A diagnostic tool or treatment for disease in humans or other animals [4].	Reviewed by the FDA	Once these applications approved Premarketing notification (510k) is submitted to FDA to demonstrate that either it is safe or effective for the human use, after which marketing of medical device is authorized by FDA [5].
2	Europe	Accessories including software. And / or therapeutic purposes, required for proper use, manufacturer is intended to be used by on, monitoring, for humans for diagnostic and preventive purposes of treatment or illness relief; injury or any physiological process [4].	There are three main directives governing the regulations of medical devices [5]	Determine the classification of our device according to EU directive and then implement a Quality Management System, and prepare CE marking technical file and audit QMS by notified body. Prepare Declaration of Conformity (DOC) after obtain the CE marking and ISO 13485 certificate from notified body [5].
3	India	Medical equipment includes anything from household appliances to computer software. It can be used by itself or in combination with other items, and is meant to be used for diagnosing, preventing, monitoring or alleviating disease [4].	Central Drug Standard Control Organization [5]	CDSCO/MD/GD/CLAA CDSCO/MD/GD/IL [7]

Comparison of Medical Devices

S. No	Point Of Comparison	USA	Europe	India
1	Regulatory Authorities	USFDA	EMA and RA of Member State	CDSCO
2	Classification Categories	Class I gadgets are characterized as non-life maintaining and present insignificant mischief potential to client. by safe use. These gadgets need to follow Class II clinical gadgets are those gadgets that have a moderate to high take a chance to the patient and additionally client. 43% of clinical gadgets fall under this classification. Most clinical gadgets are viewed as Class II Data on Class II excluded gadgets is situated inside the gadget guideline, 21 CFR 862 through892. Class III gadgets generally support or support human existence, are critical [4].	Class I - Provided non-sterile or don't have an estimating capacity (generally safe) and furthermore gave sterile or potentially have an estimating capacity (low/medium gamble); the MDR adds to this gathering, reusable careful instruments as Class I reusable careful instruments. Class III gadgets are viewed as high-risk and are dependent upon the most severe necessities, including clinical assessment of the gadget [5].Class IIa clinical gadgets are viewed as medium-risk gadgets by the MDR. This implies that not at all like a Class I gadget, the producer should get an announcement of congruity from an advised body following its similarity appraisal [5]. Class IIb clinical gadgets are viewed as medium-to high-take a chance with gadgets under the MDR, and in this way their CE course additionally requires the inclusion of a told body. This hazard class incorporates gadgets like hatcheries, insulin pens, long haul contact focal points, and ventilators [5].	The grouping of clinical gadgets in India is finished by CDSCO under the affected by Drug Controller General of India (DCGI) [6]. Class A - Low Risk Level Accreditation by advised body as a piece of local area appraisal isn't needed. It is the sole liability of the producer. Class B-Low moderate gamble level [6]. Confirmation by informed body as a piece of local area evaluation is expected for the assembling office quality administration framework. Class C-Moderate high Certificate by told body as a piece of local area evaluation is expected for the plan and production of such kind of clinical gadgets [6]. Class D-High gamble level. Accreditation by informed body as a piece of local area evaluation is expected for the plan [6].
3	Regulatory Pathway	510(K) application Premarket Approval (PMA).	By Notified Bodies and CE Markings [5].	Market Authorization application to Competent Authority.

Discussion

Case Studies on Medical Devices

➢ **Medical Device Product Development Case Study**

- Product development for medical devices is a difficult task.
- Even the simplest product development project might take a number of unexpected turns before it is ready for market.
- Few would argue that designing a medical gadget is done too quickly.
- Regulations are a quick and easy solution.
- The FDA, to be precise, in the United States. Those three letters can be frightening, and they're frequently used as a convenient scapegoat by medical equipment firms [6].
- At First
- During the first few months of the project, at least 38 hours were lost.
- Where did all the time go?
- 20 hours were spent sending, receiving, retrieving, and changing documents via email. To communicate and coordinate, the crew had to rely primarily on email [1].
- When the Project Team is changed
- It took some time to get the original team up to speed and running. When the team members changed, more time was required.
- It just took 10 hours to get the correct
- Between the Occasion
- Dealing with document modifications took another 30 hours.
- Deep Dive into Development
- There is an increasing amount of documentation. Email! Ugh.
- On Getting the Clearance by FDA
- Did I mention that we communicated primarily via email? A total of 40 hours have been lost.
- Ending
- I'm not sure how much you get paid each hour. That's a simple calculation [6].
- Consider how much time you could have saved if you could have saved 312 hours during the project. What is the price of each item? In a month, how many do you sell? Could you picture making money 8 weeks sooner? [6].
- Would it make a difference?

The goal

- Put regulatory notions into practice with an infusion device.

➢ **FDA Warning Letters Related to Medical Devices**

- This letter was issued on April 28 2022
- Medtronic issued an Urgent Medical Device Correction External Link Disclaimer earlier this week to alert health care providers to the pump weld fault. Medtronic is doing research to determine which HVAD pumps are affected. The FDA does not support the elective removal of perfectly working systems, as noted in the FDA's June 2021 letter. Health care practitioners and patients should make case-by-case decisions about removing or swapping the Medtronic HVAD System, taking into account the patient's clinical status and surgical risks.
- Patient's clinical status and surgical risks [6].

Recommendations

- Pump thrombosis should be addressed first in patients who have one or more of the signs or symptoms of the condition.
- Only examine if the patient is a candidate for pump exchange, heart transplant, or pump explant for recovery if symptoms do not improve, taking into account the patient's clinical condition and surgical risks.
- If any of the signs and symptoms described below apply to the patient right away.
- The controller's csv logfiles, as indicated in Medtronic's Urgent Medical Device Correction [7].
- Be note that the FDA's June 2021 communication's recommendations have not changed. Including:
- Follow the directions in the Instructions for Usage (IFU) and current best clinical practises, including as stringent blood pressure and International Normalized Ratio (INR) [7].

Background

Medtronic received three complaints from patients who suspected pump thrombosis, and inspection of the returned pumps revealed a problem with the Medtronic HVAD System's internal pump. All three patients received a pump exchange, and two of them died as a result of the procedure. One or more of the following signs or symptoms were present in the three patients:

- a grinding noise
- High Watt warnings and transient power surges in log files
- Lactate dehydrogenase levels are high.
- Low perfusion due to low motor speed
- Lightheadedness or dizziness [7]

Actions Taken by FDA

The FDA and Medtronic will continue to work together to:

- Keep an eye out for any problems caused by faulty pump welds [7].
- The second study, "Freedom From Unacceptable Risk: Making a Case for Safety Assurance and Risk Management
- The Goal
- To identify the essential ideas of medical device safety

assurance.

- The Goal
- Describe the medical gadget. Investigational Device Exemption (IDE) Application for the First in Human (FIH).
- PMA is a medical gadget that will be introduced.
- To comprehend the steps involved in obtaining a PMA application, as well as the data necessary.
- The purpose of this study is to look at the general concepts of nonclinical and clinical research.
- The goal
- Have a better understanding of how a 510(k) submission's "substantial equivalence" determination is made.
- To look at the entire 510(k) submission process.

Importance of Quality Systems

The Quality System Regulation specifies the procedures, controls, and facilities that must be utilised in the design, manufacture, labeling, packaging, storing, purchasing, installing, and servicing of medical devices. The FDA's quality control system is also known as Current Good Manufacturing Practices (CGMP) [8].

The CGMP does not provide explicit guidance on how to make a certain device compliant under the Quality System Regulation due to the broad range of medical devices. Its purpose is to act as a framework for all devices.

Need for Medical Device Reporting

Medical Device Reporting (MDR) was created to assist the FDA and manufacturers in quickly identifying and monitoring the harmful consequences of a specific device. Under the MDR programme, any deaths or major injuries must be reported to the FDA. Both manufacturers and importers share this duty. Importers are only required to report device malfunctions to manufacturers, who must then report the matter to the FDA [8].

How does the FDA ensure that registration and listing are accurate?

- By checking the submitted information with CDRH's establishment registration and listing database, we ensure that the reported manufacturer and shipper are registered with the FDA. We also check the data system of the CDRH to see if the declared importer is registered.
- By comparing the claimed product description to CDRH's establishment registration and listing database, listing for the declared product is also validated.
- Compliance is validated if the information submitted matches the CDRH establishment registration and listing database; if the information does not match, the FDA may request more information or detain the product. The goods will be refused if the company does not have the necessary registration and listing [8].

How does the FDA ensure that medical device regulations are met?

- The FDA's internal data systems are compared to the information in these entry statements. Internal data systems are used by the FDA to check registration, listing, device approval (if applicable), and other product requirements, as well as to establish if a company is subject to DWPE. Compliance is validated if the information submitted matches; if the information submitted does not match, the FDA may request additional information or detain the product.
- Correct and precise entry data, as well as the appropriate A and C codes, can help speed up the entry review process. Because the FDA's screening technology, PREDICT, can validate the declared information against the database, providing accurate information increases the possibility that your shipment will be processed electronically and not kept for human review [8].

What methods does FDA use to check premarket submissions?

- When a product requires premarket approval, the FDA will compare the supplied information to CDRH's data systems to validate the stated.
- Compliance is validated if the information submitted matches the CDRH data system; if the information does not match, the FDA may request additional information or detain the How can I figure out what I need to bring a medical gadget into the country.

Affirmation of Medical Device Compliance Codes

Affirmation of Compliance (A of C) codes is three-letter codes that can be provided at the time of import to help the FDA process the paperwork. The FDA employs A and C codes to help ensure that your product satisfies the necessary standards. When you provide the correct A and C codes, your cargo is less likely to be held for further FDA entrance review during the FDA's import screening procedure. A or C codes are only necessary in some situations and are not required in other scenarios. In addition to any necessary A of C codes, submitting voluntary A of C codes may speed up initial screening and assessment of your entry. Medical device A and C codes are also available [9].

Article 117

Article 117 of Regulation modifies Annex I of requiring that the DDC marketing authorisation dossier contain, where possible, the results of the device part compliance assessment (i.e. the declaration of conformity or the relevant EU certificate issued by a notified body). If the results of the

conformity assessment are not included in the dossier, and an EU certificate from a notified body would be required if the device were used separately, the applicant will be required to submit an opinion from a notified body on the conformity of the device part with relevant requirements of Annex I to Regulation as part of the Marketing Authorisation Application [9].

European Public Assesment Report

An EPAR informs the public about a pharmaceutical product, including how it was evaluated, and reflects the EMA/scientific NCA's conclusions. The EPAR will summarise information on the medical device part that is important to the medicinal product's usage, including whether a declaration of conformity, an EU certificate, or a notified body opinion was submitted as part of the medicinal product's marketing authorisation application. The applicant/MAH will be asked to identify information in the EPAR that is regarded commercially sensitive and submit a proposal with arguments for deletions/alternative phrasing. The opinion of the notified body will not be published separately [9].

In European Union How do MDR Affect the Co-Packaged Medical Device?

Applicants for marketing authorizations of medicinal products in which a medical device is provided within the secondary packaging of the marketed medicinal product (i.e. co-packaged) and does not form an integral product with the medicinal product must ensure that their co-packaged [9].

Discussions from Table

In case of medical device regulations in Unite States it is USFDA (US Food And Drug Administration)

- Device Advice is CDRH's flagship text-based resource that covers the complete product life cycle and discusses many elements of medical device laws, regulations, guidance's, and policies.

In case of medical device regulations in Europe it is EMA and RA of Member State.

- The EU has revised the legal framework of 3 directives to reflect progress over the last 20 years.
- The European Commission publishes a number of publications to aid parties in implementing the medical device legislation.
- These are legally non-binding advice texts whose principal goal is to ensure that regulations are applied consistently.

In case of medical device regulations in India it is CDSCO

- Only registered medical devices are now regulated as drugs in India under the Drugs and Cosmetics Act 1940 and Rules promulgated there under in 1945.

Classification Categories for USA, Europe and India

- Class I gadgets are characterized as non-life maintaining and present insignificant mischief potential to client. by safe use. These gadgets need to follow Class II clinical gadgets are those gadgets that have a moderate to high take a chance to the patient and additionally client. 43% of clinical gadgets fall under this classification. Most clinical gadgets are viewed as Class II
- Data on Class II excluded gadgets is situated inside the gadget guideline, 21 CFR 862 through892. Class III gadgets generally support or support human existence, are critical.
- Class I - Provided non-sterile or don't have an estimating capacity (generally safe) and furthermore gave sterile or potentially have an estimating capacity (low/medium gamble); the MDR adds to this gathering, reusable careful instruments as Class I reusable careful instruments.
- Class IIa clinical gadgets are viewed as medium-risk gadgets by the MDR. This implies that not at all like a Class I gadget, the producer should get an announcement of congruity from an advised body following its similarity appraisal.
- Class IIb clinical gadgets are viewed as medium-to high-take a chance with gadgets under the MDR, and in this way their CE course additionally requires the inclusion of a told body. This hazard class incorporates gadgets like hatcheries, insulin pens, long haul contact focal points, and ventilators [5].
- Class III gadgets are viewed as high-risk and are dependent upon the most severe necessities, including clinical assessment of the gadget.
- The grouping of clinical gadgets in India is finished by CDSCO under the affected by Drug Controller General of India (DCGI) [6].
- Class A - Low Risk Level
- Accreditation by advised body as a piece of local area appraisal isn't needed. It is the sole liability of the producer.
- Class B-Low moderate gamble level.
- Confirmation by informed body as a piece of local area evaluation is expected for the assembling office quality administration framework.
- Class C-Moderate high
- Certificate by told body as a piece of local area evaluation is expected for the plan and production of such kind of clinical gadgets.
- Class D- High gamble level.
- Accreditation by informed body as a piece of local area evaluation is expected for the plan.

Regulatory Pathway

USA

- The 510 (K) process is used to bring about 90% of medical devices to the US market, whereas PMA is used to bring about 5% of medical devices to market, and the remaining five pathways are used to bring the remaining 5% of products to market.
- In 2014, the 510 (K) pathway cost roughly $31 million to get a medical device to market, compared to about $94 million for PMA.
- In 2022, the 510(K) pathway cost roughly $55 million to get a medical device to market, compared to about $99 million for PMA.
- A 510(K) is a premarket notification that is sent to the FDA to guarantee that a device is safe and effective before being sold.
- A 510(K) application establishes that a device is essentially the same as a reference device (one that has been cleared by the FDA or has been on the market since 1976) [10].
- Substantially equal means that the new device serves the same purpose as the old one and has the same technological capabilities.
- During the pre-market approval (PMA) process, the FDA's scientific and regulatory review department assesses the safety and effectiveness of Class III medical devices.
- Any gadget that is considerably different from previous devices requires a PMA [10].
- A medical equipment classified as a Class III carries a higher level of risk. A PMA application under section 515 of the FD&C Act was required because general and special control investigations were insufficient to verify and assure safety and efficacy.
- A clinical trial is required to demonstrate the safety and efficacy of the product. The PMA must be granted within 180 days, according to FDA standards [11].

Europe

- By Notified Bodies and CE Markings
- Medical device manufacturers must obtain CE certification in order to ensure that their goods are safe and appropriate for their intended use.
- The French term "Conformite Europeenne" is represented by the letter "CE."
- The CE Marking on a product is a manufacturer's certification that the product complies with the essential requirements of relevant European health, safety, and environmental regulations, and it ensures the product's free movement between the EFTA and European Union single markets [11].
- CE marking is the responsibility of the Notified Bodies (NBs).
- It's a company or government agency that has been given permission to certify that the device conforms with the European Directive.
- Manufacturers can choose from any of the EU's member states for their NBs.
- Competent authorities in each state will propose Notified Bodies, and the NBs will have the authority to grant the CE mark.

India

- Market Authorization application to Competent Authority.
- Medical devices are regulated in India by the Ministry of Health and Family Welfare's CDSCO (Central Drugs Standard Control Organization).
- On June 29, 2006, the FDA released medical device recommendations. Appendix MIII of the Pharmaceuticals and Cosmetics Regulatory Guidelines was published to regulate the manufacture of medical devices and ensure that they are of good quality.
- India, like the EU, is considering a notifying body's third-party compliance evaluation, and it is working to apply ISO 13485: 2003 QMS for medical devices [11].
- We'll need a valid CDSCO wholesale licence in Forms 20B and 21B, as well as an import licence in Forms 8&9, to market medical devices in India.
- Medical devices that fall under the Notified Medical Devices & IVDs category must register with the CDSCO before going on the market.
- The Government of India provided guideline documents on Medical Device Marketing Authorization through CDSCO. The CDSCO detailed its expectations for the grant of a License for the Import and Manufacture of Medical Devices in these documents [11].

Conclusion

The medical device sector is made up of many different sorts of items that are used for a variety of purposes. Medical devices must be governed by tight rules according to the different risk categories since their safety and effectiveness are critical to human health. A common framework for medical device regulations is a comprehensive Medical gadgets, on the other hand, are diverse and inventive, putting current regulatory systems to the test. As a result, competent authorities in charge of medical devices around the world are constantly updating their regulatory systems [11].

The medical device industry is a powerful economic driver around the world. Although the post-marketing research programs are similar, the medical device approval process is historically different between the US FDA and EU systems. There was no difference in security between the two systems [6,7].

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