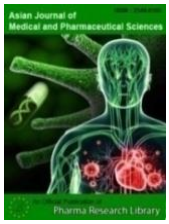

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A study on Approval and Marketing of medical products in EU, USA AND INDIA and AUSTRALIA

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A B S T R A C T

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. We believe that the future of India's innovative biomedical industry will depend on the upgradation of several national policies. Whereas this study was not designed to inform such policies, and tools such as stakeholder analysis are better suited for this purpose than the case study method adopted here, we would like to make three recommendations for the development of an innovative medical device sector in India: First, the national regulatory bodies need to offer guidance to industry about product development as the FDA, European Medicines Agency and WHO do. Currently, the scientific capabilities of the relevant agencies are inadequate to do this. Second, government procurement of innovative devices needs to be increased. India has advanced into a "World Pharmaceutical Hub" whereas its regulatory authority is still struggling to keep pace with the international industrial growth. According to the report commissioned by Indian parliamentary committee in 2012, CDSCO struggled with staffing shortage and infrastructural issues affecting its responsibilities to ensure public safety. (16) Following this criticism, CDSCO not only updated its mission statement as "To safeguard and enhance the public health by assuring the safety, efficacy and quality of drugs, cosmetics and medical devices," but has also moved beyond the past issues to correct its flaw and become a world class regulator comparable to the US FDA and EMA (European Medicines Agency).

Keywords: FDA, CDSCO, European Medicines Agency, EU systems, World Pharmaceutical Hub, cosmetics

A R T I C L E I N F O

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C O N T E N T S

1. Introduction

ThemainpurposeforMedicalDeviceregistrationistohavecomp leteassessmentofdocuments provided by the applicant to regulatory authorities, ensuring quality, safety, and efficacy of the device in view of public health. Medical Device registrations are different from country to country - much more complicated, never truly be "SIMILAR". Medical Device registrations approval requires special regulatory process & guidelines toensure quality, safety and efficacy of the device. But still, there is a lack of clear regulatory guidance in diaasthe regulationsvary in many countries like Taiwan, Korea, China, Brazil, Russia, etc. To overcome the medical device registrations process hurdles, understanding the regulatoryrequirements in clear and to ensure compliance across the globe, this project workwasinitiated. Devices which are classified as drugs) fall under the category of non-notified medical devices for which registration is not required. However, amendments have been made in the recent past to address the lack of

standardization across the devices portfolio and the list of notified devices has expanded nowto coverover 160devices. Several recommendations have also been made to make the regulatory framework morestringent and covering aspects such asclassifying medical devices along global guidelinesand directives, setting up notified bodies to conduct quality audits of manufacturing facilities, adopting international quality management standards, conducting clinical trials and evaluation of medical devices asper Global Harmonization task Force (GHtF) guidelines (asat present there is no document detailing the guidelines for conducting medicaldevicesrelated trials) and finally, adopting post-market surveillance of approved devices. Due to lack of a well-documented orarobust regulatory frame work such as the FDA‟s, indigenous device manufacturers adopt international quality standards on their own as they progress on theirmaturity curve. However, the level of adherence to such standards is questionable and there isageneral lack of trust intheproducts manufactured inIndia.

New Medical Device Rules

As medical devices deal with the health and safety of the patients, their manufacturing is done in a strictly regulated environment, and they fulfill stringent regulatory requirements and guidelines. While the drug regulations in India are well established for decades, a well-defined regulation for medical devices was missing for long. Nevertheless, the Indian regulatory regime for medical devices has recently been very active. Medical Devices and Diagnostics Division of Central Drug Standard Control Organization (CDSCO) has developed structured regulations for medical devices, IMDR which was released in January 2017 and came into force from January 2018. IMDR was amended in February 2020 as "Medical Devices (Amendment) Rules, 2020"and came into force in April 2020. The 2020 amendment was released with an addition of "registration of certain medical devices". Though many of the medical devices still continue to be controlled as drugs under the Drugs and Cosmetics Act, 1940, the advent of the IMDR and other supporting guidelines has paved the way for India to move its first step towards enhanced patient safety with respect to medical devices. Future amendments of IMDR can focus on fulfilling the gaps that would have equated these regulations with that of MDR and IVDR of EU, which are the most recent international regulations for medical devices for device safety and performance.

Medical devices approval process in India

Before manufacturers of certain medical devices can sell within India, they need to be in compliance with India's medical device regulations. Indian authorities overhauled the medical device regulatory process in 2017 with the publication of the Medical Device Rules. The rules came into force in January 2018 and devices are regulated by the Central Drugs Standard Control Organization (CDSCO), an agency of the Ministry of Health and Family Welfare. For an overview of the regulatory process, see or download the approval chart below.

India's medical device and IVD approval process

The chart shown illustrates India's approval process and is available for download in PDF format. However, if you would like to explain the steps to someone else in an email, you can cut and paste the text below or send them a link to this page.

Medical Device Market Approval Process in the United States: The United States remains the largest medical device market in the world with $156 billion which is 40 percent of the global medical device market in 2017 and by 2023; it is expected to grow to $208 billion. The medical technology industry (commonly referred to as medical devices) consists of articles, instruments, apparatuses, or machines that are used in the prevention, or for detecting, measuring, restoring, correcting, or diagnosis or treatment of illness or disease or modifying the structure or function of the body for some health purpose.

- The regulatory body for medical devices in the United States
- The U.S. The Food and Drug Administration's Center for Devices and Radiological Health (CDRH) oversees medical devices marketed in the United States.

2. Materials and methods

Harmonization of Medical Device

Regulations: The International Medical Device Regulators Forum (IMDRF) is a voluntary group of Medical device regulators from around the world who have come together to build on the strong foundation work. Previously it was known as Global Harmonization Task Force (GHTF).In Southeast Asia-The Medical Device Product Working Group (MDPWG) was formed for Medical Devices regulatory harmonization.

Benefits of Harmonization

Ensure the Safety, effectiveness, performance & quality of Medical Device.

- To promote technological innovation.
- Facilitating international trade.
- Improve the efficacy of national economies & their ability to adopt change and remain competitive.
- Reduce the cost to market the product.

Currently different countries have to follow different regulatory requirements for approval of new drug. For marketing authorization application (MAA) a single regulatory approach is applicable to various countries is almost a difficult task. Therefore it is necessary to have knowledge about regulatory requirement for MAA of each country.

Drug approval in United States:

The United States has perhaps the world's most stringent standards for approving new drugs. Drug approval standards in the United States are considered by many to be the most demanding in the world.

Investigational New Drug (IND) Application

It's an application filed to the FDA in order to start clinical trials in humans if the drug was found to be safe from the reports of Preclinical trials. A firm or institution, called a Sponsor, is responsible for submitting the IND application. A pre - IND meeting can be arranged with the FDA to discuss a number of issues:

- The design of animal research, which is required to lend support to the clinical studies. The intended protocol for conducting the clinical Trial

- The chemistry, manufacturing, and control of the investigational drug

Such a meeting will help the Sponsor to organize animal research, gather data, and design the clinical protocol based on suggestions by the FDA.

New Drug Application (NDA)

If clinical studies confirm that a new drug is relatively safe and effective, and will not pose unreasonable risks to patients, the manufacturer files a New Drug Application (NDA), the actual request to manufacture and sell the drug in the United States.

Abbreviated New Drug Application (ANDA)

It's an application made for approval of Generic Drugs. The sponsor is not required to reproduce the clinical studies that were done for the original, brand name product. Instead, generic drug manufacturers must demonstrate that their product is the same as, and bioequivalent to, a previously approved brand name product.

Drug approval in Europe:

Similar to the US requirements, there are two regulatory steps to go through before a drug is approved to be marketed in the European Union. These two steps are clinical trial application and marketing authorization application. There are 28 member states in the European Union (as of July, 2013); Clinical Trial Applications are approved at the member state level, whereas marketing authorization applications are approved at both the member state and centralized levels.

Centralized procedure

The centralized procedure is one which allows applicants to obtain a marketing authorization that is valid throughout the EU.Results in a single authorization valid in EU, Norway, Iceland and Liechtenstein.

Application evaluated by an assigned Rapporteur.

Timeline: EMA opinion issued within 210 days, and submitted to European Commission for final approval.

Centralized process is compulsory for:

- Those medicines which are derived from any biotechnology processes, such as genetic engineering.
- Those medicines which are intended for the treatment of Cancer, HIV/AIDS, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions.
- Medicines officially designated 'Orphan medicines' (medicines used for rare diseases).

Mutual Recognition Procedure

The Mutual Recognition procedure allows applicants to obtain a marketing authorization in the concerned member states (CMS) other than the Reference member state (RMS), where the drug is previously approved.Applicant submits identical dossier to all EU member states in which they want marketing authorization, including required information. As soon as one Member State decides to evaluate the medicinal product (at which point it becomes the "RMS"), it notifies this decision to other Member States (which then become the "CMS"), to whom applications have also been submitted.

- RMS issues a report to other states on its own findings.
- Generic industry is the major user of this type of drug approval procedure. This process may consume a time period of 390 days.

Nationalized Procedure

The Nationalized procedure is one which allows applicants to obtain a marketing authorization in one member state only. In order to obtain a national marketing authorization, an application must be submitted to the competent authority of the Member State.

- New active substances which are not mandatory under Centralized procedure can obtain marketing authorization under this procedure.
- Timeline for this procedure is 210 Days.

Decentralized procedure

Using this procedure, companies may apply for authorization simultaneously in more than one EU country for products that have not yet been authorized in any EU country and essentially do not fall within the centralized procedure's essential drugs list. Based on the assessment report which is prepared by the RMS & any comments made by the CMS, marketing authorization should be granted in accordance with the decision taken by the RMS & CMS in this decentralized procedure.

- Generally used for those products that has not yet received any authorization in an EU country.
- Time: 210 days.

Approval of New Drug in India:

When a company in India wants to manufacture/import a new drug it has to apply to seek permission from the licensing authority (DCGI) by filing in Form 44 also submitting the data as given in Schedule Y of Drugs and Cosmetics Act 1940 and Rules 1945. In order to prove its efficacy and safety in Indian population it has to conduct clinical trials in accordance with the guidelines specified in Schedule Y and submit the report of such clinical trials in specified format. But a provision is there in Rule - 122A of Drugs and Cosmetics Act 1940 and Rules 1945 that the licensing authority may waive certain trails if he considers that in the interest of public health he may grant permission for import of new drugs basing on the data of the trials done in other countries. Similarly there is another provision in Rule - 122A which says that the clinical trials may be waived in the case of new drugs which are approved and being used for several years in other countries.

3. Results and Discussion

Authorized representatives

This is the executive body within the European Union which has responsibility for proposing legislation. The Commission determines the requirements for medical device regulation and seeks approval at a European level from the European Parliament and the European Council of Ministers. Once approval is obtained, a Directive become binding across the European Union and by agreement the EFTA (European Free Trade Area).

Competent Authorities:

Are the regulatory bodies, appointed by the respective governments within each European State, with the purpose of monitoring compliance with the relevant European directives as applied into national laws, i.e. the Competent

Authority will seek to ensure that the medical device directives are fully implemented within their own country167. It is important to understand that the European Commission will determine the directives which apply across the full European Union and European Free Trade area. For example the Medical Devices Directive MDD 93/42/EEC equally applies to all European markets. The directives are not legally binding, therefore in order to enforce in law, each individual country will transpose the directive into their national laws. In this process, due at times to language and historical reasons some variations between the national laws of countries may arise. This can result in some variations in requirements between European countries for the medical device regulations. Note however, the substantive requirements are essentially the same across the EU and EFTA.

Notified Bodies and Medical Device Approval:

Are third party non-governmental agencies involved in conformity assessment. Notified Bodies are and must remain third parties, independent of their clients and other interested parties. All medical devices need the employment of a Notified Body to certify the product except those that fall into Class I.

Authorized representatives:

Where a medical device is manufactured outside the European Union, then an authorized representative that is based within the EU must be appointed. There should only be a single authorized representative for non-EU / EFTA manufacturers, i.e. there should not be different authorized representative for the various EU countries (reference Article 14.2* of Council Directive 93/42/EEC amended by Directive 2007/47/EC).The authorized representative will be the contact for submitting the required regulatory requirements to the various Notified Bodies and Competent Authorities and for communicating with these bodies where questions arise, information is required, etc.

Stages in the European Medical Device Approval process

1st stage in the medical device approval process.

The manufacturer, in preparing for CE marking, should first determine if their product falls within the scope of a relevant Directive either as a medical device or as an accessory to a medical device. Definitions of what constitutes a medical device will be defined in the relevant directive.

2nd stage: Having confirmed that the product under consideration is subject to a European Medical Device Directive, confirm which directive specifically applies, also confirm if the regulations see the medical device as a product within its own right, or as an accessory to a related medical device. Identify other European Directives which may be impacting on the product. For example, if the medical device has an active power source, then the AIMD Directive (Active Implantable Medical Devices Directive) may apply, however, equally the medical device may have to comply with Directive 2004/108/EC which relates to electromagnetic compatibility.

3rd stage: Determining the level of risk.

General medical devices and related accessories must be classified into one of four classes, which are based on the perceived risk of the device to the patient or user. The classification of a device determines the conformity assessment options that are applicable to the device, with higher risk devices undergoing higher levels of assessment. Devices are grouped into 4 classes as follows:

- Class I – low risk
- Class IIa – medium risk
- Class IIb – medium risk
- Class III – high risk

Duration of contact:

In determining the correct classification of a device the duration that the device is in continuous contact with the patient is defined as transient, short term or long term.The longer the device is in contact with the patient or user, the greater the potential risk, and therefore contact duration needs to be taken into account when determining classification.Continuous use is defined in MEDDEV 2.4/1 as the uninterrupted actual use for the intended purpose. Where use of a device is discontinued in order that the device is immediately replaced with an identical device (e.g. replacement of a urethral catheter) this shall be considered as continuous use of the device. Duration of contact can be difficult in some instances to determine.

Degree of invasiveness:

A device, which in whole or in part, penetrates inside the body either through a body orifice or through the skin surface, is invasive. Invasiveness is generally categorized as invasive of a body orifice (including the surface of the eye), surgically invasive devices and implantable devices.An implantable device is one which is intended to be totally introduced into the human body or to replace an epithelial surface or the surface of the eye by surgical intervention and which is intended to remain in place after the procedure. Any device intended to be partially introduced into the human body through surgical intervention and intended to remain in place after the procedure for at least 30 days is also considered an implantable device.

Is the device active or non- active:

A medical device is considered to be active if operation of the device depends on a source of electrical energy or any source of power other than that directly generated by the human body or gravity and which acts by converting this energy. Medical devices intended solely to transmit energy between an active medical device and the patient where there is no significant change in the energy (e.g. nature, density, level) are not considered to be active medical devices.The concept ‘act by converting energy’ includes conversion of energy in the device and/or conversion at the interface between the device and the tissues or in the tissues of the human body.

Authorized representatives:

Where a medical device is manufactured outside the European Union, then an authorized representative that is based within the EU must be appointed. There should only be a single authorized representative for non-EU / EFTA manufacturers, i.e. there should not be different authorized representative for the various EU countries (reference Article 14.2* of Council Directive 93/42/EEC amended by Directive 2007/47/EC). The authorized representative will be the contact for submitting the required regulatory requirements to the various Notified Bodies and Competent

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- Class I – low risk
- Class IIa – medium risk
- Class IIb – medium risk
- Class III – high risk

Duration of contact:

In determining the correct classification of a device the duration that the device is in continuous contact with the patient is defined as transient, short term or long term. The longer the device is in contact with the patient or user, the greater the potential risk, and therefore contact duration needs to be taken into account when determining classification. Continuous use is defined in MEDDEV 2.4/1 as the uninterrupted actual use for the intended purpose. Where use of a device is discontinued in order that the device is immediately replaced with an identical device (e.g. replacement of a urethral catheter) this shall be considered as continuous use of the device. Duration of contact can be difficult in some instances to determine.

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A medical device is considered to be active if operation of the device depends on a source of electrical energy or any source of power other than that directly generated by the human body or gravity and which acts by converting this energy. Medical devices intended solely to transmit energy between an active medical device and the patient where there is no significant change in the energy (e.g. nature, density, level) are not considered to be active medical devices. The concept 'act by converting energy' includes conversion of energy in the device and/or conversion at the interface between the device and the tissues or in the tissues of the human body.

Part of the body affected

The anatomy affected by the use of the device must be considered. Devices in contact with the central nervous system or the central circulatory system are automatically placed in a higher risk category.

4th stage: Technical File, Design Dossier

The device developer and manufacturer will need to maintain a Design File (Design Dossier) and ongoing Technical File which provides evidence of conformity to the essential requirements of the relevant Medical Device Directive. Clinical data or in the case of some lower risk devices, peer product review data will need to be available to assure the effective functioning of the device. The Technical File is a requirement for class I, IIa, IIb devices. The Design Dossier is a requirement of class III devices. The Technical File will provide information (or point to the location of information) on development and performance aspects of the device.

5th stage: Quality Management System.

The product manufacturing process will need to comply with basic quality management system requirements. For the majority of medical device manufacturers this will require compliance with the ISO 13485 standard. Specifically compliance with the ISO 13485 standard will be demanded for products which reside within the IIa, IIb, and III levels of risk, in addition to class I products with a sterile aspect or a measurement function. Class I devices need a lower level of quality system elements, however compliance with all aspects of the ISO 13485 standard could be seen as good business practice even for Class I medical devices.Certification to the ISO 13485 standard will require 3rd party Notified Body certification and on-going surveillance auditing.

6th Stage: Labelling: Each European country may require labelling to be in their official language, or in a widely utilized language within their territory.

7th stage: Registration.

The following device classes must be registered with the Competent Authority where the manufacturer or their Authorized Representative is located. Most EU countries do not require registration for class IIa, class IIb, or Class III devices as these will require review via the independent Notified Bodies.All class I devices. All class I devices which may have been refurbished or re-labelled under a

new name. All system or procedure packs containing at least one medical device. Custom-made medical devices. All in vitro medical devices. In vitro diagnostic medical devices (IVDs) undergoing performance evaluation.

8th stage: EC (European Community) Declaration of Conformity: The EC declaration of conformity is a written document which states that the manufacturer of a medical device has complied with all relevant EU requirements relevant to the device i.e. completed the medical device approval process. The declaration may cover a single device or multiple devices, all of which will be clearly identified on the declaration via product name, product model, etc.. Also detailed where relevant will be the applicable directives, the EU Authorized Representative (where the manufacturer is not based in the EU), Notified Body engaged for audit and technical files review, key standards applied in meeting the requirements of the directive.

9th stage: Market vigilance. Post market surveillance.

All medical devices placed onto the European market need to be subject to an appropriate post market surveillance process. A medical device manufacturer needs to have a pro-active surveillance system in place, which will include monitoring customer feedback, identifying investigating and addressing complaints, complaint trending, the implementation of an effective and efficient corrective and preventative action process, for higher level risk devices maintenance of a database which links devices to customers, maintenance of records which will allow forward and reverse tracking of manufactured devices, i.e. if a problem is identified for example with a raw material after devices have been manufactured, then the manufacturer needs to be able to identify affected devices in the field, alternatively if a fault is identified with a device in the field, then the manufacturer needs to be able to track back to manufacturing data. The higher risk devices will need more comprehensive tracking records and processes.

10th stage:

Medical Device Approval, Affixing the CE label: Where all relevant directive requirements have been met (i.e. medical device approval), the Notified Body if applicable has confirmed that the quality system, technical file, design files are all to expectations, product labels meet individual country requirements, a market surveillance system is in place, then the CE label can be affixed to the product and the device placed onto the European market. Where the manufacturer is located outside the EU, an Authorized.

Medical devices fees in Australia

License Transfer To change the Australian Sponsor associated with an ARTG listing, the existing sponsor must complete, sign and submit a transfer form to TGA. After the transfer is complete the new Australian Sponsor must take the following steps:

Submit manufacturers evidence (no TGA fee)

Prepare and submit Device Change Requests to update the ARTG entries with the Manufacturers evidence (TGA fee is $360/application and the TGA allows up to 10 ARTG entries per application

Medical Device Regulations and Classification in Australia

Regulatory authority:

Therapeutic Goods Administration (TGA)

Classification system:

Medical Devices: I/Is – sterile/Im – incorporating a measuring function/IIa/IIb/III/AIMD

IVDs: 1/2/3/4

Timeframe: Medical Devices and IVDs (based on experience) Approximately 1-2 months to complete both the conformity assessment and ARTG inclusion, except for Class I medical devices (non-measuring, non-sterile), Class 1 IVDs, and Class 1,2,3 in-house IVDs that are exempted from conformity assessment.

Special requirements:

On-site audits are necessary for all manufacturers (both domestic and foreign manufacturing sites) applying for a TGA Conformity Assessment Certificate. However, the audits might not be required for the manufacturer that has been audited by EU Notified Bodies, MDSAP – Medical Devices Single Audit Program, FDA, Health Canada, etc.

Local testing is only required for HIV testing devices.

LOCAL FEES (New Application): – as of July 2022

Medical Device: Conformity Assessment: varies depending on type of assessment from USD 18,500 to USD 46,750

ARTG Inclusion:

Class I (non-sterile & measuring device): USD 450

Class I (sterile & measuring device)/Class IIa/Class IIb: USD 800 Class III/AIMD: USD 1,050

Application Audit (if applicable): varies depending on type of application audit from USD 3,000 to USD 5,500

In-vitro Diagnostics (IVDs): Conformity Assessment: varies depending on type of assessment from USD 13,500 to USD 50,750

ARTG Inclusion (all classes): USD 800

Technical File Review (TFR) – if applicable:

Class 1/2/3: USD 5,500

Class 4 (in-house IVDs): USD 50,000

Class 4 (in-house immunohaematology reagent IVD): USD 12,100

LOCAL FEES (Manufacturer):

If on-site audits are applicable, there will be surveillance inspections fees (the amount varies depending on type of QMS inspection and other additional fees such as assessor fee, travel expenses, etc.).

License validity:

Conformity assessment certificate: 5 years

ARTG inclusion certificate: no validity; however, to maintain a medical device in the ARTG, annual fees will be charged depending on the classification of the device.

License Transfer: License transfer is possible. Both new and former sponsor must complete a notification form after the transfer has occurred. No fee is required.

Authorized representative:

Foreign manufacturer must designate local authorized representative who will be known as "Sponsor".

Additional information:

From the 1st of October and 4th of December 2020, applicants of class I medical devices (non-measuring, non-sterile) and class 1 IVDs, respectively, need to provide a manufacturer's Declaration of Conformity with their application to include the device in the ARTG, rather than simply holding it at the time they apply for inclusion. If TGA is not satisfied with the application, TGA will select

the application for non-mandatory audit but if TGA is satisfied, TGA will include the device in the ARTG within 4 working days. There are several ways to expedite the conformity assessment/ARTG inclusion process. Priority Review Designation – through this process, the device will be allocated "front-of-queue" priority throughout the relevant assessment process. This is applicable for devices intended for serious condition in which the devices' need in Australia is currently unmet and/or the devices could bring a breakthrough technology. Abridged Procedure – some overseas evidence (such as certificates issued by EU notified bodies, MDSAP, FDA, Health Canada, MHLW, etc.) can be used to support the application for conformity assessment or ARTG inclusion.

US FDA's Regulations on Medical Devices: The legal authority of US, the FDA (Food and Drug Administration) assures safety and effectiveness of the medical product. (4) FDA's Centre for Devices and Radiological Health deals with pre and post marketing regulations of medical devices. The FD&C (FDA Drug and Cosmetic) Act contains provisions or regulatory requirements that define FDA's level of control over these products. FDA formulates, publishes and enforces regulations in order to fulfill the provisions of the FD&C Act that apply to medical devices.Most of FDA's medical device and radiation-emitting product regulations are in Title 21 CFR Parts 800-1299. This final regulation cover various aspects of design, clinical evaluation, manufacturing, packaging, labeling, post market surveillance of medical devices and also provides standards and product reports that apply to radiation-emitting products. Currently, the CFR is updated to e-CFR (Electronic Code of Federal Regulations). It is an unofficial editorial compilation of CFR material and Federal Register amendments produced by the National Archives and Records Administration's Office of the Federal Register (OFR) and the Government Printing Office. The OFR updates the material in the e-CFR on a daily basis.

US FDA Registration Process for Medical Devices

All companies planning to manufacture, sell or import medical devices in the United States need to register their products with the US FDA. The Medical Device Amendments of 1976 to the Federal Food, Drug and Cosmetic Act categorised medical devices into three regulatory classes (6) (Figure 6). These classes are based on the degree of control that is required to assure their safety and efficacy. Figure 7 highlights the regulatory procedure for registration of different classes of medical device in US.

Comparing Indian and US Regulations

The Indian regulations as opposed to the US regulations are very new and in their infant stage. However, both of them have their own rules and regulations that need to be followed.US FDA has classified medical devices into three classes based on the risk associated with the device and their registration depends on the class in which they fall. Whereas, in India according to CDSCO guidelines medical devices are either notified or notified devices depending on utility and not according to their safety. Notified devices require registration whereas non-notified may or may not require any registration. In India if product is registered in US or Europe, there is no need to conduct clinical trials in India but if no predicate is available in US or European market, clinical trials are required. In US, if no predicate is available.

Table1: Administrative Requirements

Requirements	US	EU	INDIA
Application	ANDA/ NDA	MAA	MAA
Debarmentclassification	Required	NotRequired	NotRequired
Numberofcopies	3	1	1
ApprovalTimeline	~18 Months	~12 Months	12 -18 Months
Fees	Under$2million-NDAApplication $51,520–ANDA Application	National fee(includinghybridapplications): £103,059 DecentralizedproceduewhereUKis CMS:£99,507	50,000 INR
Presentation	eCTD & Paper	eCTD	Paper

Table2: Finished Product Control Requirements

Requirements	US	EU	INDIA
Justification	ICHQ6A	ICHQ6A	ICHQ6A
Assay	90 -100 %	95 -105 %	90 -110 %
Disintegration	NotRequired	Required	Required
Colour Identification	NotRequired	Required	Required
WaterContent	Required	NotRequired	Required

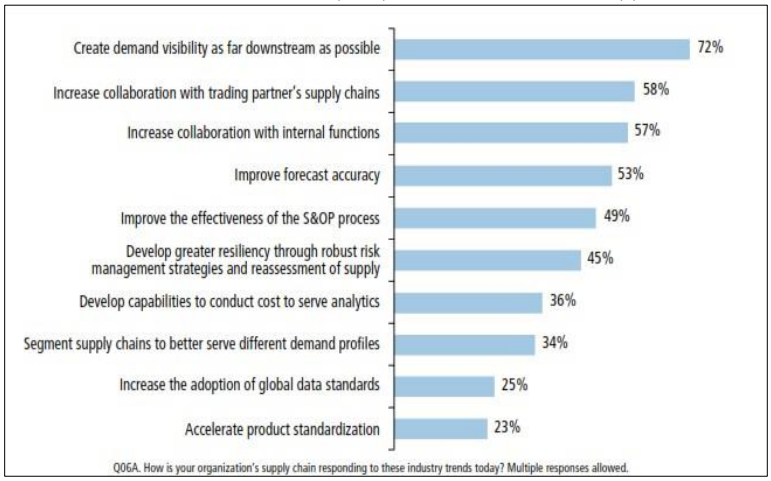

Figure.1: Increasing collaboration to improve the supply chain

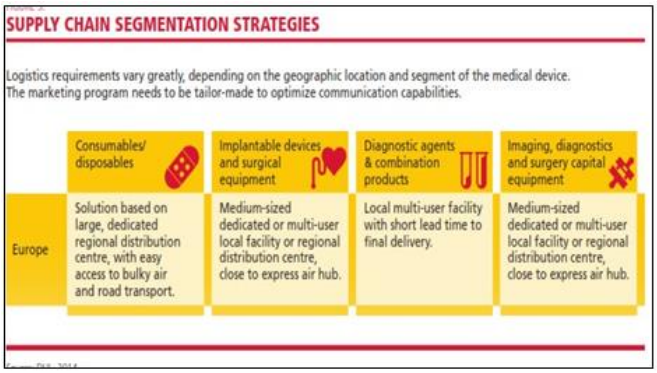

Fig.2. European risk based medical device regulatory system and supply chain segmentation strategies

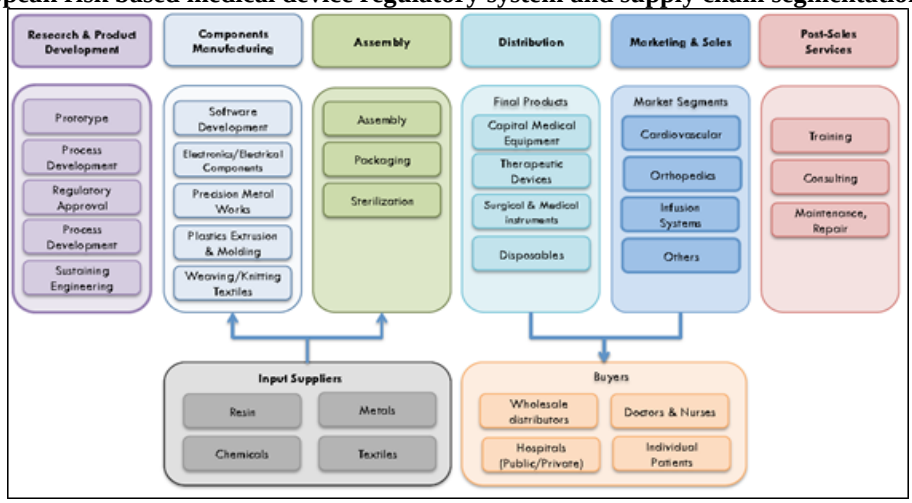

Fig.3 Medical deviceglobal valuechain

Table3: Manufacturing &Control Requirements

Requirements	US	EU	INDIA
Number of batches	1	3	1
Packaging	Aminimum of 1,00,000Units	NotRequired	Notaddressed
Process Validation	Not required at the time of submission	Required	Required
BatchSize	1pilotscaleorminimumof1lakhunitsWhicheverishigher.	2 pilot scale plus 1 lab batch orminimumof 1 lakh units Whicheverishigher.	Pilotscalebatch

Table4: Stability Requirements

Requirements	US	EU	INDIA
Number ofbatches	3 Pilot Batch or 2 PilotBatch&1Smallscale	2PilotScale(IfAPIStable)3PrimaryBatches (IfAPIunstable)	2 Pilot Scale/Productionscale(If APIStable)3 Primary Batches (If APIunstable)
Condition: Long term stability, Accelerated stability,	Longterm:25°C/60%RH Accelerated:40°C/75%RH(0,3,6months); Intermediate:30°C/65% RH	Long term: 25°C/60%RHAccelerated:40°C/75%RH(0,3,6 months)Intermediate:30°C/65 %RH	Long term: 30°C/70%RHAccelerated:40°C/75%RH (0,3,6months)
Minimum time period at Submission	6 Months Accelerate &6Monthslongterm	6MonthsAccelerate&6Monthslongterm	6MonthsAccelerate&6Monthslongterm
Container orientation	Inverted&Upright	Donotaddress	uprightandinverted
Clause	21CFR part 210&211	Volume 4 EU Guidelines formedicinalproducts	ICHQ1F
QPCertification	NotRequired	Required	Required

4. Conclusion

This study suggests that many new devices do receive regulatory approval but often lack clinical trial data supporting their safety and effectiveness. The IDEAL model makes several proposals for the staged introduction of innovations in surgery (and other disciplines that offer complex interventions), including randomised controlled trials to assess safety and effectiveness. At present, few relevant randomised controlled trials are published, and fewer still meet current quality standards for optimal reporting. Changes in the regulatory approval of devices that would require trials for proof of safety and effectiveness might promote adherence to the IDEAL model.

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