IJPSR (2023), Volume 14, Issue 10 (Review Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 12 January 2023; received in revised form, 20 May 2023; accepted 31 May 2023; published 01 October 2023

CURRENT REGULATORY REQUIREMENTS FOR MEDICAL DEVICES IN US, EU, AND INDIA

N. Suganthi, Kaviya Suresh and B. Anbarasan *

Department of Pharmaceutics, Sri Ramachandra Faculty of Pharmacy, SRIHER (DU), Porur, Chennai - 600116, Tamil Nadu, India.

Keywords:

IMDRF, Medical devices, FDA, harmonization, Legislation, Safety, EUMDR

Correspondence to Author:
Dr. B. Anbarasan

Lecturer,
Department of Pharmaceutics,
Sri Ramachandra Faculty of Pharmacy, SRIHER (DU), Porur,
Chennai - 600116, Tamil Nadu, India.

E-mail: anbarasan.b@sriramachandra.edu.in

ABSTRACT: Clinical results of various medical treatments using medical devices demonstrate continuous advances, dealing with multiple types of products covering a vast range of applications in the last two decades. Millions of people rely on medical devices to diagnose and manage illnesses. A typical framework for medical device regulations is a whole product life cycle regulatory system that covers product design, production, premarket gatekeeping, and post-market monitoring. Nevertheless, the present regulatory frameworks are being tested by the diversity and innovation of medical devices. This comparative study serves as the basis for the research, which then examines the function of litigation in regulation and ensuring patient safety by placing medical device litigation within the context of the pertinent regulatory frameworks.

INTRODUCTION: A medical device is any appliance, equipment, substance, apparatus, or another item, whether used alone or in conjunction with another device, including the software required by the maker for its intended purpose to be used by human beings. Whereas the effectiveness and safety of medical devices are crucial to maintaining human health, the devices must be governed by restrictive laws based on the various risk categories. Additionally, certification processes for various activities must be completed per specifications [1]. In terms of sales, the United States dominates the global medical tech sector, and the European Union (EU) has consistently been its principal export destination.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.14(10).4733-40

This article can be accessed online on www.ijpsr.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.14(10).4733-40

Understanding EU rules has been a key factor in the success of American medical technology companies in Europe. Additionally, the EU is recognized as having one of the world's quickest pathways to market for Med Tech products [2]. A major point of comparison for device regulation in the United States & European Union with lower regulated markets. This study aims to provide an informative review, investigate why these devices are regulated and provide a response through a critical evaluation and comparison of the laws governing medical devices in three vices in three different countries: the United States, European Union, and India.

Overview of Global Medical Device Regulations: A risk-based classification approach is used internationally to govern Med Tech devices in almost all emerging markets. These systems are comparable to those proposed by the Global Harmonization Task Force (GHTF), a non-governmental organisation with the goal of

harmonizing global medical device standards. The International Medical Device Regulators Forum (IMDRF), which has subsequently taken the role of the GHTF, which was abolished in December 2012, follows the principles of its predecessor. The current IMDRF members represent medical device regulatory authorities in Australia, Brazil, Canada, China, Europe, Japan, Russia, Singapore, South Korea & United States [2, 3].

Working Groups:

1. Clinical Evidence for IVD Medical Devices.
2. Good Regulatory Review Practices.
3. Medical Device Cyber Security Guide.
4. Adverse Event Terminology.
5. Personalized Medical Devices (PMD).
6. Artificial Intelligence Medical Devices.

Medical Device Regulations in United States (US): The Federal Food, Drug, and Cosmetics (FD & C) Act was amended in 1976, expanding the authority of the US FDA to manage medical equipment beneath the Centre for Radiological Devices Health (CDRH). The rules governing pharmaceuticals and medical devices share a lot of similarities. The speed of invention in these two sectors, however, varies. Moving a new medical device from concept to market takes an average of three to seven years, as opposed to the 10 to 15 years it often takes to approve a new drug [4].

Classification of Medical Device as Per US Food Drug Administration: The FDA's Centre for Devices and Radiological Health (CDRH) oversees pre- and post-market medical device oversight in the United States. Based on their risks and the regulatory measures required to ensure safety and effectiveness, the FDA divides medical devices into Class I, II, or III categories.

TABLE 1: CLASSIFICATION OF MEDICAL DEVICES UNDER THE USFDA [4]

Classes	Risk description	Safety/Effectiveness controls	Example
Class-I	Low Risk	General Controls	Elastic bandages, examination gloves
Class- II	Moderate Risk	General Controls & Special Controls	Infusion pump, surgical drapes
Class-III	High Risk	General Controls & Premarket Approval	Heart valves, Breast implants

Levels of Regulatory Pathway of Medical Devices in US: The 510(K) procedure accounts for around 90% of medical device introductions to the US trade, PMA accounts for 5% of medical device releases, and the remaining five routes account for the remaining 5% of devices introductions [6]. FDA bases its decision approval or clearance on the data the manufacturer presents to the agency. The Food and Drug Administration Modernization Act of 1997 (FDAMA; P.L. 105-115) granted the FDA the power to set up protocols for conversing with manufacturers before submitting a submission. By allowing FDA and a company to resolve queries and concerns before the planned studies that will be used to support the marketing application are started, and the application is filed, the processes attempt to hasten the review process [7].

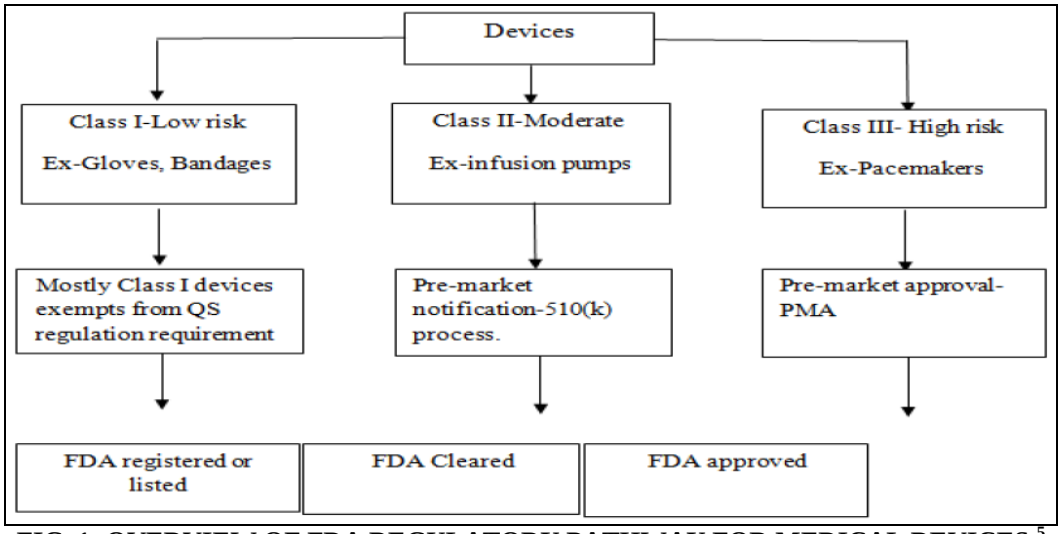

FIG. 1: OVERVIEW OF FDA REGULATORY PATHWAY FOR MEDICAL DEVICES [5]

510 (K) Premarket Notification: Any moderate-risk medical device that is not excluded from the premarket review must submit a 510(k) application. A 510(k) is a premarket notification submitted to FDA to authorize that the product being marketed is substantially equivalent, substantially safe and effective to a lawfully marketed "predicate" product. Devices that were lawfully marketed prior to May 28, 1976 (amendments devices), that were deemed SE out through the 510(k) procedure, or that have obtained marketing authorization through the De Novo classification phase under section 513(f) (2) of the FD & C Act are not distinct from the premarket notification requirements. The de novo 510(k) method is another option for innovative devices without a predicate [9].

Premarket Notification 510(k)s can be filed to the FDA in one of three formats: traditional, special, or abbreviated. The FDA created the Special and Abbreviated 510(k) Programs in 1998 to speed up the review of specific submissions subject to 510(k) requirements. These programmes are designed to make it easier to submit, review, and approve changes to a manufacturer's own legally marketed predicate device (an "existing device") that has already received 510(k) clearance.

Premarket Approval: To independently assess the efficacy and safety of Class III medical devices, the FDA uses the PMA scientific and regulatory evaluation process. These devices sustain human life, play a significant role in avoiding health impairment, or pose an unreasonably high risk of disease or harm. Since the FDA has determined that general and special controls are insufficient to minimize the degree of risk associated with Class III devices, these devices need a PMA application to get marketing clearance under Section 515 of the FD & C Act [10].

FDA has 45 days after receiving a PMA to ensure that the application is administratively finished. If everything is in order, FDA formally applies. Further, the agency has 75 days to finish the preliminary investigation and decide if seeking a meeting of the advisory committee is needed. The FDA may ask advisory groups for their opinions on any scientific or regulatory issue. FDA often accepts suggestions from advisory committees for an application (approvable, approvable with conditions, or non-approvable). However, the PMA review and decision-making process must be completed within 180 days. To speed up PMA reviews, MDUFA performance measures have been developed [8].

Humanitarian Device Exemption (HDE): The Humanitarian Device Exemption (HDE), granted by the Safe Medical Devices Act of 1990 (SMDA, P. L. 101-629), promotes the creation of devices that help in the diagnosis and therapy of illnesses or ailments that impact fewer than 4,000 people annually in the United States. Like a PMA, an HDE application is excluded from the effectiveness standards to encourage manufacturers to create products for these specific markets [8]. An HDE is exempt from the effectiveness requirements of Sections 514 and 515 of the FD & C Act and is subject to certain profit and use restrictions. An HDE cannot be authorized for a device with the same planned application as the humanitarian use device once it has received approval or clearance. However, if a similar device has already received approval under another HDE or is currently being investigated by an IDE, the agency will "consider an HDE application."

Medical Device Regulations in European Union (EU): The European medical device market's involves therapeutic and surgical equipment, health monitoring, diagnostic and medical scanners. Regulation (EU) 2017/745 on medical devices (MDR) significantly upgrades the regulatory framework in the European medical device sector [11]. New MD Regulation (EU) 2017/745 and IVD Regulation (EU) 2017/746 came into force on May 25, 2017. This would merge two current legal provisions and replace both the present medical device directive (93/42/EEC) and the active implantable MD directive (90/385/EEC). It also repeals the three amending directives, regulations (EC) no 2001/83/EC, (EC) no 178/2002, and regulations (EC) no 1223/2009 [12].

Classification of Medical Devices as Per Eu-Mdr (European Union): The classification of medical devices in use by the EU medical device legislation is a risk-based system considering the human body's resilience and the potential hazards associated with the devices. According to MDR Article 51, devices are divided into classes I, IIa,

IIb, and III, considering the devices' intended use and the risks they entail. Classification is to be carried out in accordance with Annex VIII to the MDR [3].

TABLE 2: CLASSIFICATION OF MEDICAL DEVICES UNDER THE EU-MDD

Classes	Risk description	Example
Class I-sterile	Reusable sterile surgical instruments	Sterile gloves. Dressings, others.
Class I-measuring	Provided sterile and/or has a measurement function (low/mediumrisk);	Volumetric urine bag
Class I-basic	Provided non-sterile or will not have measurement feature (low risk)	Non-Sterile Gloves
Class IIa	Medium risk	Suction equipment, Surgical Blades.
Class IIb	Medium to high risk	Radiotherapy equipment, orthopaedic implants
Class III	High-risk	Drug-eluting cardiac stents

Levels of Regulatory Pathway of Medical Devices in the European Union:

CE Marking: To assure that their devices are secure and suitable for the indicated use, medical device manufacturers must display CE marking on their devices [1]. Additionally, the CE mark permits unrestricted marketing of medical device within the whole European Economic Area (EEA). The manufacturers are responsible for ensuring that their product complies with the fundamental criteria of the applicable EU regulation.

The initials "CE" in the following format contribute the CE conformity mark:

Although this minimal dimension may be waived for small-scale equipment, the vertical aspects of the various CE marking components must be approx. the same and cannot be less than 5 mm [13].

Post Marketing Surveillance (PMS): Manufacturers of medical devices will be expected to gather post-market clinical data as part of their ongoing evaluation of impending safety hazards under the supervision of new rules. They must evaluate existing PMS procedures and specify precisely who oversees providing this new information and the supporting documentation [12]. Since, 2011, it has been required to report any adverse occurrences to the European Databank on Medical Devices (EUDAMED). The makers of authorized devices, a history of certifications that have been issued, altered, withdrawn, or denied, and active clinical trials into the device are all listed on Eudamed. If the device's long-term safety is uncertain, the notified authority may ask businesses to do post market research as part of the CE mark certification [14]. According to different frequency and submission criteria, new electronic vigilance reporting (MDR article 92) and periodic safety update reports (PSUR) for all devices will be added.

UDI (Unique Device Identification): Article 27 of Regulation (EU) 2017/745 (the "MDR") and Article 24 of Regulation (EU) 2017/746 (the "IVDR") state that the UDI system must include the creation of a UDI that includes a UDI device identifier (the "UDI-DI") specific to a manufacturer and a device, allowing access to the information, and a UDI production identifier (the "UDI-PI") that identifies the unit of device. Due to the new MDR's requirement that all devices be completely traceable through the UDI system, careful preparation for UDI deployment in the EU will be needed.

The Medical Device UDI assists manufacturers in improving adverse event management, better control innovation, lower health care fraud, and foster transparency across the distribution chain [12].

Medical Device Regulations in India: Prior to 2005, India failed to offer any medical device regulation. In 2008, the government suggested amending the current 1945 Drug and Cosmetics Rules to include regulatory criteria for premarket clearance of medical devices. The Medical Devices Rules, 2017, officially came into effect on January 1st, 2018. For the aim of legislative clarity, the new regulation has categorically separated "medical devices" from "drugs/pharmaceuticals" along with the other revisions [15].

Classification of Medical Devices as Per Medical Device Rues, 2017 (India): The DCGI is governed by the CDSCO categories for medical devices, associated with regulatory clearance and

registration from the CDSCO. Every single medical device in India pursues a regulatory framework that depends on the drug guidelines under the Drug and Cosmetics Act (1940) and Drugs and Cosmetics runs under 1945. Medical Devices are generally based on risks; the actual risk-based classification of the medical device depends upon its intended use and purpose.

TABLE 3: CLASSIFICATION OF MEDICAL DEVICES UNDER THE MDR-2017

Classes	Risk Description	Example
Class A	Low risk	Surgical dressings, thermometer
Class B	Low-moderate risk	Nebulizers, Hypodermic needles
Class C	Moderate– High risk	Lung ventilator, Bone cement
Class D	High risk	Pacemakers, Coronary stent

Levels of Regulatory Pathway of Medical Devices in India:

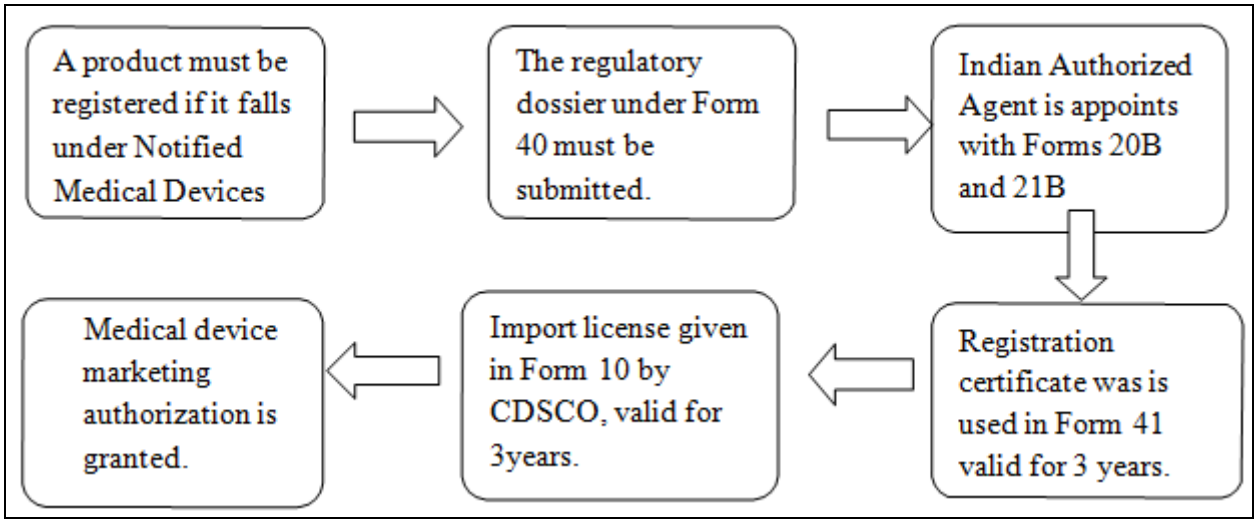

FIG. 2: REGISTRATION OF MEDICAL DEVICES IN INDIA

License for Sale of Medical Devices: There are no specific rules under the 2017 rules for selling medical devices. The D & C rule's regulations governing the sale of medications other than homeopathic medicines will apply to medical devices as if they were included in the 2017 rules. Within three months following the publication of these are commendations, importers, stockists, and retail dealers of medical devices must receive the necessary sale prints from the state licensing authorities. The distributor must document Any sale or distribution, as per D& C rules. A stock transition is not a sale or distribution; hence the distributor doesn't record it therefore, the stocks presence at the facility may be seen as a distribution action [16].

Mandatory Recalls on Knowledge of Risk to Safety: Manufacturers and importers are required under the 2017 Rules to initiate are called right once if a medical device poses a threat to a patient's health while being used, indicating that it may be harmful. The purpose of their call should before move the medical equipment from patients' and the market, along with a statement of the grounds for the removal. The licensing authority must be informed about the specifics of their call by the manufacturer and importer [17].

Legislative Standards for Medical Device Clinical Research: The GHTF Study Group 5's suggestions for clinical assessment and research have been supported by industry. Additionally, it will offer a document of ISO 14155 on clinical studies and correlate it with the ICH standards on good clinical practises for pharmaceuticals.

A new regulatory framework for the clinical research of medical devices will be introduced by the 2017 Rules. Among this framework's important clauses are:

A. The licensing authority must decide within a set timeframe of ninety (90) days. Regarding performing a clinical experiment.

B. The first participant must be enrolled in a clinical study within one year of approval.

C. Pilot Study (also known as an exploratory study) and Pivotal Study (also known as a confirmatory study) new concepts have been introduced in relation to the authorization of a research medical device [18].

Comparison of Regulatory Requirements of Medical Devices in United States, European Union, and India:

Sr. no.	Parameters	United States	European Union	India	Similarity/ differences
1.	Regulatory Authority	US Food and Drug Administration (USFDA)	European Medicines Agency.	Central Drugs Standard Control Organization (CDSCO)	Different
2.	Guidelines	Federal Food, Drug and Cosmetic Act (FD & C Act).	Regulation 726/2004 - Regulation (EC) No 726/2004 of the European Parliament and the Council of March 31st, 2004, set forth Community processes for licencing and oversight of medical devices for human and animal use by the European Medicines Agency.	The Drugs & Cosmetics Act, 1940 regulates the import, manufacture, distribution and sale of drugs in India.	Different
	Website	https://www.fda.gov	https://www.ema.	https://cdsco.gov.	Different
3.	Regulation of Medical Device	21CFRPART800-898	EU Medical Devices Regulation (MDR2017/745)	Medical Device Rule 2017	Different
4.	Articles	21	NA	NA	Different
5.	Quality Management Systems requirement	ISO1348 52 01 6 21 CFR Part 820. Quality System Regulation	ISO13485:2016	ISO13485:2016	Same
6.	Applicant	Manufacturer/Authorized representative	Manufacturer/Authorized representatie	Manufacturer/Authorized representative	Same
7.	Application in The form of	Technical file	Technical file.	Technical file	Same
8.	Mode of submission	FDA Electronic Submissions Gateway (ESG)	e-Submission gateway or web client.	Hardcopy/Online SUGAM portal	Different
9.	Format for Dossier submission	Electronic Common Technical Document (eCTD)	Electronic common technical document (eCTD) format	Common Technical Document (CTD)-Paper/Electronic	Different
10.	Registration fee for Medical device	Premarket Notification 510(k)-$12,745 PMA,PDP, PMR, BLA -$374,858 De Novo Classification Request-$112,457	For a single strength associated with one pharmaceutical form and one presentation 286900 EUR, for each additional strength or pharmaceutical form including one presentation, submitted at the same time as initial application for authorization 28800 EUR.	**For class A and B**$ 1,000 Registration Fee $ 50- Premises Registration **For class C and D** $ 1,500-Registration Fee $ 3000-PremisesRegistration	Different
12.	Labelling regulations of Medical Devices	21 CFR Part 801	93/42/EEC	Drugs & Cosmetics Act, 1940 GSR 703	Different
13.	Outcome of Review Process	Approval Letter (PMA) Marketing Clearance 510 (k)	CE mark with NB number	Import/ Manufacture License number	Different
14.	Approval time frame	Class-I: 1 Month Class-II:9-12 Months Class-II: 18-30, Months Class-III: 18-30	Approximately 6 months for class I and class II a devices, upto 12 months for class II b and class III devices	Registration of Medical Devices is generally 6-9 months, post submission of complete documentation to obtain Registration certificate.	Different
15.	Shelf life	5 years	5 years	The Medical Device's shelf-life shall not exceed 60 months from the expiration date.	Same
16.	Unique device	The FDA published the draft	A manufacturer and device-		A medical

Identification of the medical device (UDI)	guide line titled Updates for Unique Device Identification-Policy Regarding Global UDI Database Requirements for Certain Devices on October 13, 2021. According to the draft guidance, the FDA doesn't plan to enforce the 21CFR 830.300 Global Unique Device Identification Database (GUDID) reporting requirements for some class I devices that are deemed product safety goods	specific UDI device identifier ('UDI-DI'), providing access to the information provided for Annex VI Part B; AUDI production identifier ('UDI-PI'), identifying the device manufacturing unit and, the packaged devices as set out in Part C of Annex VI;	product that has been licensed for sale, delivery, import, or export must be are UDI Containing the device beginning January 1, 2022

CONCLUSION: Medical devices are governed differently in the US, Europe and India, but in each of these regions, pre- and post-market processes are carried out to ensure the marketing of high-quality products. 90% of manufacturers in the US complete the 510(k) process, but the pre-market approval process is trickier(k). For high-risk technologies, clinical evaluations are essential. Several gadgets, known as notified devices in India, are governed by CDSCO through gazette notifications. Several items are categorized as medications in India but as devices in other nations [19].

This system doesn't adhere to international norms. It seems elementary when comparing the current system to the US and EU regulatory frame works. However, the Global Harmonization Task Force (GHTF) standards can be followed to strengthen the industry, and the emphasis must be placed on clinical trials due to the existing regulatory structure's lack of active engagement from the government [20].

ACKNOWLEDGEMENT: I am thankful to my guide who initiated me to work on this topic and I am also thankful to my co-author who contributed to my manuscript preparation throughout.

CONFLICTS OF INTEREST: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the paper.

REFERENCES:

1. Chen YJ, Chiou CM, Huang YW, Tu PW, Lee YC and Chien CH: A Comparative Study of Medical Device Regulations: US, Europe, Canada, and Taiwan. Ther Innov Regul Sci 2018; 52(1): 62-69. doi: 10.1177/2168479017716712. Epub 2017 Jul 7. PMID: 29714608.
2. Daigle, Brian and Mihir Torsekar: The EU Medical Device Regulation and the U.S. Medical Device Industry. Journal of International Commerce and Economics 2019.
3. International Medical Device Regulators Forum (IMDRF). Available at: Working groups | International Medical Device Regulators Forum (imdrf.org)
4. Wilkinson, Anthony. Medical Device Regulation and Litigation: A Comparative Analysis of Australia, the United Kingdom and the United States of America. Queensland University of Technology 2021
5. Agung Purnama and Daniela Drago: "FDA regulatory pathways for medical devices,"
6. Judith A. Johnson: FDA Regulation of Medical Devices. 2016; 14.
7. Jonathan P. Jarow and John H. Baxley: Medical devices: US medical device regulation. Urologic Oncology: Seminars and Original Investigations 2015; 33(3): 128-132. ISSN 1078-1439. Available from: https://doi.org/10.1016/j.urolonc.2014.10.004
8. Shluzas and Lauren: "Review of U.S. Medical Device Regulation. Journal of Medical Devices 2007; 1: 283-292.
9. Agrahari N, Lakshameesha C, Goli D and Awadhesh NC: Gap Assessment on New Medical Device Rules in India and EU. J Drug Des Res 2021; 8(2): 1083.
10. Impact of changes under the new EU Medical Devices Regulation (EU) 2017/745 to international registration 26 May 2020. https://www.medtecheurope.org/resource-library
11. Maresova P, Hajek L, Krejcar O, Storek M and Kuca K: New Regulations on Medical Devices in Europe: Are They an Opportunity for Growth? Administrative Sciences [Internet] 2020; 10(1): 16. Available from: http://dx.doi.org/10.3390/admsci10010016
12. Sridhar S and Venkatesh MP: Impact of New Medical Device Regulation in European Union. Journal of Chemical and Pharmaceutical Research (ISSN: 0975-7384)
13. French-Mowat E and Burnett J: How are medical devices regulated in the European Union. J R Soc Med 2012; 105 1(Suppl 1): 22-8. doi: 10.1258/jrsm.2012.120036. PMID: 22508970; PMCID: PMC3326593.
14. Maak, Travis & Wylie, James: Medical Device Regulation: A Comparison of the United States and the European Union. Journal of the American Academy of Orthopaedic Surgeons 2016; 24: 1. 10.5435/JAAOS-D-15-00403.
15. Lahiry S, Sinha R and Chatterjee S: Medical device regulation in India: What dermatologists need to know. Indian J Dermatol Venereol Leprol 2019; 85: 133-7.
16. Analysis of Medical Devices Rules, 2017. Available at: https://www.nishithdesai.com/fileadmin/user_upload/pdfs/NDA%20Hotline/Analysis_of_Medical_Devices_Rules-2017.pdf
17. Manu M and Anand G: A review of medical device regulations in India, comparison with European Union and way-ahead. Perspectives in Clinical Research 2021; 0(0): 0

18. GNK G, B N and T. Vidhya L: Medical device regulation in US, Europe, china and India. International Journal of Drug Regulatory Affairs 2017; 5(2): 17–25.
19. S NS, K VR and Nl P: A comparative study of medical devices and their regulations in US, EU, India, and China. Asian Journal of Pharmaceutical and Clinical Research [Internet] 2023 Mar 7 [cited 2023 Apr 14]; 6–14. Available from: https://innovareacademics.in/journals/index.php/ajpcr/article/view/46624
20. Nitika Agrahari, Goli D and Shantha Kumar GS: 32nd International Conference on Healthcare, Biomedical, Statistics and Public Health. Journal of Biomedical Engineering and Medical Devices [Internet] 2022 Aug 5 [cited 2023 Apr 14]; 7(8):1–5. Available from: https://www.longdom.org/open-access/comparative-regulatory-insight-for-medical-device-in-india-and-eu-93736.html

How to cite this article:
Suganthi N, Suresh K and Anbarasan B: Current regulatory requirements for medical devices in US, EU, and India. Int J Pharm Sci & Res 2023; 14(10): 4733-40. doi: 10.13040/IJPSR.0975-8232.14(10).4733-40.

All © 2023 are reserved by International Journal of Pharmaceutical Sciences and Research. This Journal licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported License.

This article can be downloaded to **Android OS** based mobile. Scan QR Code using Code/Bar Scanner from your mobile. (Scanners are available on Google Playstore)