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Evolution of Medical Device Sector in India and Comparison of Registration Processes of Medical Devices in India with Countries like China, Australia, U.S. and Europe

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Abstract

The medical device market in India is a sunrise sector in the pharmaceutical industry and has achieved a milestone in the last few years securing 4th position in the medical device market in Asia with increasing foreign direct investments through governments Make in India Campaign 2017, and PLI (Product linked incentive) schemes. To enter the medical device market in any country, one has to go through different procedures and regulatory requirements of that country. Medical devices are regulated in India by the DCGI (Drug Controller General of India) under the CDSCO (Central Drug Standard Control Organization). In China, the registration approval process is under NMPA (National Medical Product Administration) and requires complying with Chinese regulatory standard notice No. 218. Europe and Australian regulations are bit same and require a CE (Conformité Européenne) mark for manufacturing and marketing. U.S. regulations for approving medical devices are stringent and 510 (k) and PMA (pre-market authorization) is compulsory. In this review, the reader would get an idea about the evolution of medical devices and legislative changes in India and also about international standards and auditing programs. There is a comparison of Indian, Chinese, Australian, U.S., and European medical device registration processes for understanding the similarities and differences.

Keywords: Medical devices; Legislative changes; Registration process; Government initiatives; ISO; IEC

Abbreviations: PLI: Product Linked Incentive; DCGI: Drug Controller General of India; CDSCO: Central Drug Standard Control Organization; NMPA: National Medical Product Administration; FDI: Foreign Direct Investment; MOHFW: Ministry of Health and Family Welfare; CDSCO: Central Drugs Standard Control Organization; PLI: Product Linked Incentive; PPO: Public Procurement Order; QCI: Quality Council of India; ICMED: Indian Certification of Medical Devices; CFC: Common Facility Center; AMTZ: Andhra Pradesh Medtech Zone; DST: Department of Science and Technology; GOI: Government of India; KSIDC: Kerala State Industrial Development Corporation; CDA: Central

Drug Authority; ISO: International Standard Organization; IEC: International Electro-Technical Committee; MDSAP: Medical Device Single Audit Program. FDA: Food and Drug Administration; WHO: World Health Organization; IVD's: In Vitro Diagnostics; CAGR: Compound Annual Growth Rate; ARTG: Australian Register of Therapeutic Goods; QMS: Quality Management System; QSR: Quality System Regulation; NB: Notified Body.

Introduction

Medical devices [1]

Medical devices as defined in sub-clause (iv) of clause (b) of section 3 of Drugs and Cosmetics Act, 1940 (23 of 1940) includes all devices like instruments, apparatus, appliances, implants, material, or articles used alone or in combination, including software or an accessory, intended by its manufacturer to be used especially for human beings or animals which does not achieve the primary intended action in or on human body or animals by any pharmacological or immunological or metabolic means, but which may assist in its intended function by such means for one or more of the specific purposes of:

- Diagnosis, prevention, monitoring, treatment, or alleviation of any disease or disorder;
- Diagnosis, monitoring, treatment, alleviation, or assistance for, any injury or disability;
- The investigation, replacement or modification, or support of the anatomy or of a physiological process;
- Supporting or sustaining life;
- Disinfection of medical devices; and control of conception.

The medical devices industry in India mostly depends on imports. Economically well-developed countries are the forerunner in the production of highly sophisticated and technologically driven medical devices. Reduction in imports of medical devices can be achieved by innovation in production in home grown industries. The global market for medical devices has grown to $456.8 billion in 2020 over US$ 228 billion in 2015. The United States of America has a major global market share of 45% of medical devices followed by a European market (30%) and Japan with a 10% market share. India's medical device manufacturing sector which is one of the top 20 markets in the world is still a minor in comparison to the rest of the globe and ranks fourth in Asia [2].

Indian Medical Devices Market Size

In September 2014 to make India a manufacturing hub the GOI started the "Make in India" campaign. The Indian medical device market stood at 77,539 crores (US$11 billion) in 2020 which is estimated to grow at a CAGR of 35.4 percent, reaching Rs. 352,450 crores (US$ 50 billion) by 2025 [3]. The GOI has taken various initiatives and campaigns to expand the medical devices sector, emphasizing research and development (R&D) and establishing FDI (Foreign Direct Investment) to uplift the pharma industry's position in the global market by understanding of the country's needs. FDI in medical devices and surgical appliances totalled US$ 2.18 billion from April 2000 to December 2020 [4].

Export in Medical Device

Medical devices in India depend on 75-80% imports from the countries such as the US, China, Germany, being exported at Rs. 14,802 crores (US$2.1billion) in 2019 and it is anticipated that it would increase at a CAGR of 29.7% to reach 70,490 crores (US$10 billion) in 2025. The Indian Ministry of Health and Family Welfare (MOHFW) and the Central Drugs Standard Control Organization (CDSCO) have begun to take the following steps: re-examination and implementation of Schedule MIII (a draft guidance on GMPs and facility requirements) and a system for labelling, clinical evaluation, and adverse reporting clarification, state licensing authority to extend free sales certificates from 2 to 5 years to allow export, and for easy access by regulatory authorities to create a list of manufacturers with exports to increase export of medical devices in-country. Medical devices will be featured in Virtual Export 2021, which will allow direct connection between Indian suppliers and buyers/importers from participating countries. Over 300 foreign buyers from the healthcare sector are anticipated to attend this event [4].

Government Initiatives in the Medical Device Sector

The Government of India has analysed the medical device industry as an important and bright sector under the "Make in India" campaign 2014 and has taken following initiatives to reduce imports regarding medical devices (Table 1).

- A PLI (Product Linked Incentive) scheme for the domestic production of medical devices has been initiated by the department of pharmaceuticals to boost indigenous manufacturing and attract investments in India., The funds valued for the period FY21-FY28 is around Rs.3420 crores (US$468.78 million).

Medical devices that are eligible for the PLI scheme include the following:

Sr. No.	Description of Medical devices
1	Cancer care/Radiotherapy medical devices
2	Radiology & imaging medical devices (both ionizing & nonionizing radiation products) and Nuclear Imaging Devices
3	Anesthetics & Cardio-Respiratory medical devices including Catheters of Cardio-Respiratory Category & Renal Care Medical Devices
4	All Implants including implantable electronic devices like Cochlear Implants and Pacemakers

Table 1: Medical Devices under PLI scheme [5].

- In January 2020, the government established a National Medical Equipment Promotion Council to promote local manufacturing of high-end medical devices and enhance investment in the sector.
- On March 25, 2021, the Department of Pharmaceuticals issued a revised notice on the Public Procurement Order (PPO). The new PPO guidelines contain 19 medical devices that are intended to promote indigenous medical device manufacture and cut import bills by roughly Rs. 4,000 crores (US$538.62 million).
- In April 2021, the government eased the standards for clearance of medical devices like as nebulizers, oxygen concentrators, and oxygen canisters under the Legal Metrology Act (Packing Rules 2011), making it easier to import these items.
- The Quality Council of India (QCI) and the Association of Indian Manufacturers of Medical Devices (AiMeD) introduced the Indian Certification of Medical Devices (ICMED) 13485 Plus system in June 2021 to verify the quality, safety, and efficacy of medical devices [4].

In support of the "Make in India" initiative, the Indian government has sanctioned the establishment of four medical device parks situated in Andhra Pradesh, Telangana, Tamil Nadu, and Kerala to deliver quality products at a reasonable price for treatment and diagnostics. Such parks are required to provide the essential infrastructure for businesses to function properly. Establishing a medical device park not only will saves import costs, but will also provide convenient access to standard testing facilities [6].

Medical Devices Park

Andhra Pradesh Medtech Zone's project to establish a Common Facility Center (CFC) for superconducting Magnetic Coil Testing and Research was approved. The program is expected to give Rs. 25 crore, or 70% of the cost of establishing CFCs. Despite the fact that India is a net importer of medical equipment, the indigenous industries accounts for only 2% of the worldwide market, which is valued at USD 250 billion [7]. Think 3D printing solutions is collaborating with Andhra Pradesh Medtech Zone (AMTZ) to provide a 3D printing facility with an investment of Rs. $ 6 million. The plant will serve over 400 businesses while also producing X-ray machines. This alliance intends to cut production costs by up to Rs. 40 and reduce the country's reliance on imports by Rs. 78 [8].

In the coming two years, India will have its first medical equipment and device manufacturing park in Northern India. This park will be developed on YEIDA 28 sector area by Yamuna Expressway Authority. YEIDA will bring out a scheme for the project which is estimated to go around Rs. 5000 crores out of which 100 crores will be given by the Central Government. In this plant, domestic and foreign companies will manufacture medical devices such as CT scans, X-ray machines, blood pressure monitors, pulse oximeters, and ventilators and the production will start by 2023 [9].

In collaboration with the Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), an autonomous institute of the Department of Science and Technology (DST), Government of India (GOI), and the Kerala State Industrial Development Corporation Ltd, a medical device park will be established in Kerala (KSIDC). Unlike other medical device sectors, this one will place a greater emphasis on medical implants and extracorporeal devices, where SCTIMST will be able to contribute more with its expertise. Establishing these types of industries might help in growing medium-sized medical devices industry [10].

Telangana state recognized that establishing the medical device park would be a sunrise sector for the economic development of the state which is spread over a 302-acre area in Hyderabad in 2017. The medical device park got a huge response and 32 companies approached for setting up their manufacturing plants.

International Standardization Organizations and Certification Bodies

Medical devices and IVD's in India are regulated by Drug Controller General of India (DCGI) which is part of the Ministry of Health and Family Welfare's Central Drug Standard Control Organization. Most medical devices in

India are notified, which means they need to be approved by the CDSCO or CDA (Central Drug Authority) before they can be sold.

To ensure their quality, safety, and market credibility as ISO (International Standard Organization) and IEC (International Electro-Technical Committee) provides worldwide standards for the manufacture of medical equipment. These are internationally recognized standardizations and hence give increased customer trust, retention, and acquisition. Because ISO and IEC do not issue certificates for the quality and safety of medical devices, these functions are done by external certification authorities, and hence organizations and enterprises cannot be certified ISO. The ISO Committee on Conformity Assessment (CASCO) has issued certification process standards that are utilized by certifying bodies [11].

The Indian Government has approved third-party conformity assessments for medical devices which include 8 private organizations that assess medical device manufacturers based on ISO13485 quality management system standard and submit the results to the regulatory authority (CDSCO or CDA) to decide on granting manufacturing licenses. This applies to medical device class IIa, IIb, and III [12].

The ISO was founded in 1947 and the standards for medical devices were introduced in year 1996.The ISO standards for medical devices along with published dates are listed in Table 2.

Sr. No.	ISO standards	Purpose	Published date
1	ISO 15223-2:2010	Specifies a process for developing, selecting, and validating symbols for inclusion in ISO 15223-1	2010-01
2	ISO13485:2016	Specifies the requirements for a quality management system (QMS), in which an organization must demonstrate its capacity to consistently supply medical device-related services that fulfil customer and regulatory requirements.	2016-03
3	ISO16142-1:2016	Essential principles of safety and performance of medical devices in addition to these specific essential principles for all non-IVDs and guidance on selection standards.	2016-03
4	ISO/TR 80002-2:2017	Applies to any software used in device design, testing, component acceptance, manufacturing, labelling, packaging, distribution, and complaint handling or to automate any other aspect of a medical device.	2017-06
5	ISO16142-2:2017	This document identifies and describes the six general essential principles of safety and performance. All medical devices, including IVD medical devices, are subject to these regulations. (In-vitro diagnostic).	2017-08
6	ISO14971:2019	Specifies terminology, principle, and a process for risk management of medical devices, including software as medical devices and in IVD's.	2019-12
7	ISO/TR 24971:2020	guides the development, implementation, and maintenance of a risk management system for medical devices according to ISO 14971:2019	2020-06
8	ISO/TR 20416:2020	guides the post-market surveillance process and is intended for use by medical device manufacturers	2020-07
9	ISO 20417:2021	specifies the requirements for information supplied by the manufacturer for a medical device or by the manufacturer for an accessory	2021-04
10	ISO15223-1:2021	this document applies to symbols used in a broad spectrum of medical devices, that are available globally and need to meet different regulatory requirements supplied by manufacturers	2021-07

Table 2: ISO standards.

The additions and editions which were carried out in ISO standards are given below:

- ISO15223-2:2010 is the first edition of ISO 1523-2 together with ISO 15223-1:2017 cancels and replaces ISO15223:2000. This edition helps in minimizing the misinterpretations of symbols that were previously accepted in ISO15223-1.
- ISO13485:2003 is cancelled and replaced by

ISO13485:2016 which was technically revised. A lot of inclusions have been made to this revised standard, and those are alerting the organization about their obligations related to regulatory requirements which are focused on quality management systems. Refines some existing definitions, relationships with ISO 9001 (Table 3).

- ISO16142:2006 was cancelled and replaced by the first edition which is ISO16142-1:2016 with the following changes; the essential principles were harmonized with the Global Harmonization Task Force, and the US, EU jurisdiction, thorough mapping of published reference standards, etc.
- ISO/TR 80002-2:2017 is the document that explains and applies the ISO 13485:2016 requirement for software validation to stakeholders, manufacturers, auditors, and regulators. This document is for software that is used to monitor and measure requirements. This document does not cover software that is utilized as a component, part, or accessory of a medical device, or software that is a medical device in and of it.
- ISO16142-2:2017 is built on ISO16142-1 this is the first edition of ISO16142-1 which cancels and replaces ISO/TR16142:2006 which has been revised and the following changes were made: the standard was developed in two parts, one for non-IVD medical devices and one for IVD medical devices, a thorough mapping to published reference standards has been included.
- ISO14971:2007 is cancelled and replaced by ISO14971:2019 which is the third and technically revised edition. The changes made in this edition are; more attention is given to the benefits of medical devices, clarification of the requirement for production and post-production activities, and also restructured.
- ISO/TR24971:2013 was cancelled and replaced by ISO/TR24971:2020 which is the second edition. The changes made were the clause of ISO/TR24971:2013 and annexes of ISO14971:2007 are combined, shuffled, revised, and incorporated additional guidance. Annexes hold guidance on specific aspects of risk management.
- ISO/TR20416:2020 is meant for medical device manufacturers to utilize to aid the post-market surveillance process. However, this paper does not provide guidance on the regulatory authority's market surveillance efforts, and it does not replace or modify existing regulatory requirements for post-market monitoring.
- ISO20417:2021 defines the information that must be provided by the manufacturer for medical devices or by the manufacturer for accessories. However, this document provides no guidance on how to provide the information.
- ISO15223-1:2021 is the fourth edition that cancels and replaces the third edition ISO15223-1:2016 and inclusions made are the addition of 20 symbols validates as per ISO15223-2, deletion of defined term labelling, the addition of 5 symbols which are previously published in ISO7000, ISO7001, and IEC60417.
- International Electro technical Commission gives standards for electrical, electronic, and related technologies to maintain quality, safety and efficacy. The standards which are given by IEC for the medical devices are as follows:

Sr. No.	IEC standard	Purpose	Published date
1	IEC 62304:2006	Specifies software for medical devices must meet certain life cycle standards. Processes, activities, and tasks that make up a system	2006-05
2	IEC/TR80002-1:2009	Application of risk management to medical devices to medical device software concerning IEC 62304:2006, Medical device software - Software life cycle processes	2009-09
3	IEC/TR80002-3:2014	Outlines the software development life cycle for medical devices. The software life cycle processes for medical devices are based on IEC 62304:2006.	2014-06
4	IEC 62366-1:2015	Specifies a process for a manufacturer to analyze, specify, develop and evaluate the usability of a medical device	2015-02
5	IEC62366-1:2015/AMD 1:2020	This amendment is about the software life cycle process which will be replaced by IEC/DIS 62304.3 which is under development	2015-06
6	IEC/TR62366-2:2016	Guidance on implementing usability engineering and as defined in IEC 62366-1:2015 and supporting goals other than safety	2016-04

Table 3: IEC standards for medical devices.

IEC standards are frequently updated to overcome shortcomings and to include newer additions.

- IEC62304:2006 is a set of procedures, activities, and tasks that provide a common foundation for the software life cycle process for medical devices. When the software is a medical device, when it is implanted, or when it is a critical component of the medical device, this standard applies. It also applies to the development and maintenance of medical device software.
- ISO/TR80002-1:2009 is a guidance document on the application of risk management included in ISO14971:2007 which was replaced by ISO14971:2019 and how to full fill requirements of risk management mentioned in ISO14971.
- ISO/TR8000-3:2014 is having a foundation of; IEC6304:2006 which gives medical device software life cycle process with equivalent safety classes which have been aligned with software life cycle development processes of ISO/IEC 12207:2008 and are given in the document in compliance with ISO/IEC 4772:2010.
- IEC 62366-1:2015: This first edition of IEC 62366, together with the first edition of IEC 62366-2, cancels and replaces the first edition of IEC 62366 published in 2007.
- IEC62366-1:2015/AMD 1:2020amendment is about the software life cycle process which will be replaced by IEC/DIS 62304.3 which is under development.
- IEC/TR62366-2:2016 holds background information and guides certain areas that can be useful for individuals implementing Usability Engineering (Human Factors Engineering) as a supporting aim other than safety as indicated in IEC62366-1:2015. This report should not be used to make regulatory decisions. It just gives suggestions and information rather than defining obligations [11,13].

Global Auditing Program for Medical devices

MDSAP Program

To monitor manufacturing of medical devices there is a global auditing program named Medical Device Single Audit Program (MDSAP). The inaugural meeting was conducted in Singapore in 2012 and the members participating in this MDSAP program are Australia (TGA), Brazil (ANVISA), Canada's Health Canada, Japan's Ministry of Health, Labor and Welfare, and the Japanese Pharmaceutical and Medical Devices Agency, and the United States Food and Drug Administration (FDA). This program is initiated keeping the objective of developing and managing a single audit program to satisfy the needs of multiple regulatory requirements [14]. While MDSAP's observers are EU (European Union), UK (Medicines and Healthcare Products Regulatory Agency), World Health Organization (WHO) Prequalification of In Vitro Diagnostics (IVD's) Program. MDSAP pilot program was conducted between 1st January 2014 to 31st December 2016. On 29th June 2017, a report was generated which the summary of outcomes was obtained from the three years of MDSAP pilot reports. And based on the evaluation of these reports the international governing body of MDSAP has demonstrated that the MDSAP program is executable [15].

By conducting an MDSAP audits there would be a decrease in audits and inspections for the manufacturer. MDSAP is an efficient program that saves time in auditing, and even reduces cost, minimizes business disruptions. Accelerates the approval process where traditional regulatory jurisdictions may take time [16].

Global Market for Medical Services

Medical devices market size: Since 2015, compound annual growth rate (CAGR) for global medical devices was 3.5 percent which has grown to reach $456.8 billion in 2020. The market fell by 3.2 percent in 2019, from $456.9 billion to $442.5 billion in 2020. The global lockdown imposed by governments interrupted the supply chain, causing the medical equipment market to collapse. The growth rate rebounded to 6.1 percent CAGR from 2021 to reach $603.5 billion in 2023 as market for ventilators and other medical devices/equipment was increased.

Medical device market segmentation: The medical devices market is divided into four categories: device type, expenditure type, end-user, and geography. We will focus on classification by geography [17].

- Asia Pacific: China, India, Japan, Australia, Indonesia, South Korea
- North America: USA
- South Africa: Brazil
- Western Europe: France, Germany, UK
- Eastern Europe: Russia
- Middle East
- Africa

In the Asia Pacific region, there are six countries and for registering medical devices from one country to the other it is required to go through the regulatory procedures and reports. The regulatory procedures for registering medical devices in India, China, Australia, U.S., and Europe are given below. And registration process of these five countries is compared [18].

- **The Registration Process for Medical Devices of India, China, Australia, U.S., Europe**

Steps for registration of medical devices in India

Step 1: To ensure notified Medical devices, see the Drugs and Cosmetics Rules, the Medical Device Rules 2017, and the Gazette Notifications. In some cases, DCGI will give NOC to

medical devices without following the registration process after reviewing product information. (4-12 weeks).

Step2: On behalf of interested importer company appoint an India-approved agent to contact with CDSCO with a valid wholesale license (Forms 20B and 21B/21C).

Step3: In-country performance testing from NIB/an accredited lab is required for Class B, C, and D IVDs. Performance testing of Class D IVDs from NIB.

Class B and C -Accredited Indian lab for performance testing under (Form 40) costs between $1000 and $1500 in the United States (6-9 months).

Step4: Compiling a device application form (Form MD-14), attaching manufacturer information, an ISO13485 certificate, IFU (Instructions for Use), testing findings, proof of approval in the United States, the European Union, Australia, Canada, or Japan, and proof of approval in the home nation (Certificate of Free Sales, Certificate of Foreign Government).

Step 5: Fill up an application for registration/Import License with the CDSCO, pay the costs, and make sure all of the documentation are in English. Registration certificate form 41 and import license.

Step 6: CDSCO reviews application, requires approx. 25% formal technical presentation, new devices goes through Subject Expert Committee (SEC).

Step 7: An import license is issued by CDSCO in the form MD-15., followed by implementing Medical devices rule 2017.Registration and import licensing process for medical devices are combined in India.

Step 8: Only Indian authorized agents are allowed to import products once they have been licensed [19-21].

- **Steps for Registration of Medical Devices in China**

Step 1: Determine the medical device classification according to the NMPA's medical device classification (National Medicinal Product Administration). If the medical device is not manufactured in China, the registered company is needed to submit a sample of medical devices from classes II and III. If clinical data is required, it must be provided when registering the application. Simplified Chinese translations of packaging and labelling are required.

Step 2: Appoint a Chinese agent to effectively communicate with the NMPA [22].

Step 3: Show the proof of home country approval with the following certificates: 1) (CFS), 2) (CFG).

Step 4: The registered firm is required to submit documentation demonstrating that the item has been approved in the parent country (for example, a CE Mark, 510(k) letter, ISO 13485 certification, or an approved Premarket Approval Application).

Step 5: Prepare product technical requirements, complying with the standards according to the national, international, industrial. In product technical requirements the main data is about performance, safety, and inspection methods of the finished product i.e. sample of a medical device. For class, I devise foreign test reports are accepted but in the case of class II and III devices it is compulsory to give a sample of a medical device to NMPA for testing and it requires reports to be submitted by foreign and local testing agencies.

Step 6: Prepare technical documents for class I submission and send to NMPA. There are no submission costs for class I devices. The only stipulation is that all of the paperwork be written in simplified Chinese.

For class II and III devices: Prepare a report that contains testing findings, an agent authorisation letter, a CFS/CFG diagnosis, a clinical evaluation, and other technical papers for submission to the NMPA. Submission fees must be paid, and all paperwork must be completed in simplified Chinese.

Step 7: Administrative approval will be required for Class I devices.

Class II and III devices will be subjected to a thorough examination, which will encompass both technical and administrative aspects. An expert panel meeting may also be required for novel and high-risk goods. For the foreign producer, the NMPA has the option of performing an on-site QMS audit.

Step 8: Class I: In the case of class I medical devices the NMPA issues a certificate of record filing and posts it on its website. Record Filing Certificate does not have an expiry date. The registrar has now been granted permission to sell the device in China.

Class II: The NMPA issues registration certificates and posts them online after a thorough inspection. This is valid for a period of five years. And there is a condition to put details such as NMPA license number, and IFU (Instruction for Use) on the device label. Now the registrar is approved to sell the device in china [23,24].

- **Steps for Registration of Medical Devices in Australia**

To put medical device in Australian market a device must be registered with the Australian Therapeutic Goods

Register (ARTG), which is regulated by the TGA (Therapeutic Goods Administration).

Step 1: Categorize the devices by referring to schedule 2 of Australian Therapeutic Good (Medical Devices) Regulations.

Step 2: If the registering medical device company is not having a local sponsor, then the sponsor should be appointed. The designation of the sponsor is impactful in expediting medical device registration process that is liaison between the manufacturer and TGA. And it is compulsory that sponsor's name must appear on the medical devices and labelling.

Step 3: Prepare the documents listed below for submission:
1) A design dossier or a technical file.
2) Declaration of Conformity from Australia.

Step 4: The sponsors should submit proof from manufacturers (e.g., a marking certificate) to the TGA Business Services (TBS) system for the purpose of evaluation of acceptance with exception of class I (Non-sterile, non-measuring).

Step 5: Intended Purpose Statement, classification, and Global Medical Device Nomenclature (GMDN) code is to be submitted when filing the medical device application in TBS system by the sponsor. There is a charge associated with applying.

Step 6: Design dossier is examined by TGA the as part of the level 2 application audit. All class III devices, with the exception of minimum percentage of Class IIb devices, require a level 2 application audit.

Step 7: At this point, the TGA will either approve or disapprove the application. If the TGA approves an application, an Australian Register of Therapeutic Goods (ARTG) listing number (ARTG Certificate of Inclusion) will be issued, and the listing will be posted to the ARTG database and the TGA website.

Step 8: The medical equipment can now be sold in Australia by the manufacturer. If we do not make any changes to the equipment that would render the ARTG listing invalid, the registration will not expire; however, annual ARTG listing costs must be paid [25-29].

U.S. Medical Device Registration Process

Step 1: Determine the class of medical devices or in vitro diagnostics (IVDs) using the FDA classification database, or identify a predicate device that is designed for the same use and uses the same technology. The recognized predicate devices with a three-letter product code and a seven-digit regulation number should be given special attention. If the classification cannot be identified, the 513(g) method can be used to obtain FDA classification.

Step 2: Most QSR regulations excludes some Class I devices with few exception, with a few exceptions. For Class I and Class II devices the implementation of a Quality Management System (QMS) that complies with Quality System Regulation (QSR) 21 CER Part 820 is required.

Step 3: Clinical trials are necessary for innovative Class II and Class III medical devices. Pre-Submission meeting request is advised before submitting the 510(k) or premarket application PMA review process.

Step 4: If clinical trials are required, an application for an Investigational Device Exemption (IDE) study must be submitted. Develop a clinical study protocol and carry out the clinical trial. Non-significant risk studies require IRB approval.

Step 5: For class II devices, a 510(k) Premarket Notification application is necessary. A Premarket Approval (PMA) application is needed for class III devices. Fees for respective applications are to be submitted.

Step 6: The FDA conducts facility inspections for Class III devices that include not just the manufacturing site but also all main supplies used in the device's design and production.

Step 7: The FDA issues a clearance letter and publishes it on the internet if the application is approved; Class II- 510(k) and Class III-PMA approval letter.

Step 8: At this step applicator must be in complete accordance with Quality System Requirements, for classes I and II the site inspections are not done before the device registration, but even after registration FDA can conduct inspections if not found compliant with the QSR then can issue Form 483.

Step 9: Appoint FDA US agent as a representative to contact with FDA on local level.

Step 10: FURLS system is used for listing of device and registration which is available on the FDA website, the charge for establishment registration and listing must be paid, and renovations must be completed every year.

Step 11: Now the applicator can sell the device in the U.S. On the FDA website, the status of the firm and the device registration will be listed. The authority is indefinite unless and until the design has been altered, and its intended application, etc. [30-32].

Europe Medical Device Registration Process

Step 1: Determine whether Regulation (EU) 2017/745-Medical Device Directive (MDD) or Implantable Medical Device Directive (AIMDD) applies.

Step 2: Use Annex IX of the Medical Device Directive (MDD) to define medical devices: The different types of instruments are Class I (non-sterile, non-measuring), Class I (sterile, measuring), Class IIa, Class IIb, or Class III/AIMD. There are similar regulatory requirements for Class III and Active Implantable Medical Devices.

Step 3: With the exception of class I (non-sterile, non-measuring) all medical device classes, can meet the Quality Management System (QMS) criteria by following Annex II or V of the MDD. Implementing a QMS for Class I (non-sterile, non-measuring) has no formal requirements. However, although the PMS procedure is needed, it is not audited by a Notified Body (NB).). To attain QMS requirements most of the companies apply ISO 13485 standards.

Step 4: Technical file is required which will give thorough information about the medical device and showing compliance with 93/42/EEC for Classes I through IIb. The devices which require clinical data should be submitted. Class III/AIMD devices will require a Design Dossier. For Class IIb and III implants, clinical study reports are needed, however existing clinical data may be justifiable. For clinical trials in Europe pre-approval by European Competent Authority is mandatory.

Step 5: Designate a European Authorized Representative (EC Rep) who is prepared to deal regulatory issues on the outer package or device label, as well as on the instruction for use, an EC REP's name and address must be mentioned.

Step 6: There is auditing by the Notified Body, of Quality Management System, Technical File, or Design Dossiers except for Class I medical devices (non-sterile, non-measuring).

Step 7: For all medical devices with exception for Class I (non-sterile, non-measuring), the CE marking certification and ISO13485 certificate will be provided after a successful audit by the Notified Body. The ISO 13485 certificate, on the other hand, must be renewed every year, while CE marking certificates are normally good for three years.

Step 8: A legal document should be prepared by the registrar affirming compliance with applicable directives which is named as Declaration of Conformity. Now the manufacturing company can affix the CE marking.

Step 9: For Class, I devise registration with competent Authority is mandatory where the registrar or registrar EC REP is based. Because there is a requirement for an additional registration of Class II a, IIb, III devices in some of the EU member states if the registrar is willing to place the device in their markets.

Step 10: Except for Class I, all other classes there is a yearly audit by the Notified bodies for verification of compliance with Regulation (EU) 2017/745. If the manufacturing company fails to comply there will be a cancelation of the CE Marking Certificate (Table 4).

Annual auditing by NB is not required for Class I (non-sterile, non-measuring). Hence carrying out CER and PMS activities are mandatory for all classes of the medical device [30,33-35].

Sr No.	Point of Comparison	India	Australia	China	U.S.	Europe
1	Regulatory authority	DCGI under CDSCO	Therapeutic Good Administration (TGA)	National Medical Product Administration (NMPA)	Federal Food Drug and Cosmetic Act (FD&C Act)	EMA & RA of Member State
2	Regulation	Medical Device Rules, 2017	Australian Therapeutic Goods(Medical devices) regulation 2002	Regulation on supervision and Administration of Medical Devices	FDA QSR (21CFR820)	Regulation (EU) 2017/745

3	Classes of Medical devices	Four	Three	Three	Three	Three
		Class A	Class I, Is, Im	Class I	Class I	Class I
		Class B	Class II-IIa, IIIb	Class II	Class II	Class II a
		Class C	Class III, AIMD	Class III	Class III	Class II b
		Class D				Class III
4	QMS Requirement	ISO13485:2016	ISO13485:2016	ISO13485:2016(Identical to Chinese GMP requirement (Notice No.218)	QSR 21CFR Part 820 (Similar to ISO13485:2016 but not same)	ISO 13485 or as per applicable in 94/42/EEC
5	Assessment of technical data	Notified bodies (NB) Under CDSCO	Conformity Assessment Body (CAB)	NMPA	USFDA	Notified bodies (NB) Under National Regulatory Authority
6	Submission format	Paper / Electronic	Electronic submission	Electronic submission	Electronic/ Paper submission	Electronic/Paper submission
7	Language	English	English	Simplified Chinese	English	English
8	Clinical test reports	Mandatory for class C and D devices	Mandatory for class II and III devices	Mandatory for class II and III devices	Innovative class II and Class III devices may require	For Class IIb and III medical devices
9	In-country Clinical test	Not strictly required	Not strictly required (Required for HIV testing devices)	not strictly required	Required and approved by IRB (institutional review board)	Must be approved by European Competent Authority
10	Registration expiry	Three years	Five years	Five years	Unless and until no change in medical device	CE mark validity indefinite for Class I 3 Years for Class IIa IIb.
11	Time required for approval	6-12 months for the notified device	Class I-Approx.24 Hrs. Class IIa, IIb-3 months Class III-5 months	Class II-60 Days Class III-90 Days	ClassI-510k exempt 1 month Class II-6to9 months Class III-PMA 18to30months	Class I (1) Class II (3-6) Class III(9-15)
12	On-site audits	Applicable (Notified Bodies)	Applicable	Applicable	Random unannounced audits	Applicable (Notified Bodies)

Table 4: A comparative study of medical devices registration regulations applicable for India, Australia, China, U.S., Europe.

Before 2017 medical devices were treated as drugs and there were no separate rules and regulations for medical devices (Table 5). The medical device rule was passed on 31st Jan 2017 and commenced from 1st Jan 2018. But before the rule came medical devices were still imported in India hence amendments were passed for medical devices. The overall legislative changes in the medical devices sector are listed in the table below [1].

Sr. No.	Year	Amendments
1	**17th March 1989** G.S.R. 365(E)- In pursuance of sub-clause (iv) of clause (b) of Section 3 of the Drugs and Cosmetics Act, 1940,	Disposal hypodermic needle, disposable hypodermic syringe, disposable perfusion rate notified as drugs with immediate effect
2	the Drugs and Cosmetics Act, 1940 (23 of 1940) sections 12 and 33 of Rule 76 **22nd Feb 1994**	after the words Schedule M the words "and Schedule M-IT1 in respect of Medical devices" s
3	In pursuance of Drugs and Cosmetics Act, 1940clause (b) of section 3 of the, sub-clause (iv) (23 of 1940)**6th Oct 2005**	10 devices notified as drugs with immediate effect
4	Drugs and Cosmetics Act, 1940 Section 3, Clause (b). Sub-clause (iv) **April 20, 2010**	22 medical devices considered as drugs
5	**4th March 2016**	In order to facilitate the implementation of e-Government, the CDSCO has created SUGAM, an online site for applying for the import and registration of medical devices and diagnostics.
6	**29th June 2016**	Quality management system –for notified medical devices and in-vitro diagnostics [1]
7	**31st Jan 2017**	Medical Devices Rules, 2017 vide G.S.R. 78 (E) which commenced from 1st Jan 2018
8	1st June 2018 S.O. 2237(E).— In pursuance of the powers conferred by sub-rule (2) of rule 19 of the Medical Devices Rules, 2017,	for the purpose of testing and evaluating medical devices, as the Central Medical Device Testing Laboratory, for the purpose of (a) testing and evaluation; (b) operating as an appellate laboratory; and (c) carrying out any other role that the Central Government may particularly assign to it.
9	**1st August 2018** amendment for the performance evaluation report of in-vitro medical devices	The applicant must submit a performance evaluation report from the manufacturer in the case of in-vitro diagnostic medical equipment.
10	**4th Feb 2019** Drugs and Cosmetics Act, 1940 of sub-section (1) of section 12 and sub-section (1) of section 33 of (23 of 1940)	Provided further that the testing laboratories of State Government and Central Government shall be exempted from the requirement of accreditation by the National Accreditation Board for Testing and Calibration Laboratories for two years from the date of commencement of this amendment.
11	**8th Feb 2019** S.O. 775(E).—In pursuance of sub-clause (iv) of clause (b) of section 3 of the Drugs and Cosmetics Act, 1940 (23 of 1940)	(ii) CT scanners; (iii) MRI scanners; (iv) defibrillators; (v) dialysis machines; (vi) PET scanners; (vii) X-ray machines; and (viii) bone marrow cell separators specified by Government of India.
12	**18th March 2019** sub-section (1) of section 12 and sub-section (1) of section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940)	Environmental requirements for medical devices such as condoms and surgical dressing.
13	**18th April 2019***	To specify the licensing authority for four classes Class A, B,C,D Central Licensing Authority for Class C and Class D medical devices and State Licensing Authority for Class A and Class B medical devices" shall be inserted.
14	**31st July 2019**	List of notified bodies registered with CDSCO

15	**13th Sept 2019***	Medical device the fourth amendment rules 2019, Inform MD-10 which is related loan license to manufacture Class c devices (for sale or distribution) (Moderate High-Risk Devices) or Class D (High-Risk Devices) medical device for the words "state licensing authority" the words: Central Licensing authority" has been substituted.
16	S.O. 3721(E).—In pursuance of clause (b) of section 3 of the Drugs and Cosmetics Act, 1940, sub-clause (iv) (23 of 1940),**16th October 2019**	Ultrasound equipment was notified by Government.
17	The Drugs and Cosmetics Act of 1940 (23 of 1940) contains sections 12 and 33 **18th Oct. 2019**	Registration of manufacturing &importer of 36 medical devices.
18	**18-Dec-19**	The Niti Aayog organized a stakeholder meeting on its draft Medical Devices Bill, 2019, where it proposed creating the Medical Devices Administration, to work parallel to the CDSCO, under the Directorate General of Health Services ('DGHS') [36]
19	In accordance with clause (b) of section 3 of the Drugs and Cosmetics Act, 1940, sub-paragraph (iv) of clause (b) of section 3 (23 of 1940)**11th Feb 2020**	Complete definition for devices that should be considered as medical devices.
20	28th May 2020	Domestic medical device manufacturing is eligible for a product-linked incentive program.
20	As per S.O.4671 [E]**28th DEC 2020**	Notified devices Nebulizers, Blood pressure Monitoring Devices, Digital Thermometer, Glucometer
21	The 1940 Drugs and Cosmetics Act (23 of 1940) contains sections 12 subsection (1) and section 33 subsection (1)**5th Feb 2021**	A new Ministry notification would amend India's Medical Device Rules, 2017 to allow medical device market applicants to use ASTM methods to demonstrate conformance; current regulations in India recognize ISO and IEC international medical device standards only.

Table 5: Legislative changes in the medical device Sector.

Conclusion

The primary aim of this review is to understand the medical device market, legislative changes, government initiatives, schemes, and the evolution of the medical device market in India. Considering India as a developing country, it has achieved a milestone by achieving 4th place in the Asian Medical device market without compromising on quality, safety, and efficacy. The review also gives Ideas about international standards, implementation, and their purposes. The registration process of medical devices in India, China, Australia, the U.S., and Europe is compared because conditions, standards, and regulations differ from country to country.

India has shown a rise in the medical device industry but the medical device regulations are not as stringent as in the US, Europe, and China. Because India wants to grow the medical device market by investing in Greenfield and brownfield projects and through automatic routes, FDI has increased. In China NMPA handles medical devices and the main condition is to submit the data in Chinese if one is registering a medical device in China. Previously parent country approval for innovative devices and the in-country clinical study was mandatory in china but now the regulation has changed from 1st June 2021 that parent country approval is not mandatory from now on and in-country clinical testing is not mandatory. Medical devices are marketed in Europe if it is having a CE mark. EU notified bodies are accountable for checking the quality standards of the medical device and approval for CE marking.

Australia has quite similar regulations to Europe. The CE mark is compulsory if one wants to enter into Australian medical device market. The in-country clinical test is not mandatory for all classes of medical devices except for HIV testing devices (clinical test data is acceptable). U.S. medical devices are handled by CDRH, having strict regulations for registering. 510(k) and PMA is required for manufacturing and marketing medical devices in the U.S.

References

1. Ministry of Health & Family Welfare (2021) Medical device & diagnostics, Central Drugs Standard Control Organization.
2. Annual Report.
3. Rashika Vij (2021) Make in India for the World: A Leap for The Indian Medical Devices Sector.
4. IBEF (2021) Medical Devices Industry in India – Market Share, Reports, Growth & Scope, Indian Brand Equity Foundation.
5. National Investment Promotion & Facilitation Agency (2021) Schemes for Medical Devices Manufacturing, Invest India.
6. (2021) Government's go-ahead for 4 medical device parks - The Economic Times.
7. (2021) Andhra Pradesh Medtech Zone: Latest News & Videos, Photos about Andhra Pradesh Medtech Zone, the Economic Times.
8. (2021) Think 3D: Think3D to open facility at Andhra Pradesh medical devices park-The Economic Times.
9. (2021) by 2023, Noida likely to get north India's first medical device park | Noida News - Times of India.
10. (2021) Medical Device Park: Kerala to have one of the first medical device parks, Health News, ET Health World.
11. ISO (2021) International Organization for Standardization.
12. (2010) Market Overview, Medical Device Regulatory Profile for India.
13. ISO (2021) ISO/TC 210 - Quality management and corresponding general aspects for medical devices.
14. MDSAP (2021) Medical device single audit program, TÜV SÜD in India.
15. FDA (2021) Medical Device Single Audit Program, Food and Drug Administration.
16. MDSAP (2021) Medical Device Single Audit Program.
17. (2021) Medical Devices Market Global Opportunities and Strategies.
18. (2021) Global Medical Devices Market Report Opportunities And Strategies.
19. (2021) India Medical Device Registration and Approval.
20. CDSCO (2021) Medical Device Registration in India, Central Drug Standards Control Organization.
21. (2021) Step by Step: Registration Process of Medical Devices in India.
22. May N, Dazhi R (2021) A Road Map To China's Medical Device Registration Process.
23. RAMS (2021) China NMPA Approval Process for Medical Devices, Regulatory Affairs Management Suite.
24. (2021) An Overview of Medical Device Regulations in China, RegDesk.
25. RAMS (2021) Australia TGA Approval Process for Medical Devices, Regulatory Affairs Management Suite.
26. (2021) Medical Device Registration and Approval in Australia, ARAZY Group.
27. TGA (2021) Auditing of medical device, including IVD medical device, applications, Therapeutic Goods Administration.
28. TGA (2021) Australian conformity assessment bodies, Therapeutic Goods Administration.
29. (2021) What classification is my medical device? Therapeutic Goods Administration (TGA).
30. Sethi R, Sethi S, Popli H (2017) Medical Devices Regulation in United States of America, European Union and India: A Comparative Study 6: 1.
31. RAMS (2021) US FDA Approval Process for Medical Devices, Regulatory Affairs Management Suite.
32. FDA (2021) Device Registration and Listing, Food and Drug Administration.
33. (2021) Europe: Medical Device Market Approval, Credevo Articles, Medical devices, European Medicines Agency.
34. (2021) Medical devices, European Medicines Agency.
35. (2021) Europe Medical Device Registration (MDR, IVDR), Kobridge.
36. (2019) NITI Aayog plans to bring all medical devices under one regulatory regime, Business Standard, pp: 1-2.