ISSN- 2230-7346
Journal of Global Trends in Pharmaceutical Sciences

THE COMPARATIVE STUDY ON PERFORMANCE OF SELECTED MEDICAL DEVICES MANUFACTURED IN INDIA AND FOREGN COUNTRIES WITH REGULATORY ASPECTS

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ARTICLE INFO

Key words:

Medical devices.
Regulatory affairs
Regulatory professionals
Manufacturing Import
World Health Organization

Access this article online
Website:
https://www.jgtps.com/
Quick Response Code:

ABSTRACT

Medical devices are the integral part o modern medical industry. The dependency of medical device has increased handsomely in treatment of diseases. This dependency has led to quality issues in medical care resulting in complications in the condition of the patients as the body does not accept them and consider them as foreign body. Therefore, for manufacturing of medical device safety and quality are given prime importance in its regulation. Initially the regulation around the world was evolving and now by introducing guidelines and policies and the revision of law has provided satisfactory guidance for the manufacturers and agencies to manufacture and check the quality appropriately. The regulation will implement the safe manufacturing, quality, and uniformity of medical devices throughout and it will also ease the importing procedures into India. The guideline implemented and regulated effectively will have a positive outcome. The objective of the present study is comparison of regulatory guidelines for medical devices in India and US and European Union. The research work involves study of Medical regulation of US, EU and its comparison with Indian regulation by conducting study of different class of medical devices. Data collected was analyzed for device problems and complications .The data for reporting of issues was further checked with regulatory websites of India and other countries. In the study four medical devices from different classes (Class A, Class B, Class C and Class D were selected and the study was conducted in various hospitals of four towns in Gujarat. The hospitals were government and private hospitals.A total of 2323 cases were studied from four cities.Maximum numbers of patients were of urinary catheter and IV cannula .Government hospital showed more number of patients compared to private hospitals. The primary reason was the treatment in Government hospital is cheaper than private hospitals and various medical schemes of Indian / State Government are available as we are a developing countries and not everyone can afford costly treatments of private hospitals. No data regarding medical device complication were available with regulatory body of India in any of the devices and when compared with other countries have reported data available. Indian doctors also prefer imported medical devices as they are more reliable and quality products as their data are available. The study shows a biggap between the Indian regulation and regulation of US and other countries. T heir system for quality is based on clinical trials while we do not have any such mechanisms in our regulations.

INTRODUCTION:

Diseases have evolved to the period of human existence. Evolution of heath and diseases evolved over more than thousand years ago. Civilizations like Egyptian, Assyrian, Babylonian, Hebrew, Abrican, Arabic, Chinese and Indian had their own traditional medicines.They used plants and animal's products for treatment of diseasese.g. The *Ebers Papyrus*dating to 1550 BC was the chief minister of Egyptian king and is considered to be the first doctor.From the knowledge and literature of past the modern medicine was nurtured in European region.During the4 CenturyBC literature like Charak Samhita were written.Sushrutais considered father of surgery where he has described surgery under eight heads Chedya (excision), Lekhya (scarification), Vedhya (puncturing), Esya (exploration),Ahrya (extraction), Vsraya (evacuation), and Sivya (suturing).All the basic principles of surgery including planning precision,hemostasis and perfection are mentioned.He has described 60types of upkarna for treatment of wound, 120 surgical instruments and 300 surgical procedures. The word "UPKARNA" means equipment's used for surgery and in today's world we term it as "device". Medical devices are thene west technology of the 90's which is used to save lives of the persons having different medical conditions.These devices are used in many forms like diagnosing ,monitoring and treating the diseaseor a condition. The devices vary from simple to complex devices like sticking plasters, syringes or latex gloves, spectacles, wheelchairs, hearing aids, heart stents, pacemakers and replacement joints for knees and hips etc. In today's world, we have more than 500,000 medical technologies used to improve and extend the lives of the patients. This is one of the major industry having worldwide sales of more than £110 billion per year. The global medical market is expected to grow at a compound annual growth rate(CAGR)of4.1%,and reach $522 billion by 2022.The market is further expected to grow at a CAGR of 6.2% in the period of 2023-2031 to reach a value of about $965.2 billion by 2031[6]. The gap of synchronization around the world has also created an issue for the recognition of different class of medical device based on design complexity, its application, and features safety concern if misused. Around the world it is defined in different categories but they are typically grouped in 3 classes: class I, II and III (orA, B, C, D). The classification is based on the risk related to health from low risk to high risk. The developed countries like USA,Europe,and Japanetc.were the first countries that adopted the guidelines and harmonized the regulation of medical devices by forming a consortium Global Harmonization Task Force (GHTF). GHTF was formed in 1992 to achieve uniformity between national regulatory systems of different countries. The aim was to enhance patient safety,effective and beneficial technologies around the world. The founding members were European Union, United States, Canada, Australia and Japan. GHTF defined medical devices in 2011 as"Any instrument, apparatus, implement, machine, appliance, implant, in vitro reagent, software, material or other similar or related article: a) intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of: diagnosis, prevention, monitoring, treatment or alleviation of disease, diagnosis, monitoring, treatment, alleviation of or compensation for an injury, investigation, replacement, modification, or support of the anatomy or of a physiological process, supporting or sustaining life, control of conception, disinfection of medical devices, providing information f or medical or diagnostic purposes by means of in vitro examination of specimens derived from the human body; and b) which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but that may be assisted in its intended function by such means". In US the term medical device means "a device as an "instrument, apparatus, implement, machine, contrivance, implant,invitro reagent,or other similar or related article, including a component part, or accessory which is

recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them, Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals. European countries have defined medical device as" instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of diagnosis, prevention, monitoring, treatment or alleviation of disease, diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap, investigation, replacement or modification of the anatomy or of a physiological process, control of conception and which does not achieve its principal intended action in or on the human body. India has its own regulation and defined medical device as "medical device used, whether alone or in combination with other medical devices,to supply information for detecting,diagnosing or monitoring, or to provide support in the treatment of, any physiological condition, state of health, illness or congenital deformity, to support, modify, replace or restore biological functions or structures, with a view to the treatment or alleviation of any illness, injury or handicap".

Discussion:

US Medical device regulation[4] In 1938, the law for Federal Food, Drug, and Cosmetic Act was formed and it covered medical device to a certainextent.In1976,the Food and Drug Administration(FDA)received its jurisdiction to regulate devices prior reaching the market and its use in US. Upon integration the medical devices were classified into three types based on the risk it had. The most significant change was in 1997 and 2016 which was "least burdensome provisions." The Federal law is under 21CFR Part 800 – 861. Premarket Notification (commonly known as 510(k) Clearance) Premarket Approval (PMA)and Humanitarian Device Exemption(HDE). There are other pathways,also such as the DeNovo, and Investigational Device Exemption (IDE).

EU Medical device regulation[3]

Medical device regulation in Europe was introduced in 1993 and known as Medical Device DirectiveMDD 93/40/EEC (MDD). The medical device directive was amended in the year 2000 (2000/70/EC) and further amended in the year 2001(2001/104/EC) incorporating devices that incorporate stable blood derivatives. Reclassification of breast implants into Class III were introduced which covered utilization of tissues of animal origin in the year 2003 (2003/12/EC, 2003/32/EC). Reclassification of hip, knee and shoulder joints into Class III was introduced in the year 2005 (2005/50/EC) and amendments were also introduced in the year 2007 and 2011 in 2011/100/EU. In the year 2017 the MDD was replaced with two different regulations Medical Device Regulation (MDR) MDR, 017/745/EU and the *In Vitro* Diagnostic Medical Device

Regulation (IVDR, 017/746/EU). The latest amendment came in year 2023 (EU) 2023/607.The new directive requires CE marking on all the medical devices from 2023 onwards. The classification is similar to US but the class II devices are further subcategorized into IIa and IIb.For regulatory approval for commercialization upon identification of the class by Conformity assessment procedures have to submit documents, such as the technical documentation, audits and others documentations.

Indian medical Device Regulation: [5] India is one of the largest markets of medical devices in the world;over 800 medical devices are manufactured in India. Still most of the devices are imported products. The regulatory framework in India for medical devices was regulated by the Drugs and CosmeticsAct,1940 and its rules which cover 15 types of medical devices under the head of "drugs" and rest was unregulated.So to regulate and promote the local industry Indian

government introduced "The Medical Devices Rules, 2017" notified under the Drugs & Cosmetics Act, 1940 on 31st January 2017 and made effective from 1st January, 2018. The risk based classification is used for medical devices in India. It is classified into four classes ClassA, Class B, Class C and Class D from low risk to high risk. This approach was selected for harmonization of with other countries.

Medical Device–IV Cannula(ClassA)[2]

The work cannula is a Latin word meaning "little reed"· It is a tube inserted into the body for the delivering o rremoval of body fluids o together samples for research and medical testing purposes.The use of a plastic cannula and withdrawal of the needle was introduced in 1945. The length of the cannula is half the length of the needle. It is also called as intravenous (IV) cannula. The size ranges from 14 to 24 gauge having different colours as code as per the gauge.

The main parts of cannula are

Flashback Chamber

1. Needle Grip
2. Luer Lock Plug
3. Luer Connector
4. Valve
5. Injection PortCap
6. Catheter Hub+wings
7. Bushing
8. Catheter and Needle

Urinary Catheters (ClassB)[7]

Urinary catheters are a hollow, partially flexible tube, which collects urine from the bladder and leads to a drainage bag attached to it. Benjamin Franklin played a part in advancing catheter technology.He created a silver catheter for and found that they are painful.The first rubber catheters were introduced in the 1700s made from rubber having more flexibility.The drawback of these catheters was it weakened easily and became brittle under coldc ondition. In1800s,Charles Good year formulated the concept of vulcanization of rubber in1800 and in1844Thomas Hancock patented it.

Intraocular Lens(IOL)(ClassC)[8-9]

Intraocular lens (IOL) is an artificial lens implanted in the eyes for the treatment of cataracts or myopia. A surgery is conducted to remove cataract it is commonly known as cataract surgery and it the most commonly performed surgical technique in the world today. The origin of intraocular lens was during the Second WorldWar, where an Ophthalmologist Harold Ridley operated air force pilots with eye injuries.

Types of intraocular lenses:

There are different types of intraocular lenses available based on the requirement and recommendation by the ophthalmologist. These are as follows Monofocal: Monofocal IOLs are standard lenses used in cataract surgery. One of the major disadvantages of these conventional IOLs is that they can only be focused for one particular distance- either optical infinity or a fixed finite distance. Multifocal: Multifocal IOLs attempt to provide simultaneous viewing of distanc vision and near vision.Trifoca lIOLs can provide intermediate vision .Many multifocal lIOL designs attempt to achieve this simultaneous

Toric: A toric IOL is used to correct preexisting corneal astigmatism at the time of cataract surgery. Astigmatism can also be treated with limbal relaxing incisions or an excimer laser procedure.Cataract surgery with implantation of atoric IOL is essentially the same as cataract surgery with a conventional IOL.Like toric contactlenses,toricIOLs have different powers in different meridian softhelens,and they must be positioned on the correct meridian to reverse the preexisting astigmatism.If thet oricIOL is not on the correct meridian, it may need to be repositioned in a second procedure.

Multifocal toric: Standard toric IOLs are monofocal, permanently focused on distant objects. Multifocaltoric IOLs provide the patient not only with correction of preexisting astigmatism, but also with multiple-focused vision at far and reading distance.

Coronary Stents(Class D)

The first stents were implanted in 1986 in Switzerland by Ulrich Sigwart Jacques Puel.Ithadamesh design were followed by

coilstents,first implanted at Emory University Hospital in1987,and slotted tube designs,implanted in Brazil, the same year. A coronary stents a tube-shaped device placed in the coronary arteries that supply blood to the heart,to keep the arteries open in the treatment of coronary heart disease as shown in Figure 14. It is used in a procedure called percutaneous coronary intervention (PCI). Coronary stents are now used in more than 90% of PCI procedures.

Types of Coronary Stents

Currently, there are three types of stents available and commonly called heart stents or cardiac or coronary stents. They are implanted in the narrowed coronary arteries through a procedure called angioplasty or PCI. Drug-Eluting Stent (DES) Bioresorbable Vascular Scaffold(BVS) Bare Metal Stent (BMS)

Strategey:

The main objective is to study the Medical device regulation of India,US and EU in depth. By understanding the differences in the regulation and its impact. We can develop better and stringent Indian regulation.To achieve the above mentioned primary objective,the study includes the following objectivesThe study the framework of medical device regulation of India, US and EU?In this section the framework history, its development from beginning to the present. It will be examined by utilizing historical and doctrinal methods.

Comparative assessment of Medical device regulation of India, US and EU?

In this section a comparative assessment of the regulation will be done with Indian regulation to identify the similarities and dissimilarities for the identification of gaps. Clinical use of medical device and its health impacts of Class A,Class B,Class C and ClassD of Indian regulation in 4 cities of Gujarat. Reporting procedure for adverse events/recalls, approvals of medical device in India,US and EU? To identify the gap between Indian, US and EU regulation and its approaches to bridge the gap to strengthen our regulation.

Table 1: Medical Devices Classification

Country	Riskbased Classification			
US	I	II	III	
EuropeanCountries	I	IIa	IIb	III
China	I	II	III	IV
Korea	I	II	III	IV
Japan	I	II	III	IV
India	A	B	C	D
Australia	I	IIa	IIb	III

Table 2:Comparison of Indian,US and European Union Medical Device Regulation

Point of Comparison	India	USA	European Union
RegulationAuthority	CDSCO	FDA	EMA and RA of Member State
Classification Categories	ClassA,B,CandD	ClassI,IIandIII	ClassI,IIa,IIb andIII
Regulatory Pathway	Application to controlling authority	510(K) and PMA Application	Multiple pathway as per class.
Fees for available pathways	Manufacturing License: Rs 6,000/-License Fee,Rs1,500/-Registration Fee Import License:$1,000/-RegistrationFee,$5,000/-Inspection of Premises	510(K) $4,690 AndPMA$ 234,495	Fee varies from each Member State of European Union
Quality Management Systems requirement	BIS15575orISO13485	21CFRPart 820	ISO13485orasper applicable Annex of 2017/745/MDR
Assessment of technical Data performed	CDSCO	FDA	National Regulatory Authority
Establishment Registration Requirement	Premises Registration	Establishment Registration	Responsible person registration
Medical Device Regulations	Medical device rules, 2017	21CFR Part 800 To21CFR Part861	MDD/93/42/EEC andRegulation2017/745 or 'MDR'
Validity of License	5years from the date of approval, for Notified Devices	Annual Establishment Registration is required, Indefinite, unless revoked or product recalled	Validity of CE markingis indefinite for Class 1 3 years for Class IIa, IIb,III

As per the data available as mentioned in the table below Total patients were 2323 and patient's issues and complications were observed and discussed below

Total No 3: No.of Patients in Government and private hospital for different medical device

City	IV Cannula		Urinary Catheter		Intraocular Lens		Coronary Stent	
	Male	Female	Male	Female	Male	Female	Male	Female
GG	68	43	58	93	47	18	34	14
GP	39	21	27	32	12	7	23	7
AG	92	77	107	167	51	40	59	21
AP	54	47	45	37	19	15	22	8
MG	47	65	37	36	14	8	25	6
MP	29	23	12	17	8	5	7	3
VG	71	65	44	78	40	27	57	9
VP	41	31	18	28	18	19	29	2
	441	372	348	488	209	139	256	70

Where GG = Government Hospital Gandhinagar, GP = Private Hospital Gandhinagar, AG = Government Hospital Ahmedabad,AP=Private Hospital Ahmedabad, MG =Government Hospital Mehsana, MP=Private Hospital Mehsana, VG = Government Hospital Vadodara and VP= Private Hospital Vadodara.

CONCLUSION:

The medical device regulation of India is very recentasitwasmadeeffectiveintheyear2018compared to European Union regulation which was made effective in 1993 and amendments made in the directive in 2007. The recent directive was framed in 2017 and is implemented since 2018. The amendments are Made in the same regulation. The US regulation is the oldest as it was introduced in late 1930 and the latest amendments are done in the year 2022.Theterm medical device is very complex and it isseen in all the definition of all the three regulation.The US and Indian regulation covers all the devices including diagnostic devices while the EU has a separate regulation for the diagnostic devices. The US regulations have separate codes and are not interlinked and sometimes difficult to understand and apply them for registration or regulatory purposes. The Indian regulation is controlled by CDSCO, US regulation is controlled by FDA under 21CFR and European council controls the European Directive. The regulation of US and EU is very stringent for classification of medical devices but in Indians cenario certain medical devices are notified as drugs to control the price. The mechanism for approval requires premarket approval in both US and EU and for class II and III devices clinical investigation and performance are required. Post market surveillance and report has to be submitted for all the medical device of the above mentioned segment. One cannot market any device from II and III category without conducting clinical investigation in US and EU while we have aprovision for direct acceptance of 21 CFR and CE approved devices without clinical investigation to market imported medical devices. The Indian devices exported do not have such exemption for market in their territory. We should also conduct clinical investigation before giving blanket permission as the seen in drugs the impact changes from region to region. The timeline for approval is maximum12 months in India compared to US and EU is around 30 months for US and 15 months for EU.

Gap analysis of US, EU with Indian regulation: As we have seen the definition and classification of medical devices are different in US, EU and India, the regulation of US and EU is almost harmonized with each other for approval process of medical devices and clinical investigations.We can improve our approval process by incorporating the methodologies adopted by US and EU of premarket approvals, PMA, de novo, for clinical performance and investigations for class B to Class D mandatorily.Clinical investigations records need to be submitted during application but for imported devices of these category study reports of country of origin is considered valid, we should encourage

to test clinical performance in India as we have seen different efficacy in case of drugs with in Indian and western population. Incorporation of penal actions in the regulations for stringent actions against the non-complying manufacturers will help the Indian population rather taking a long criminal code procedure. As India imports more than 70% medical devices by implementing and bridging the above mentioned gaps we will improve the quality and clinical performance of the domestically manufactured medical devices and make them global. It will bring revenue to the country and help in the vision of "Make in India" given by our Prime Minister Mr.Narendra Modi. It will also decrease our dependence on costly imported medical devices and will create job opportunities and new entrepreneurs.

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