

Medical devices in India: a perspective of guidelines and the way forward

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ABSTRACT

In recent times, emerging countries including India have become favored destination for medical device companies to leverage the growth opportunities. However, the Indian regulatory system is not ready to meet the challenges that may come up with growing medical device business. It needs major amendments to current Drugs and Cosmetic Act 1940, to include medical device as a separate entity. Like in developed world, the challenges could be addressed by defining medical devices, risk based classification of devices, guidelines for device safety surveillance, and clinical trials for medical devices. Drugs and Cosmetic (Amendment) Bill 2013, which is yet to be released has addressed the concerns to some extent. However, it needs a major revamp to establish effective regulatory framework for medical devices.

Keywords: Medical device, Device classification, Clinical trial, Device safety, Risk

INTRODUCTION

In an earlier part of 20th century, medical device industry was practically nonexistent.¹ However, medical technology was revolutionized over the period of years. If we look back to medical device history, technology inventions such as the stethoscope, electrocardiography, and X-ray medical imaging, led to many further innovations and developments in this health care area.

The regulatory authorities mainly from developed countries have defined medical devices categorically to distinguish it from drugs, primarily based on the mechanism of action. The drugs or pharmaceutical products are dependent on pharmaceutical and metabolic pathway. However, medical devices are an extremely heterogeneous group of health care products, mainly function by physical, mechanical, or thermal means for their primary intended effect.² The combination products

like drug eluting stents or bone cements containing antibiotics, where a drug component that assists in achieving the primary intended effect of the device by pharmacological means.

This article revisits the definition and risk-based classification of medical devices, Drugs and Cosmetic Act 1940 pertaining to medical devices, and International Organization for Standardization (ISO) 14155 guideline. It also highlights the changes proposed for medical devices in Drugs and Cosmetic (Amendment) Bill 2013.

MEDICAL DEVICES: DEFINITION

The ISO document - ISO 14155:2011(E)- "Clinical investigation of medical devices for human subjects - Good clinical practice (GCP)" defines medical devices as:³

1. Any instrument, apparatus, implement, machine,

appliance, implant, 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
 - b. Diagnosis, prevention, monitoring, treatment, or alleviation of disease
 - c. Diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury
 - d. Investigation, replacement, modification, or support of the anatomy or of a physiological process
 - e. Supporting or sustaining life
 - f. Control of conception
 - g. Disinfection of medical devices, and
2. Which does not achieve its primary intended action in or on the human body by pharmacological, immunological, or metabolic means, but which may be assisted in its intended function by such means.

United States Food and Drug Administration (US FDA) under the section 201 (h) of the Federal Food Drug and Cosmetic (FD and C) Act, defines medical device similar way.⁴

In India, medical devices are regulated under Drugs and Cosmetic Act 1940 and Rules 1945, and are defined as “devices intended for internal or external use in the diagnosis, treatment, mitigation or prevention of disease or disorder in human beings or animals, as may be specified from time to time by the Central Government by notification in the Official Gazette, after consultation with the board.”⁵

MEDICAL DEVICE: CLASSIFICATION

Regulatory authorities across the world have classified medical devices based on various factors such as associated

risk, level of control necessary to assure safety and efficacy, as well as the device designs. US FDA has classified medical devices into three categories (Table 1).⁶ Other developed regulatory authorities such as UK, European Union and Australia also classify medical device on the basis of associated risk.⁷⁻¹⁰ Current Drugs and Cosmetic Act 1940 does not classify the medical devices. However, the amendment bill 2013 has given provision to classify devices if required. The Association of Indian Medical Device industry has proposed a risk-based classification in the draft amendment to Schedule M-III of Drugs and Cosmetic Act 1940.¹¹

Devices as “drugs” in drugs and cosmetic act 1940

An import, manufacture, sale and distribution of medical devices are regulated in India under the provisions of the Drugs and Cosmetic Act 1940.⁵ However, not all the medical devices are regulated but the devices which are notified under the Drugs and Cosmetic Act, through various gazette notification, are listed in Table 2. In addition, other products such as blood grouping sera, ligatures, sutures and staplers, intra-uterine devices (Cu-T), condoms, surgical dressings, tubal rings, umbilical tapes, and blood/blood component bags are regulated as “drugs” under Drugs and Cosmetic Act.¹² All notified devices cannot be imported only for demonstration purpose.

A “new” medical device is one which does not have a predicate medical device registered and/or approved in India. A “predicate” medical device has the same approval indications or intended use as the device which is proposed for registration in India. It is registered or approved in India and has similar material of construction and design characteristics. Notified medical devices for which predicate devices are not registered in India are classified as “new”

Table 1: Classification of medical devices.

US FDA	<p>Class I: Minimal risk involved, general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device</p> <p>Class II: Complex in design compared to Class I, required special controls such as the promulgation of performance standards, post-market surveillance, patient registries, etc., to assure safety and effectiveness of the devices</p> <p>Class III: Insufficient information exists to provide reasonable assurance of its safety and effectiveness which is usually provided by general or special controls, needs regulatory approval before marketing, device presents a potential unreasonable risk of illness or injury, are for life-sustaining or life-supporting</p>
EU	Classified on the basis of potential risk associated with the medical devices, ranging from low risk to high risk. Class I (including I sterile and I measure), Class IIa, Class IIb, Class III. EU directives also classify devices in various ways (e.g., Duration of contact with the body, degree of invasiveness and local vs. systemic effect)
India (as proposed in Schedule M-III by AIMED)	<p>Class A: Low risk</p> <p>Class B: Low - Moderate risk</p> <p>Class C: Moderate - High risk</p> <p>Class C: High risk</p>

US FDA: United States Food and Drug Administration, EU: European Union, AIMED: Association of Indian Medical Device

medical devices. These medical devices are referred to the Medical Device Advisory Committees (MDAC) to comment on safety, effectiveness, essentiality, and desirability of proposed new devices. Currently, MDAC reviews new medical devices under various specialties—Cardiovascular, Dental, Ophthalmic, Orthopedic, Reproductive and Urology and Miscellaneous Devices Committees.¹³

Drugs and cosmetic (amendment) bill, 2013

Drugs and Cosmetic Act, 1940 is currently under revision. The Drugs and Cosmetic (Amendment) Bill, 2013 has been submitted to Indian parliament for approval. The key highlights of the bill with respect to medical devices are as follows.¹⁴

1. Change in title: Addition of “medical devices” to the short and long title of the act, which now read as “an act to regulate the import, export, manufacture, distribution and sale of drugs, cosmetics and medical devices to ensure their safety, efficacy, quality, and conduct of clinical trials and short title amended as “Drugs, Cosmetic and Medical Devices, Act 1940”
2. Medical Device Technical Advisory Board has been introduced
3. The definition for medical devices is similar to ISO 14155:2011(E) with additional three points to the above definition; accessory to devices, devices used for

4. Medical device clinical trials defined as “the systematic clinical investigation or study of a medical device, investigational medical device or a new medical device, in or on human subjects to assess the safety or performance of the medical device.”
5. Bill also defines investigational medical devices as “a device, which is an object of a clinical investigation or research or development involving one or more subjects to determine the safety or effectiveness of a device.”
6. New chapter IIA on “import, manufacture, sale, distribution, and export of medical devices” has been inserted.

ISO 14155: GCP for clinical investigation of medical devices

In the absence of uniformity in regulatory requirements around the world for conducting medical devices clinical trials, the challenges such as generating quality data and acceptability of clinical trial data generated in other countries, would become a major hurdle for sponsors to get regulatory approvals for marketing as planned.

ISO is a worldwide federation of national standard bodies, preparing International Standards for various activities. ISO 14155 was prepared by Technical Committee ISO/TC 194, Biological evaluation of medical devices, which provides guidelines for requirements for clinical investigation of medical devices. The principals of ISO 14155 standards are similar to ICH E6 Guideline for GCP guidelines. This International Standard addresses GCP for the design, conduct, recording, and reporting of clinical investigations carried out in human subjects to assess the safety or performance of medical devices for regulatory purposes. It specifies the procedures/requirements for clinical trial/investigations of medical devices to safeguard patients participating in the clinical investigations, ensure scientific conduct of clinical trial and generation of reliable clinical data defines the roles and responsibilities of sponsors and investigators. This standard also assists them and other stakeholders such as ethics committee, and regulators involved in the conformity assessment of medical devices.³

Clinical studies of medical devices

The primary objectives of the clinical trials of medical device are the risk assessment through safety analysis and the performance of the device. Unlike drug development process, there are three stages in clinical development of medical devices (e.g., a new medical device or change in design) are:¹⁵

1. Exploratory clinical study: First in human or feasibility studies
2. Pivotal clinical study: To assess the safety, effectiveness/performance of medical device

Table 2: List of notified devices under Drugs and Cosmetic Act 1940.

Name of the device	Gazette notification number	Date of notification
Disposable hypodermic syringes	GSR 365 (E)	17-03-1989
Disposable hypodermic needles	GSR 365 (E)	17-03-1989
Disposable perfusion sets	GSR 365 (E)	17-03-1989
In vitro diagnostic devices for HIV, HbsAg, and HCV	GSR 601(E)	27-08-2002
Cardiac stents	S.O.1468 (E)	06-10-2005
Drug eluting stents	S.O. 1468 (E)	06-10-2005
Catheters	S.O. 1468 (E)	06-10-2005
Intra ocular lenses	S.O. 1468 (E)	06-10-2005
IV cannulae	S.O. 1468 (E)	06-10-2005
Bone cements	S.O. 1468 (E)	06-10-2005
Heart valves	S.O. 1468 (E)	06-10-2005
Scalp vein set	S.O. 1468 (E)	06-10-2005
Orthopedic implants	S.O. 1468 (E)	06-10-2005
Internal prosthetic replacements	S.O. 1468 (E)	06-10-2005

IV: Intravenous, HCV: Hepatitis C virus, HbsAg: Hepatitis B surface antigen

3. Post market study: For design improvement, better understanding of device safety and effectiveness and development of new intended uses.

Indian regulatory authority does not approve the registration of medical device product if it is not being sold in any of the developed countries, i.e., USA, Europe, Japan, Health Canada, or Australia. In such case, clinical trial data on safety and effectiveness of the product generated in India are mandatory for the registration. All applications under classification of “new” medical devices are referred to the specialty specific MDAC to comment on safety, effectiveness, essentiality, and desirability of proposed new devices. MDAC may ask for conduct of clinical trial in India to generate safety and effectiveness/performance data in India.¹²

The way forward

Medical device industry is one of the fastest growing industries in India. Emerging markets such as India and other Asian countries become growth drivers for major medical device companies. The advances in medical devices such as robotic devices, computerized diagnostic systems, various drug-device combinations, artificial organs, etc., have posed a unique challenge to entire healthcare system including regulatory authorities. Hence, Indian regulatory system needs up gradation to meet the challenges such as new product opportunities, product registration process, guidelines for conducting device trial, and device safety surveillance in India. It is now essential to establish effective regulatory framework to safeguard patients and help industry stakeholders such as surgeons, hospitals (government and corporate), and device companies. Medical device industry also needs to be proactive to acquire growth opportunity. Like pharmaceutical industry, the specialized functions such as medical affairs, clinical operations, health economics, and market access have to be established within the device industry to take the advantages of growth opportunities as well as to manage the challenges such as local evidence generation and device safety.

Indian regulatory authority has taken the right step by establishing MDAC/Expert Committees and amending Drugs and Cosmetic Act 1940 to include medical device as a separate entity. However, the amendment – Drugs and Cosmetic (Amendment) Bill 2013 is still to see the light. The need of the hour is to create a platform for all the stakeholders to leverage the growth opportunity in the medical device field.

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