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Requirements for introducing Medical devices in India and US market - A comparative study of regulations

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ABSTRACT

Medical devices are widely used in the healthcare sector and are manufactured by the pharmaceutical industry. The Government of India has periodically come out with certain guidelines, to be followed by the companies that are manufacturing medical devices. There are some challenges which have to do with the medical devices. Medical devices are designed by manufacturers in answer to the demands and expectations of doctors. They are then evaluated by doctors and are used in patients. Phase I trials are not possible for them as they cannot be tested on healthy volunteers. Adverse Drug Reactions are not detected in medical devices as easily as for medicines. There are no separate regulations (apart from Schedule M III of Drugs and Cosmetics Act) for Medical Devices in India before 2017. U.S. FDA has robust regulations for medical devices. If any company wants to market its medical device in the U.S.A, it should be proved to be substantially equivalent to a chosen predicate device that is already there in the market in the USA. This paper studies the current scenario in India and the USA regarding regulations concerning medical devices. It concludes that India cannot have a policy of "accept in India if it is accepted abroad". Acceptance requirement should include certification from Notified Technical Bodies of India. India should have better connectivity between regulators and doctors as far as medical devices are concerned. A National Registry should be developed for each variety of Class D medical devices, such that "recall action", if necessary, can be taken in a fast and systematic manner.

Keywords: USFDA, CDRH, PMA, IDE, PMN, NMD, CLAA, CDSCO, ISO.

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1. Introduction

The present study attempts to review the regulations regarding showing "substantial equivalence" in the USA and showing "conformity" in India in order to get clearance or marketing approval for a medical device. Substantial equivalence is not just a part of the process of getting clearance for marketing approval, but the clearance totally depends on the substantial equivalence. Selection of predicate device or the device, to which equivalence is being shown, plays an important role because the new medical device is compared to one or more predicate devices and the clearance is given by FDA. This research paper attempts to

- To study the regulations and procedures prescribed in India and in the USA regarding showing equivalence of generic medical devices to innovator devices or predicate devices.
- To come out with interpretations and suggestions that would be useful to the society and the pharmaceutical industry.

A medical device is defined according to Schedule M-III of the Drugs and Cosmetics Act. Medical devices are different from drugs. A medical device is defined as a medical tool "which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means". Medicinal products covered by the Drugs and Cosmetic Act will not fall under Schedule M-III. If there is any uncertainty about whether the product falls under the drug or medical device category of the Drugs and Cosmetic Act under this Schedule, regulators will consider the principal mode of action of the products. In India, medical Devices are divided into 4 classes, according to their risk level:

- Class A – low - risk devices

- Class B – low - risk to moderate risk devices
- Class C – moderate to high - risk devices
- Class D – high - risk devices

The medical devices industry in India was unregulated till recent times because of the absence of a medical device specific legislation, specifying standards of safety and quality, for most of the medical devices. However, this has changed with the introduction of the Medical Device Rules, 2017, which became effective on January 1st, 2018. Presently, there are certain medical devices which have been regulated by creating a statutory section. These devices have been deemed as "drugs" by this section. By virtue of this section, a few medical devices get regulated by the Drugs and Cosmetics Rules, 1945. They are referred to as "Notified Medical Devices". It has been clarified by the authorities vide a notification that any device that does not appear in the said list of Notified Medical Devices, does not require any registration certificate or other approval from the authority. If a medical device is safe and performs as intended by the manufacturer and it conforms to the essential principles of safety, and performance, then it would be deemed to be a medical device with conformity assessment.

If any company wants to market a product in the United States, first, the company must determine the classification of the device and the predicate to their device and submit the Substantial Equivalence data in the form of premarket notification 510(K) and premarket application. After submitting the Substantial Equivalence report, FDA starts the decision - making process. It contains parameters like intended use, classification of the device, technological characteristics, safety and effectiveness data. If the device is found to be substantially equivalent to the predicate device, FDA issues approval for market of medical devices in the United State and if the device does not show any equivalence, it will reject the device. If the clearance is not given by the FDA, the medical device cannot be marketed in the United States market.

Global Medical Device Medical Outlook 2018 by Aus Med tech gave the following observations in its review of sales of medical devices in the year 2017-2018: The revenue (in billions of $) of pharma and biotech increased from 1,195 to1,246 and its growth rate is 4.3%; that of medical technologies increased from 371-390 and its growth rate is 5.2%; that of medical imaging equipment increased from 29 to31 and its growth rate is 4.4%; that of in vitro diagnostics increased from 65 to72 and its growth rate is 10%; and that of health care IT increased from 108 to 115 and its growth rate is 6.4% (1).

2. Regulations

The Government of India brought in the Medical Devices Rules 2017 in the year 2017. Till the year 2017, the government was following the Drugs and Cosmetics Act 1940 and its rules and different guidances brought out by the Government of India. Sources such as the guidelines given by USFDA in its web site, power point presentations offered by members of USFDA on its web site, and research articles were searched and studied for the purpose of obtaining material regarding the regulations in the USA. The Centre for Devices and Radiological Health (CDRH) is one among the six branches of the USFDA that governs and controls all aspects of safety and efficacy of food and medicines in the USA. The Centre for Devices and Radiological Health has six branches through which it conducts its operations. The USFDA controls the field of medical devices through the following regulations: (2, 3)

1. Federal Food, Drug and Cosmetic Act

2. Code of Federal Regulations

   a. 21 CFR part 807: Establishment, Registration and medical Device Listing

   b. 21 CFR part 807 subpart E: premarket notification (510k)

   c. 21 CFR part 814: premarket approval (PMA)

   d. 21 CFR part 812: investigational device exemption (IDE)

   e. 21 CFR part 820: quality system regulation (QS regulation)

   f. 21 CFR part 801: labelling

   g. 21 CFR part 803: medical device reporting

The concern of the present research is regarding how the USFDA permits new medical devices entry into its market and regulates on how equivalence has to be shown. The CDRH controls the entry by taking any one of two actions: (a) exempts medical devices, (b) permits any one of two official routes for obtaining authorisation to market medical devices: (1) 510 K premarket clearance and (2) premarket approval. These actions are taken based on the regulations b, c, and, d of 2 described above.

21 CFR part 807 subpart E: premarket notification (510k) (4)

Salient features

This regulation gives the requirements that a manufacturer of a new medical device must follow in order to introduce his/her product into the US market. Any company that wishes to market its new medical device in the US must apply to the USFDA in the form of a premarket submission, i.e., 510(k). This form contains the requirements to be shown to USFDA, to prove that the product is at least as safe and effective as a device that is already marketed in the USA. This device that is already legally marketed in the USA is termed as the "predicate". A company can sell its device only after the device is declared to be substantially equivalent to its predicate. The FDA does not carry out any inspection before giving clearance of substantial equivalence but it conducts inspections after giving clearance for checking for quality. Substantially equivalent means that the new device, in comparison to its predicate has the same intended use and the same technological features as the predicate or it has the same intended use but has different technological features, but these features do not raise new questions of safety. Any company intending to market its device in the USA has to submit this application. These companies have to also follow design controls, which are given by 21 CFR

820.30 when they are carrying out their device development activity. This rule also explains when a 510(k) application is required. It also explains the word "pre-amendment devices", i.e., those devices that were marketed in the USA before May 28, 1976 and were not subsequently modified.

21 CFR part 814: premarket approval (PMA) (5)

Salient features

The USFDA brought in medical device amendments (MDA) in May 1976. FD&C Act, by section 513(a) (1), defined three classes of medical devices, Classes I, II and III. The risk associated with the use of the medical device increases from Class I to Class III. Class I devices require only general controls such as reporting to USFDA about possible adverse effects and giving details of establishment registration and so on. Class II devices require special controls such as post marketing surveillance and reporting of performance standards. Devices belonging to Class III show the highest risk. They are usually used for supporting or sustaining human life. Examples for Class III devices are implantable pacemakers and replacement heart valves. These devices can be introduced into the US market only after obtaining a Premarket Approval (PMA). This is given only after the company carries out a substantial clinical trial, and goes through an advisory panel review and a manufacturing inspection. The PMA is the most stringent type of application needed by the USFDA to generate permission for the marketing of medical devices in the USA. The PMA applicant is usually the owner of the rights on the new medical device. A PMA application must be complete, accurate, and consistent in its content and must be subjected by the company to thorough scrutiny before it is filed with the USFDA. It is a scientific regulatory document, meant to demonstrate the safety and effectiveness of the Class III device. It should have valid clinical information and sound statistical analysis. The data requirements of the PMA are as follows:

Technical sections

These contain data and information under two categories.

1. Non- Clinical Laboratory Studies section: information on microbiology, toxicology, immunology, biocompatibility, stress, wear, shelf life, and other laboratory or animal tests.

2. Clinical Investigations section: This section contains information drawn from clinical studies on humans. The section includes study protocol, safety and effectiveness data, adverse reactions, device failures and replacements, patient information, and statistical analysis. Study protocol must contain all elements described in the device specific guidance documents.

21 CFR part 812: Investigational Device Exemption (IDE) (6)

Salient features

This is an application filed by companies that wish to conduct clinical studies in order to show proof of the safety and efficacy of their products to the USFDA. Companies file this IDE and get it approved before conducting a clinical study. The requirements of a clinical evaluation study are:

- Institutional Review Board (IRB) approval of the plan of investigation.
- If the study contains a high risk, the plan must also get the approval of the USFDA.
- Informed consent must be obtained from all the patient participants.
- Proper labelling
- Monitoring
- Documentation
- Good clinical practices must be followed by the companies while carrying out the clinical studies on medical devices.

Technological Characteristics

The FDA first establishes that there is a valid predicate device and then that the intended use of the new medical device and the predicate device are one and the same. The next step involves comparing the technological features of the new device to the predicate and proving that they are safe.

Step 1: Identification of Technological Characteristics of the New and Predicate device

The manufacturer must clearly describe the technological features of his/her product. These features include materials, design, energy source and such aspects. He/she should provide details regarding similarities in materials, design, energy source and other features.

Features to be described include:

- Design of the device
- Complete description including engineering drawings
- Diagram that explains how all the components work together
- Physical specifications, dimensions and tolerances.
- Purpose of components and features.

Materials

- Complete identification of the detailed chemical formulations (7, 8)
- Additives including colors, coatings, and surface modifications
- Processing activities involved in the materials
- States of the materials

Energy sources

- Energy delivery to the device (batteries)
- Energy delivery that is a part of the functional aspect of the device (laser, radiofrequency, ultra sound)

Other key features

- Software/hardware features
- Density
- Porosity
- Degradation characteristics
- Nature of reagents
- Principle of assay

Step 2: Identification of Differences in Technological Characteristics between the New and the Predicate Device

This involves comparison of

- Detailed specifications
- System-level technological characteristics of the device

This information must be supplied in the form of a table.

Step 3: Determination of whether the differences in technological characteristics raise different questions of safety and effectiveness

If FDA finds that there are differences in technological features between the New Device and the Predicate Device, then, they will

- Review and evaluate all relevant information bearing on such differences to find out whether they raise questions of safety and effectiveness.
- FDA gives examples for such significant differences in its guidelines.

FDA examples (9, 10)

Once these steps are done, FDA starts the decision making process to give approval to the manufacturer to market his/her product. Five decisions are involved regarding five aspects.

Decision 1has to do with whether the new device is compared with a legally marketed predicate device.

Decision 2 has to do with whether the new device has the same intended use as the predicate device.

Decision 3 has to do with whether the new device is having the same technological features as the predicate device.

Decision 4 has to do with whether there are differences in the technological features between the new device and the predicate device, and if they are there, whether they raise any new and different questions of safety and effectiveness.

Decision 5a has to do with whether the methods for evaluation of the different characteristic effects on safety and effectiveness are acceptable.

Decision 5b has to do with whether the data submitted by the manufacturer demonstrates equivalence and supports the indications.

If the USFDA finds that the data submitted is sufficient to take it through the decision process and finds substantial equivalence, then, it will declare so; otherwise, it may ask for more data or may decline to grant substantial equivalence. USFDA must be assured of statutory standard of "reasonable assurance of safety and effectiveness" before it can give approval for marketing.

Table 1: U.S. FDA Examples

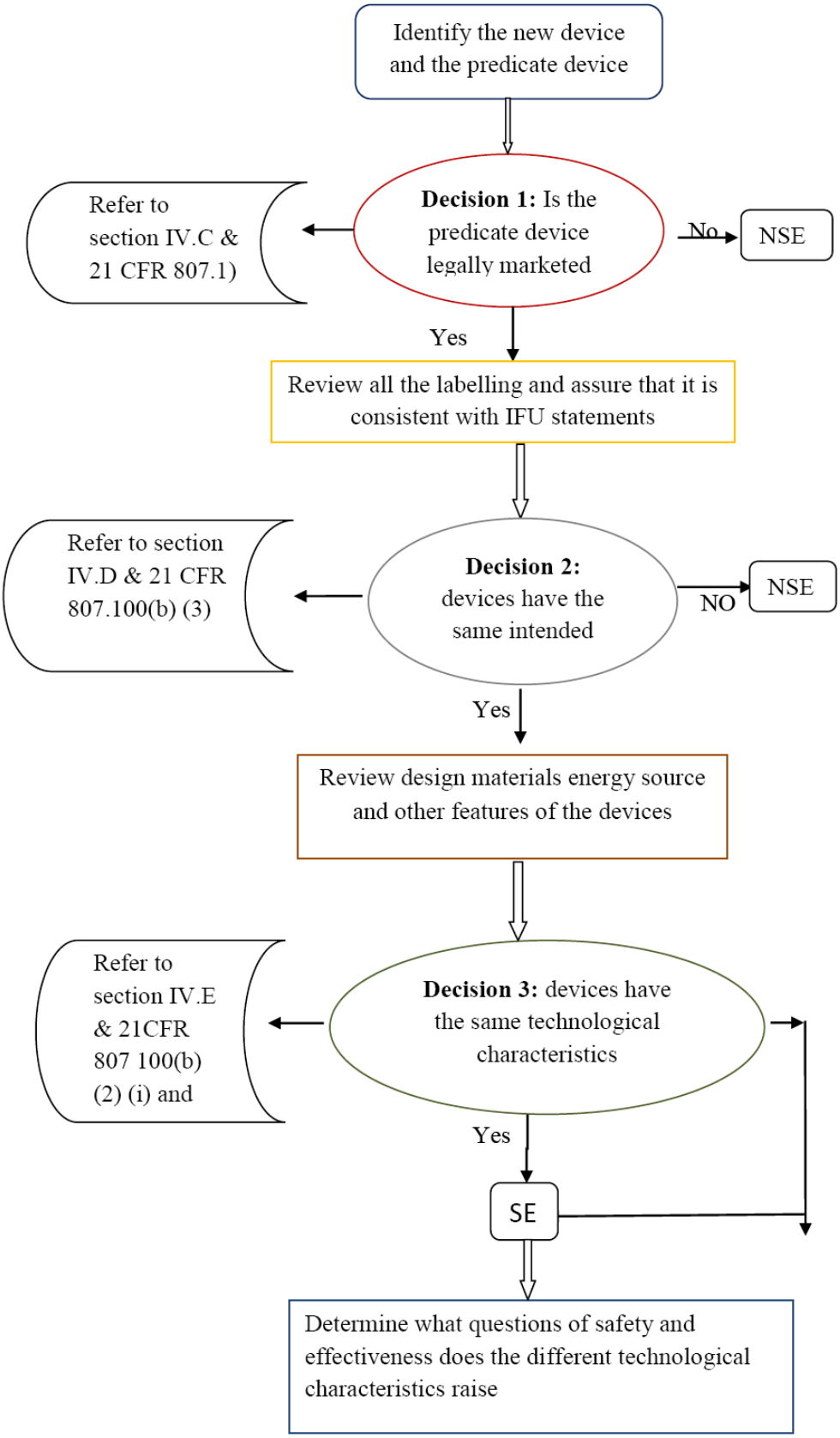
S.no	Device	Use
1.	Biomet, Inc.'s Vanguard TM XP Knee System	1. Painful and disable knee joint resulting from osteoarthritis, rheumatoid arthritis, or traumatic arthritis where one or more compartments are involved. 2. Correction of varus, valgus, or posttraumatic deformity. 3. Correction or revision of unsuccessful osteotomy, arthrodesis, or failure of previous total joint replacement procedure
2.	Gyrus EUro EZdilate Ureteral Balloon Dilation Catheter	It is indicated for "dilation of the urinary tract," which is a function not a disease state. When a device has a tool type indication, the intended use is generally the same as the indication.
3.	Hem dialysis catheter	Blood is put throughout a filter outside the body

3. Medical devices (Indian scenario)

Showing equivalence of new devices to known devices and proving their safety and efficacy, in India, is governed by the following regulations

- Schedule M III
- Guidelines for import and manufacturer of medical devices in India.
- Guidance document on common submission format for import license of medical device in India.
- Requirements for conducting clinical trials of medical devices in India.
- Guidance document on application for grant of license in Form 28 for manufacturer of medical device in India under CLAA (Central Licensing Approval Authority) Scheme
- Draft copy of guidance document for medical devices issued by the Indian Pharmacopoeal Commission, National Co-ordination Center – Materiovigilance Programme of India, Ministry of Health and Family Welfare, Government of India in February 2018

A medical device is defined by Schedule M3 of the Drugs and Cosmetics Act 1940, and Rules 1945.


Identify the new device and the predicate device
Decision 1: Is the predicate device legally marketed
Refer to section IV.C & 21 CFR 807.1)
No
NSE
Yes
Review all the labelling and assure that it is consistent with IFU statements
Decision 2: devices have the same intended
Refer to section IV.D & 21 CFR 807.100(b) (3)
NO
NSE
Yes
Review design materials energy source and other features of the devices
Decision 3: devices have the same technological characteristics
Refer to section IV.E & 21CFR 807 100(b) (2) (i) and
Yes
SE
Determine what questions of safety and effectiveness does the different technological characteristics raise

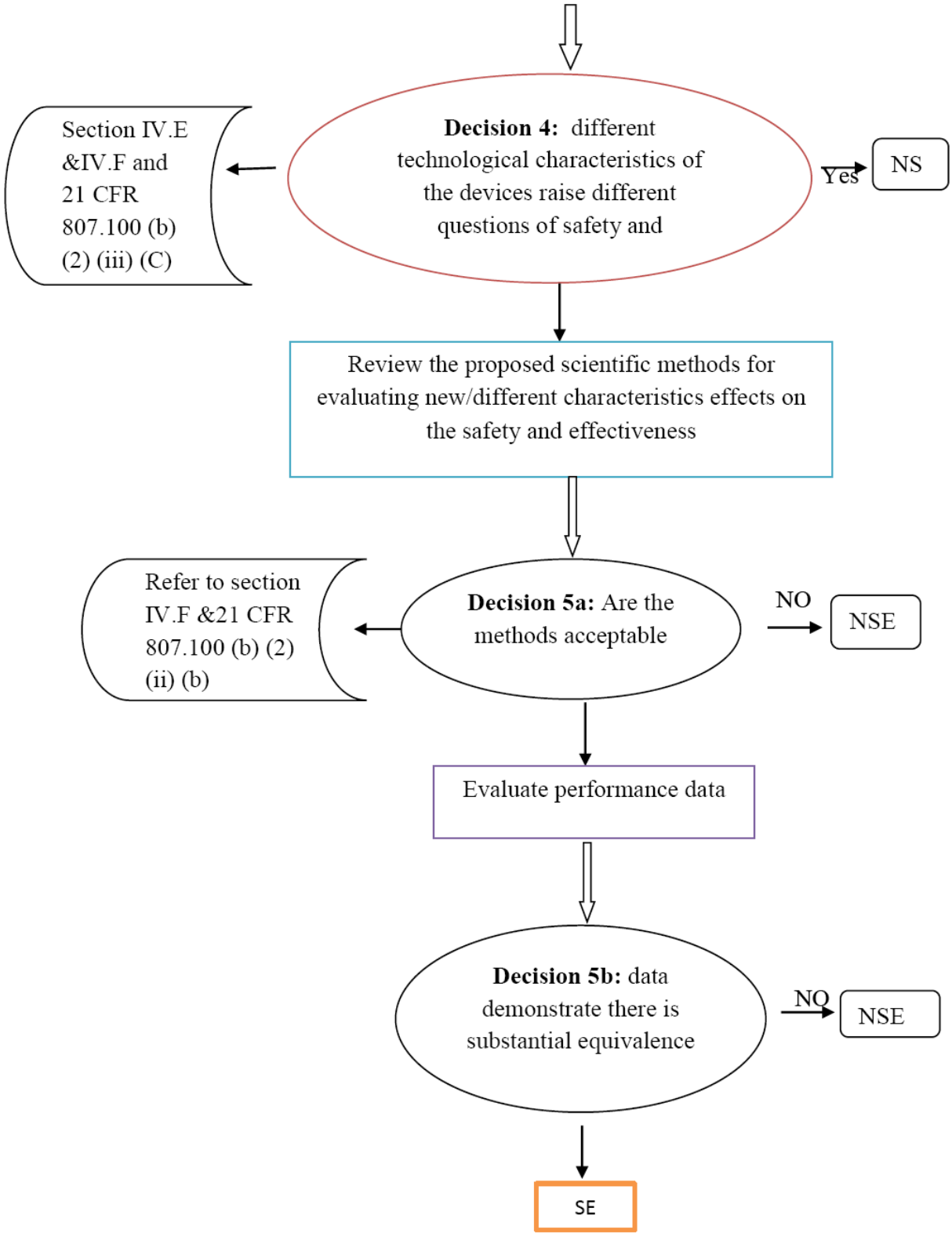


Figure 1. Decision making process flow chart (9)

It is defined as a "medical tool" and is differentiated from a drug or a medicine in this way: it "does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means".

Salient features of different regulations in India Schedule M III (11)

- Classifies medical devices into A, B, C and D.
- Class A includes- low risk devices such as thermometers.
- Class B includes low to moderate risk devices such as hypodermic needles.
- Class C includes moderate to high risk devices such as lung ventilators.

- Class D includes high risk devices such as heart stents.

The Central Licensing Approval Authority (CLAA) which is a branch of CDSCO is the main regulatory body for medical devices. All new medical devices must undergo conformity assessment and the manufacturer must provide proof of standards of their quality and safety. Then only they will be allowed into the Indian market.

The CLAA will adopt the regulatory standards of the Bureau of Indian Statistics (BIS) and those of the International Organization for Standardization (ISO).

The new devices must be so manufactured that they can achieve their intended purpose and are acceptable with respect to the health and safety of patients.

Requirements with respect to different classes (11)

- Class A: manufacturers may carry out their own conformity assessment procedures.
- Class B, C and D: CLAA in consultation with BIS will publish a list of notified bodies. These bodies will perform the conformity assessment.
- Manufacturers of medical devices must submit an application for assessment to one of these notified bodies, which include technical documentation, corrective and preventive action procedures as well as information about the organization and goals of the business.
- Names of clinical investigators and further information are required in applications of Class C and D devices.
- After receiving all the application materials, the notified body will examine and assess whether the device conforms to BIS and ISO standards. They also conduct sudden audits of manufacturing process.
- The medical devices that meet all the standards will bear the Indian conformity assessment certificate mark, which will allow them to move freely in the Indian market.
- For imported devices separate conformity assessment is not necessary, if they have already been approved in the US or in the EU that they are equivalent to an EU market or FDA approved device.

Clinical trials (11)

Clinical trials and clinical evaluation of medical devices in India are carried out as per Global Harmonization Task Force (GHTF) guidance. This task force contains members from countries like USA, Australia, Japan, Canada and European Union. Industry follows the recommendations of the GHTF study group on clinical evaluation and investigations.

- All the general principles of clinical trials described for drug trials should also be considered for trials of medical devices.
- The safety, evaluation and premarket efficacy of devices with data on adverse reactions for 1- 3 years should be obtained for medical devices before they can get premarket certification.
- The duration of the trial and extent of use may be decided on case to case basis by the appropriate authorities.

Important factors

- Safety data of the medical devices in animals should be obtained.
- Phase 1 trials are not necessary for medical devices because they cannot be conducted on healthy volunteers.
- Medical devices used within the body (orthopaedic pins) may have greater risk potential than those used on or outside of the body (crutches).
- Medical devices that are not used regularly (contact lenses) have lesser risk potential than those used regularly (intraocular lenses).
- Safety procedures should be followed while introducing a medical device into a patient's body.
- Informed consent procedures should be followed.

Technical data should be submitted along with the application for the subject medical device:

- For all medical devices

a. Design analysis data

b. biocompatibility data

- For moderate or high risk medical devices

a. Phase I study

b. Phase II study

Salient Features of Guidance Document on Medical Devices (2018) (12)

Definition of Conformity Assessment

Conformity assessment means the systematic examination of evidence generated and procedures undertaken, by the manufacturer to determine that a medical device is safe and performs as intended by the manufacturer and therefore conforms to the essential principles of safety and performance for medical devices.

1. Purpose
   - Definitions
   - Notification of Central Licensing Authority, State Licensing Authority and Notified Bodies.
2. Classification of Medical Devices
3. Essential Principles
4. Quality Standards for Medical Devices
   - Conformity Assessment
5. Life Cycle and Technical Standards
6. Post Market Vigilance and Safety Requirement

These are two sections which are issues of concern in this guidance, with relevance to the present research

paper, namely, Essential Principles and Conformity Assessment.

Essential Principles applicable to all medical devices, IVD medical devices (3.1) (12)

Section 3.1.1

- Medical devices should be designed and manufactured in such a way that, when used under the conditions proposed, for the purpose intended, they will perform as intended by the manufacturer. They should not compromise the safety of the patients. Any small risk should be an acceptable risk when weighed against the benefit caused by the usage of the device.
- The manufacturer should design and manufacture the device in such a way that it conforms to standards of safety. He/she should control the risks. Any residual risks should be acceptable.

The following are some of the risk reduction principles:

- Estimate the associated risks arising from the intended use and misuse and identify them.
- Eliminate risks through safe design and manufacture.
- Reduce the risks by taking protective measures like alarms and inform users of any residual risks.

Section 3.1.3

Medical devices should be designed to achieve the performance intended by the manufacturer. The devices should be so prepared that under normal conditions, they are suitable for their use.

Section 3.1.4

The characteristics and performances of the devices should not be affected as long as the patients maintain them properly during their use. They should not be affected by normal stress conditions.

Section 3.1.5

Medical devices should be designed in such a way that they are not affected by stress conditions during transport. Their characteristics and performances should not be affected as long as they are transported under conditions suggested by the manufacturer.

Section 3.1.6

All known risks and any undesirable effects, should be minimised.

Section 3.1.7

Every medical device requires clinical evidence to support its classification and intended use.

This guideline gives the essential principles to be followed for ensuring the safety and standards of the devices. It also gives voluntary and mandatory standards, standards development process, conformity assessment with standards, national and international standards system, current trends in the use of standards in medical device regulation, and standards of notified medical devices.

It notifies the names of some notified bodies that are authorised to carry out all the clinical trials and audits. These bodies carry out the trials and submit their data to CLAA.

Section 9.5

Conformity Assessment with Standards (12)

The following are the four common methods for assessing conformity to standards:

- Direct testing for conformity to standards.
- Determination by audits. Regulatory authorities attest that products/processes conform to a standard by authorizing the display of their certification mark.
- Formally established audit procedures supported by technical experts of the domain conduct audits. This is known as management systems registration. Management system registration bodies (Registrars) issue registration certificates to companies that meet a management standard such as ISO9000, or to medical device manufacturers that meet the ISO 13485/ISO9001 standards.
- An authoritative body is accredited to give formal recognition that an organization or a person is competent to carry out a specific task. Examples of

Table 2: Examples of Medical Devices introduced in India in 2017 (13, 14)

S.no	Drugs	Device name	Risk class	General intended use
1.	Ablation device	RF conduct MR steerable electrode catheter	Class C	It is intended for intracardiac ablation
2.	Bone cements	Bone cement	Class C	Intended for use in arthoplastic procedures of the hip, knee, and other joints for the fixation of polymer or metallic prosthetic implants to living bone
3.	Cardiac stents	Coronary stent	Class D	A coronary stent is 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
4.	Cardiac stents	Bioresorbable scaffold (BVS) system	Class D	An adorable stent which is placed into a blood vessel (coronary artery) during angioplasty to help keep the coronary artery open
5.	Cardiac stents	Bifurcation stent	Class C	Intended for improving the side branch luminal diameter of arterial bifurcation liaisons

6.	Catheters	Fiberoptic oximeter catheter	Class B	Intended for monitoring the balance between oxygen delivery and consumption at the bedside
7.	Catheters	A-V shunt or Fistula Adaptor	Class B	A blood access device and accessories is a device intended to provide access to a patient's blood for haemodialysis or other chronic uses
8.	Catheters	Transcervical (amino scope) endoscope	Class B	It is device designed to permit direct viewing of the foetus and amniotic sac by means of an open tube introduced
9.	Disposible perfusion sets	Y-connecter as an accessary to perfusion sets	Class A	It can be used to connect to a perfusion sets or catheter for infusion of contrast media etc.
10.	Disposible perfusion sets	Iv flow regulator	Class B	An iv system and administration device offering precision care and consistent delivery

4. Discussion

Medical Devices have helped the doctors immensely in diagnosis as well as in treatment. Their role in the healthcare field, especially in the field of orthopaedics, is phenomenal. But the regulatory field regarding control of medical devices has not kept pace with the rate at which the medical devices industry is growing. Till a few years ago medical devices were also treated as drugs and were controlled by the sections of Schedule M III of the Drugs and Cosmetics Act. The Central Licensing Approval Authority (CLAA), a branch of CDSCO, served as the main regulatory body for medical devices. Medical Devices are expected to undergo conformity assessment and the regulatory standards are given by the Bureau of Indian Statistics (BIS) and the International Organization for Standardisation (ISO). Medical devices that conformed to proper standards are given the Indian Conformity Assessment Certificate Mark. This mark allowed them to be freely marketed throughout India. A new draft copy of a guideline was introduced in 2018. This guideline enunciated certain essential principles and defined Conformity Assessment. It said certain centres would be notified as notified bodies and they would carry out clinical trials and submit data to the CLAA which would pronounce the decision on the acceptability of the medical device.

As opposed to this, rather liberal system in India, the USA has very systematic and rigorous procedures that govern the standards of medical devices in the USA, since a few decades. Very clear guidelines and presentations with examples help the manufacturers of medical devices to conduct their clinical trials and submit their data in a proper format.

Medical devices are sometimes implanted in the bodies of patients and their structure, sterility and composition are to be very strictly controlled. It appears that in India, till now, the structure and composition of implantable medical devices are only issues between the manufacturers and the doctors. Manufacturers learn the needs from the doctors and suitably engineer their products. The patient is a passive acceptor with no knowledge of the complexities of the system that is being planted in his/her body.

The regulatory mechanism with respect to granting permission for sale to companies that show conformity assessment, the mechanism to look out for adverse reactions and the mechanism to do a recall is not as clear, simple and transparent as the mechanism for drugs. The issue regarding a faulty hip implant that caused a debilitated life in several patients that was reported in popular press (The Hindu, 15th September, 2018) is given below to illustrate the point made above.

The medical device in question is a metal-on-metal (MOM) articular surface replacement (ASR) hip by DePuy, a subsidiary company of the global pharmaceutical company Johnson & Johnson (J&J). J&J observed in the year 2010, eight years ago, that this device, ASR was a failure, and recalled it globally. The medical device was a failure for two reasons, it left large quantities of metal debris in the body and it had a very high failure rate. The device on being placed in the body leaches metals, like cobalt and chromium. These cause severe pain, neuropathy, fluid accumulation and metal poisoning. The company, J&J, recalled the product and tried to reach out to the several doctors in the world who have already implanted the ASR in patients, to advise them to remove the device by surgery. But there was no response from India. The number of patients in India, who received this faulty implant, is 4500. These people did not come to know of the recall and they suffered in silence. All the institutions who should take active part in the recall, the implant manufacture, doctors, drugs regulators and the government systematically neglected the patients and their suffering. The patients trusted the doctors and the doctors failed them.

In 2006, the Drug Controller General of India (DCGI) granted permission to implant and market Depuy's ASR hip implant. In 2009, in India, distributors were busy marketing this product to Indian doctors. In this year, Australia withdrew it from its market. The Australian Orthopaedic Association's National Joint Replacement Registry gave an alarm regarding the failure rate of this device. The cost of a single MOM implant could be anywhere between Rs. 90,000 to RS. 1.2 lakhs and the range of the cost of the procedure is Rs. 2.5 lakhs to RS.4 lakhs. Failure of Regulatory Bodies: The FDA of Maharashtra filed a case against J&J in 2011. They sent this issue to the CDSCO. So, the CDSCO knew of this issue from 2011 onwards. CDSCO took two years to issue a "medical device alert". The ministry concerned formed a committee to probe the issue in February 2017.

They gave a report in January 2018. The findings are:

- The committee found J&J evasive and delaying the passing of information about the failure of ASR.

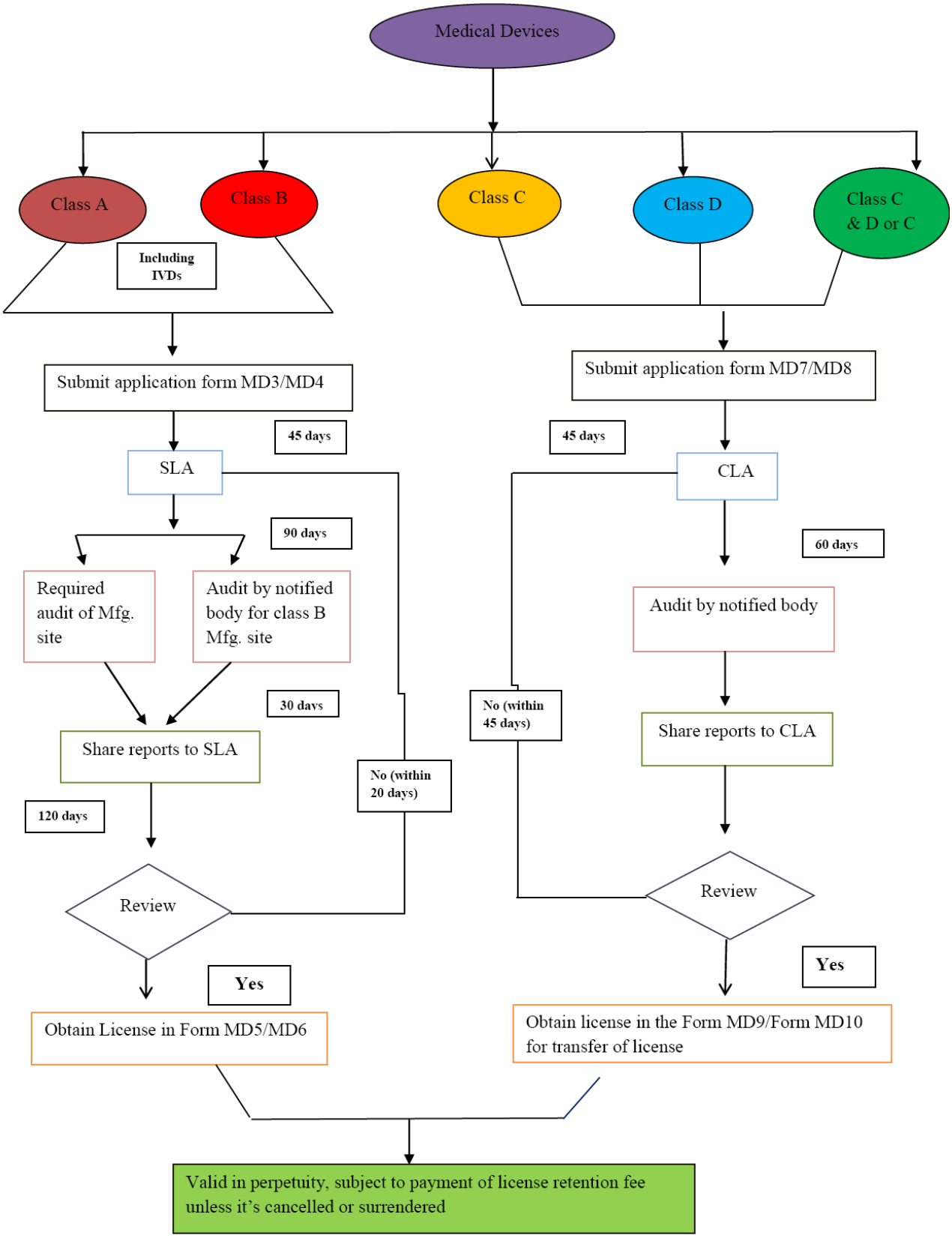


Figure 2. Regulatory approval process for manufacture/distribution of medical devices (12)

- A base compensation of Rs. 20 lakhs is to be given by J&J to each and every one of all the affected patients.
- The CDSCO did not react with the urgency that was required. They showed negligence.
- The blame is on the "deep-seated necrotic rot" commandeered by the pharmaceutical industry. This is the reason for the regulator turning a blind eye.
- Blame is on the pharma company, on the doctors and on the regulators. (15)

Innovation is the key to progress today. Several educational institutes in India are coming out with advances that are trying to integrate the advanced fields of technology and digitalisation and basic fields such as physics and chemistry. They are working as multidisciplinary teams to come out with medical devices that are extremely useful in the healthcare field. A good example is a device developed by a team of chemists from IIT-Bombay. They developed a platform that detects volatile organic compounds such as benzene, acetone, benzaldehyde, and ethanol in a gas phase at single molecular levels. This equipment can be used to detect lung cancer in its early stages and also to detect the presence of explosives (16).

These types of devices are necessary for good healthcare. But at the same time, their testing for clinical safety, efficacy, and their testing for validation is also necessary. The regulations on medical devices should be notified to make them more rigorous. Devices certified abroad should be certified in India only after they undergo some trials such as Phase III trials. The direction given by the highest court of India, the Supreme Court, to the CDSCO, seeking its response on why the medical device called articular surface replacement (ASR) was introduced into the market, without due procedure, must be perceived with significance, in this regard (17).

5. Conclusion

1. India cannot have a policy of "accept in India if it is accepted abroad". It should have its own robust mechanism for making conformity assessment. Acceptance requirement should include Phase III trials and certification from Notified Technical Bodies of India.

2. India should have better connectivity between regulators and doctors as far as medical devices are concerned. Doctors should be accountable for every device they implant into the bodies of patients. This is especially important for Class D products.

3. The system adopted by the Australian Orthopaedic Association of having a National Joint Replacement Registry gave the timely alarm in Australia. Such registers must be started in India either by professional associations of doctors or by the CDSCO.

4. Innovative devices useful in healthcare are necessary. The CDSCO must come forward and give assistance to innovators so that they can introduce their products in a fast manner, especially, if they belong to Class A or Class B.

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Conflict of interest

The authors declare that there are no conflicts of interest.

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