

OVERVIEW OF MEDICAL DEVICES AMENDMENTS 2017 IN INDIA WITH EMPHASIS ON IN-VITRO DIAGNOSTICS

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Article Received on
08 July 2018,
Revised on 30 July 2018,
Accepted on 20 August 2018
DOI: 10.20959/wjpr201816-13217

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ABSTRACT

In the last two decades, the Medical Devices Industry has undergone a transformation - from being a domestic-industry- dominated sector prior to 1991 to import-dependent sector, to being a non-regulated sector prior to 2006, to regulation of 15 notified devices, to the new Medical Device Rules announced in 2017. The government has taken various steps to ensure that the medical devices sector is considered as significant as the other sectors. The new set of regulatory practices aims to prepare India to meet the medical devices sector requirements such as safety of patients, capping of devices, availability of safe devices, strict clinical investigation protocols to increasing innovations, ease of doing business and meeting international requirements. This article provides a comprehensive review of the

major high lights of medical devices bill 2017 with focus on medical devices and in vitro diagnostics, describing the major changes and various procedures from applying for certificate to manufacture medical devices to import.

KEYWORDS: Medical Devices, Import Policy, Notified Bodies, Diagnostics Equipment, Japan, USA.

INTRODUCTION

Medical devices are instruments, apparatus, appliances, software, material, in vitro reagent that can be used alone or in combination for prevention, diagnosis or treatment of a disease for human beings. It aids in assessing, rectifying and modifying the structure or function of the body. It is also used for the purpose of supporting and sustaining life. The purpose of a medical device cannot be achieved by any pharmacological, immunological or metabolic

means alone. Medical devices range from a variety of devices such as bandages, cardiac stents, pacemakers, optical imaging devices, catheters, surgical gloves etc.^[1-3]

Indian medical device industry is currently valued at USD \$ 5.2 billion and is growing at a compound annual growth rate (CAGR) of 17%. India is counted among the top 20 global medical device markets and 4th largest in Asia.

Medical devices market can be broadly classified into four major sectors^[4]:

Table 1: Major sectors of medical devices.

Sector	Examples of devices
Diagnostic Imaging and equipment	Computed topography, Magnetic resource imaging, positron emission tomography, Ultrasound and X ray machines
Consumables and Implants	Catheters, hypodermic needles, infusion pumps, optical lens, cardiac stents, heart valves, orthopedic implants
Patient aid equipment	Ventilators, Incubators, Dialysis machines
Instrument and appliances	Anesthesia machine aspirations, Suction pumps, Autoclave/ Sterilizer, Blood chemistry analyzer, C-arm system unit, monitor, table, Cast saw, Centrifuge, Coagulation analyzer

Most of the medical devices are imported in India. The market contains about 70% of imported products. Liberalized government policies have allowed up to 100% foreign direct investment (FDI) by the automatic route. USD 1.57 billion worth FDI came into the country between April 2000 and March 2017. An increasing number of multinational companies (MNCs) are setting up their manufacturing bases in India due to this. Supportive state- level policies as well as the availability of skilled labor have paved way for emergence of new medical device clusters.

REGULATION OF MEDICAL DEVICES GLOBALLY

Globally, medical devices were controlled by Global harmonization task force (GHTF) which was established in 1992. The organization was disbanded in 2012 and has been taken over by the International Medical Device Regulators Forum (IMDRF), a successor organization composed of officials from around the world.^[5]

Europe

In Europe, four directives cover the medical device sector. A directive is an instruction to the member states of the European Union (EU) to implement a law through national regulations.

The first directive, 90/35, was concerned with active or powered implants. It was followed by the main general medical device directive, Directive 93/42, and then more recently by Directive 98/79, which covers *in vitro* diagnostics, and Directive 2000/70, which covers human blood and plasma derivatives. More detailed implementing directives (there are five in Europe) will be enacted by the European Commission, considering the views of the member states.

Those directives are known in Europe as New Approach legislation. That legislation covers all consumer goods except pharmaceuticals. The New Approach incorporates self-regulation and imposes the minimum level of regulation that is necessary to protect public health. The legislation reflects the dynamics of the device industry, which are different from those of the pharmaceutical industry.^[6]

Japan

Japan has been changing both its pharmaceutical and its device legislation following the GHTF classification. The Japanese, like the Europeans, have been using third-party certification for class II devices, and Japan has designated 12 certification bodies. Japan's Ministry of Health, Labor and Welfare (MHLW) receives a dossier at a superficial level and decides whether it is appropriate for third-party assessment. After reviewing a favorable report from a third-party assessor, MHLW issues a certificate. Using the GHTF principles, the third-party assessors use the Summary Technical Documentation for Demonstrating Conformity to the Essential Principles of Safety and Performance of Medical Devices (STED) for the product application.^[7]

China

Medical devices are controlled by both the central State Food and Drug Administration (SFDA) and local provincial controls. The system is risk-based and similar to that in India in that class II and class III devices undergo sample testing (type testing) in an approved laboratory. Selected products are required to undergo further clinical evaluation in designated SFDA-approved hospitals.

The SFDA has its own evaluation center and its own expert technical committees. Chinese regulations require a local, Chinese-based distributor. Inspections are handled by provincial authorities. In the case of overseas manufacture, the country of origin must attest its approval.

For example, a US-based company cannot bring a new device into China if it is not already registered with the US FDA.^[8-10]

REGULATION OF MEDICAL DEVICES IN INDIA

Before 2005

In India, there were no regulations for medical devices before 2005. Medical devices were considered as “Drugs” under the Drugs and Cosmetic Act 1940. These devices were subjected to the restricted code/ laws of the pharmaceutical sector. Lack of specific regulatory framework resulted in poor quality as compared to global standards. In 2004, the Mashelkar Committee called for the creation of a specific medical devices division within the Central Drugs Standard Control Organization to address the management, approval, certification and quality assurance of medical devices.^[11] Prior to 2005, only medical devices such as disposable hypodermic syringes, tubal rings, condoms, metered dose inhalers, were required to be registered in India.

Amendments in 2005

In October 2005, the manufacturing of devices came under the control of the Central Licensing Approving Authority. It declared 10 devices, such as cardiac stents, drug-eluting stents, catheters, intraocular lenses, bone cements, heart valves, scalp vein sets, orthopedic implants, internal prosthetic replacements to be considered drugs under section 3 (b) (iv) of the act. A period of 60 days was provided to importers to make application for import and registration of devices. It required good manufacturing practices by the manufacturers to ensure quality of the devices. The rules were approved by the Ministry of health and family welfare and were to be enforced by the Drug controller general of India.^[12]

Amendments in 2006

In 2006, the Medical Device Regulation Act was recommended to consolidate laws for medical devices and to establish the Medical Device Regulatory Authority of India (MDRA), at New Delhi for establishing and maintaining a national system of controls relating to quality, safety, efficacy, and availability of medical devices that are used in India, whether produced in India or elsewhere and exported to India. The bill was proposed by the Ministry of Science and technology. MDRA consisted of 9 members appointed by the Central government. CDSCO notified 15 medical devices for which registration was required. Risk based classification was introduced. It also introduced the application of quality management systems, certification of compliance, monitoring and inspection of design of medical devices.

The Central Government, by notification, shall establish one or more tribunals to be known as the Medical Device Safety Appellate Tribunal (MDSA) to hear appeals from the decisions of the MDRA. It was recommended that the provisions of this Act should come into force by December 31, 2009, but the bill was not passed by the Rajya Sabha and the bill was abolished. It was expected that a definition of medical devices and other likely changes shall be incorporated in Schedule M(III) by 2010. With the initiation of such amendments, it was addressed to include medical device with the Drugs and Cosmetics Act and Rules in a press released from the Medical Device Regulatory Authority of India.^[13,14]

Amendments in 2007

CDSCO in 2007 notified that for registration of medical devices approved in other countries, a free sale certificate is mandatory which have to be issued by the ministry of health or national regulatory agency of the country of origin. Along with it, approval of drug controller general of India (DCGI) must be obtained before doing any change in the design, material or composition of pre- registered device.^[15]

Amendments in 2008

A draft notification was released in February 2008 which states that the manufacturer should comply with good manufacturing practices (GMP) and requirements of premises, plants and equipment as specified in Schedule M-IV. The schedule M-IV was inserted after schedule M-III.

It stated that each licensee should evolve appropriate methodology, system and procedure which shall be documented and maintained for inspection and reference. The manufacturing premises should be specifically used for production of in -vitro diagnostic reagents/ kits and or no other manufacturing activity should be carried out in the premises. It contained the requirement criteria for location, buildings, premises, water system, waste disposal, warehousing area, storing facilities, ancillary areas, A notification was also released in June 2008 which stated that a group or family of devices manufactured by or for the same manufacturer and which has the same basic design, performance characteristic relating to device safety, effectiveness of the device and its intended use (which includes variation in sizes and shapes) would be considered one single device for the purpose of registration of medical devices and to calculate the fees required to be deposited with the application. A device may also include package of various devices or sub systems that are required to be used together as a single functioning device.^[16]

Amendments in 2009

Central Drugs Standard Control Organization (CDSCO) clarified that sterile medical devices such as endotracheal tubes, cardiac patches, spinal needles, insulin syringes, and extension tubes were also required to be registered. and included another 19 sterile medical devices (on March 20, 2009) such as extension tubes, arterial venous fistulas and spinal needles, volume measuring sets, heart lung packs, and so on, under the provisions as such.^[17]

Amendments in 2010

For medical device product registration, CDSCO released new guidelines for document submission on August 04, 2010 under which medical devices requiring registration need approval from the DCGI and evaluation should begin after receipt of the application with fees. Clinical testing in India or information on clinical trials performed abroad may be required by DCGI.^[18]

Amendments in 2012

Government upon the recommendation of the DCGI and examination by the Expert Committee on March 5, 2012 confirmed the inclusion of 11 more devices such as Introducer sheath, Cochlear implant, Close wound drainage set, AV fistula needle, Extension line as an accessory of Infusion set, ANGIO kit/PTCA/ Cath Lab kit, Measure volume set, Spinal needle, Insulin syringes, three way stop cock as an accessory of I.V. Cannula/Catheter/Perfusion Set and Flow regulator as an accessory of Infusion set as drugs. These laws were made effective from January 1, 2013.^[19-21]

Amendments in 2014

In March 2014, a notification was released by the CDSCO which ordered for constitution of In-vitro diagnostic device advisory committee which had to advise the DCGI, India so that the essentiality, desirability, effectiveness of IVDs could be ensured.^[22]

Amendments in 2015

CDSCO in June 06, 2015 released a revised format of schedule M(iii) which was prepared by a sub- committee of drug technical advisory board. It revised guidelines on quality management system that shall be used by the manufacturer for the design and development, manufacture, packaging, labeling, testing, installation and servicing of medical devices and in-vitro diagnostics. In-vitro Diagnostics, mechanical contraceptives (Condoms, intrauterine Devices, Tubal Rings), surgical dressings, surgical bandages, surgical staplers, surgical

sutures and ligatures, Blood and Blood Components Collection bags, intended for human or animal use that were manufactured in India were covered under this. It stated that manufacturer should establish, document, implement and maintain a quality management system and maintain its effectiveness in accordance with the requirements of this schedule and identify the processes needed for the quality management system and their application throughout the organization, determine the sequence and interaction of these processes, criteria and methods needed to ensure effective operation, control, availability of resources, information to support the operation and monitoring of these processes. It also stated that the manufacturer should monitor, measure and analyses these processes and implement actions necessary to achieve planned results and maintain the effectiveness of these processes. It also directed for maintenance of a site master file which should contain general information about the manufacturer, personnel employed, premises and facility, equipment, sanitation, production, quality control, storage facilities etc. A circular was issued to all State Licensing Authorities by Drugs Controller General (India) for extending the validity from of Free Sale Certificate from 2 years to 5 years subject to the validity of manufacturing license held by the firm.^[23-26]

LIMITATIONS OF THE OLD REGULATORY FRAMEWORK

The existing regulatory framework for medical devices in India has been inadequate for a USD 4.9 billion industry with proper regulations on only 15 devices. These medical devices are treated as 'drugs' under the Drugs & Cosmetics Act, 1940 due to which they were under the restrictive code/laws of the pharmaceutical sector. Uncertainty in the clinical trial mechanism and the absence of specific regulatory framework in manufacturing standards and quality control systems has resulted in low product quality compared globally. Lack of support policies for foreign exchange laws, duty structures, etc. has resulted in an unattractive environment for investors and ultimately blocked technological advancements and innovations.^[27]

MEDICAL DEVICES AMENDMENTS^[28-30]

The government has notified the Medical Device Rules 2017 which will come into effect from January 01, 2018. Complete separation of regulatory norms for manufacturing medical devices from drugs has been ensured. The new Rules have been framed in allegiance with global harmonization task force (GHTF) framework and to meet with best international practices. The prime focus of these practices is to make rules easier and simpler for obtaining

a license and conducting clinical trials and also allowing 100% FDI in medical device industry. The medical devices rules 2017 are divided into 12 chapters which lists various rules regarding manufacturing, selling, testing, importing etc. of medical devices.

The various high lights of different chapters and rules enlisted in them are as follows:

Definitions of various terms used in the rules such as “notified body”, “central licensing authority (CLA)”, “body orifice”, “clinical investigation”, “ethics committee”, “quality management system”, “post market surveillance” etc. are covered in **chapter 1**.

According to new rules, medical devices are specific devices that are used internally or externally in the diagnosis, treatment, mitigation, prevention of disease/disorder in human beings/animals or intended to affect the structure or any function of the human body notified under the Drugs and Cosmetics at 1940.

E.g. condoms, intra-uterine devices, tubal rings) and disinfectants, surgical dressings, surgical bandages, surgical staples, surgical sutures, ligatures, blood and blood component collection bag with or without anticoagulant, mechanical contraceptives (condoms, intrauterine devices, tubal rings), disinfectants and insecticides etc.

Regulation of medical devices is covered in **chapter 2**. It highlights the risk-based classification system for medical devices and in vitro diagnostics (IVDs), guidelines for grouping of medical devices, products standards, essential principles for manufacturing. The CLA is responsible for grouping of devices according to their use and a class wise list should be published on the website of CDSCO.

Documents to be submitted with the application for grant of license to manufacture or import Class B, Class C or Class D medical device

Manufacturing site.

- (a) Constitution details of domestic manufacturer or authorized agent
- (b) Site or plant master file
- (c) Device master file for medical devices other than *in vitro* diagnostic medical devices, *in vitro* diagnostic medical devices
- (d) Essential Principles checklist
- (e) Test license obtained for testing and generation of quality control data

- (f) Undertaking signed stating that the manufacturing site follows the provisions of the Fifth Schedule.
- (g) A copy of performance evaluation report issued by the central medical device testing laboratory or medical device testing

Grouping of medical devices^[31] have been done to have a single application for medical devices intended for same use or having same technology for import, manufacturing, sale, stock, exhibit or offer for sale. A **single** medical device is sold individually and in packages (if desired) and does not come under any family such as IVD test kit. Medical devices **family** are collection of devices from the same licensee, of common use, identical risk class and with similar design and manufacturing process.

E.g. of single medical devices are toric spherical lens, condoms (sold in packages of 3, 10 or 16). On the other hand, different types of condoms that differ in color, size, texture but are made from the same material and process can be licensed as family. Steerable guidewires that are available in various lengths and possess various tip shapes and tip flexibilities can be grouped as a “family” if their variations fall within the scope of permissible variants.

E.g. Cardiac catheters that are available in a different number of lumens, lengths and diameters can be grouped as a FAMILY.

Contact lenses with additional features of UV protection can be grouped as a FAMILY, as this feature does not affect the basic design and manufacturing of the lens.

Medical device **system** contains compatible devices of a same manufacturer and licensee intended to be used in combination for same purpose sold under an individual trade name. E.g. A hip replacement system comprising of femoral and acetabular components can be grouped as a system if components are used in combination to achieve a common intended purpose of total hip replacement. The size of the components may vary.

A catheter placement set/kit comprising of scalpels, syringes, needles, surgical gloves, gauze, drapes and flushing solution that is validated for compatibility and assembled by a single product owner under a single system name for use in combination during a surgical catheter placement procedure can be grouped as a system. **Group** is a collection of two or more devices in the same package by same licensee and sold under single trade name. The number of devices can vary in the same group keeping in mind not to destroy the purpose of group.

E.g. a first aid kit consisting of medical devices such as bandages, gauzes, drapes and thermometers, when assembled together as one package, can be licensed as a group.

NON-INVASIVE DEVICES^[32]

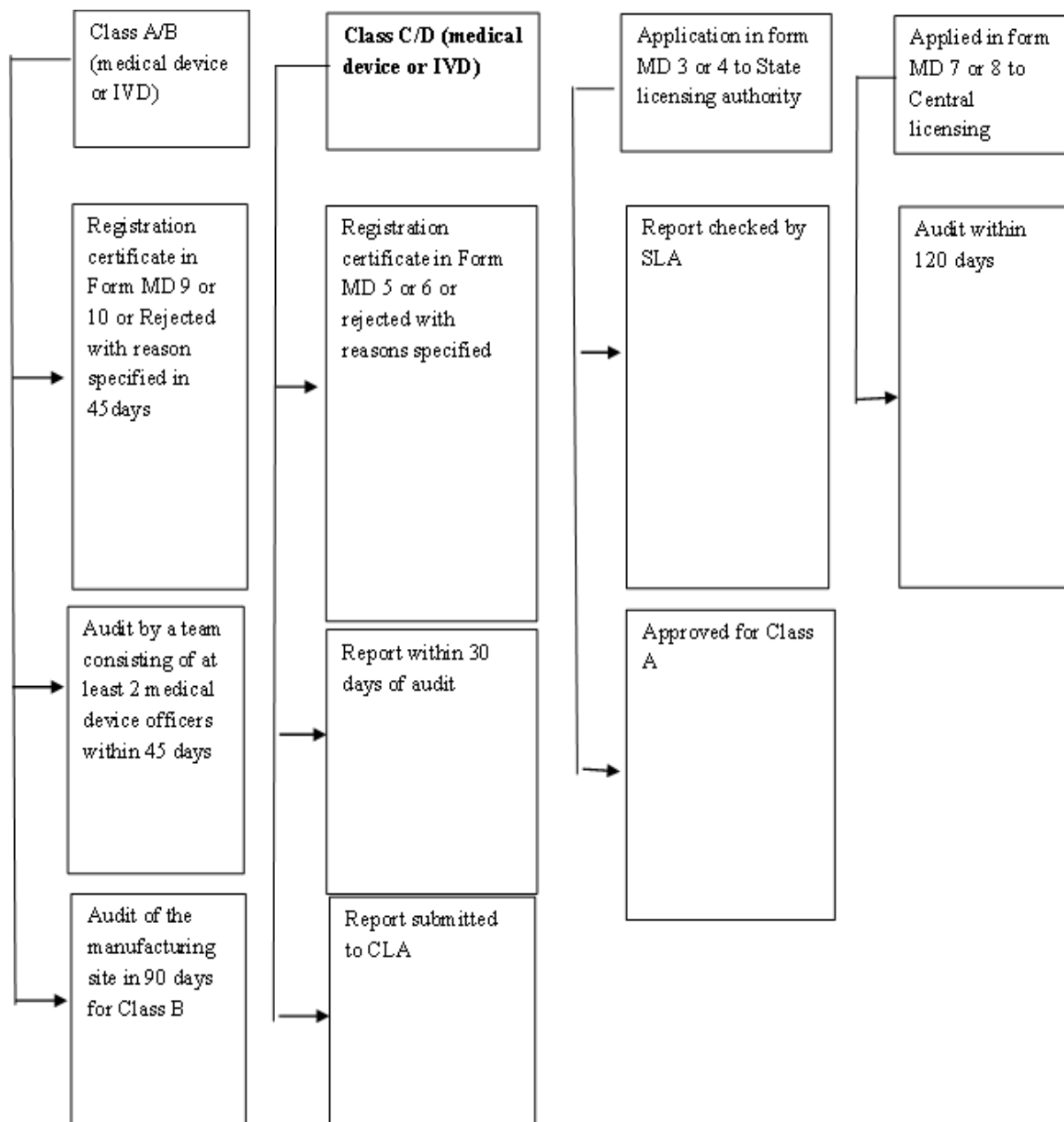


Figure 1: Classification of Non-Invasive devices.

Class A: Island dressings, cotton wool, wound strips, adhesive bandages, gauze dressing, anti-static tubing for anesthesia, anesthesia breathing circuits, pressure indicator, pressure limiting device, syringes for infusion pumps, syringes without needles.

Class B: Polymer film dressings, hydrogel dressings, non-adhesive for topical use, refrigerators specially intended for storing blood, medical devices used for filtration of blood or the removal of carbon dioxide.

Class C: Dressings for severe decubitus wounds, dressings for chronic extensive ulcerated wounds, dressings incorporating to provide a temporary skin substitute, blood bag, sperm separators.

INVASIVE MEDICAL DEVICES^[33]

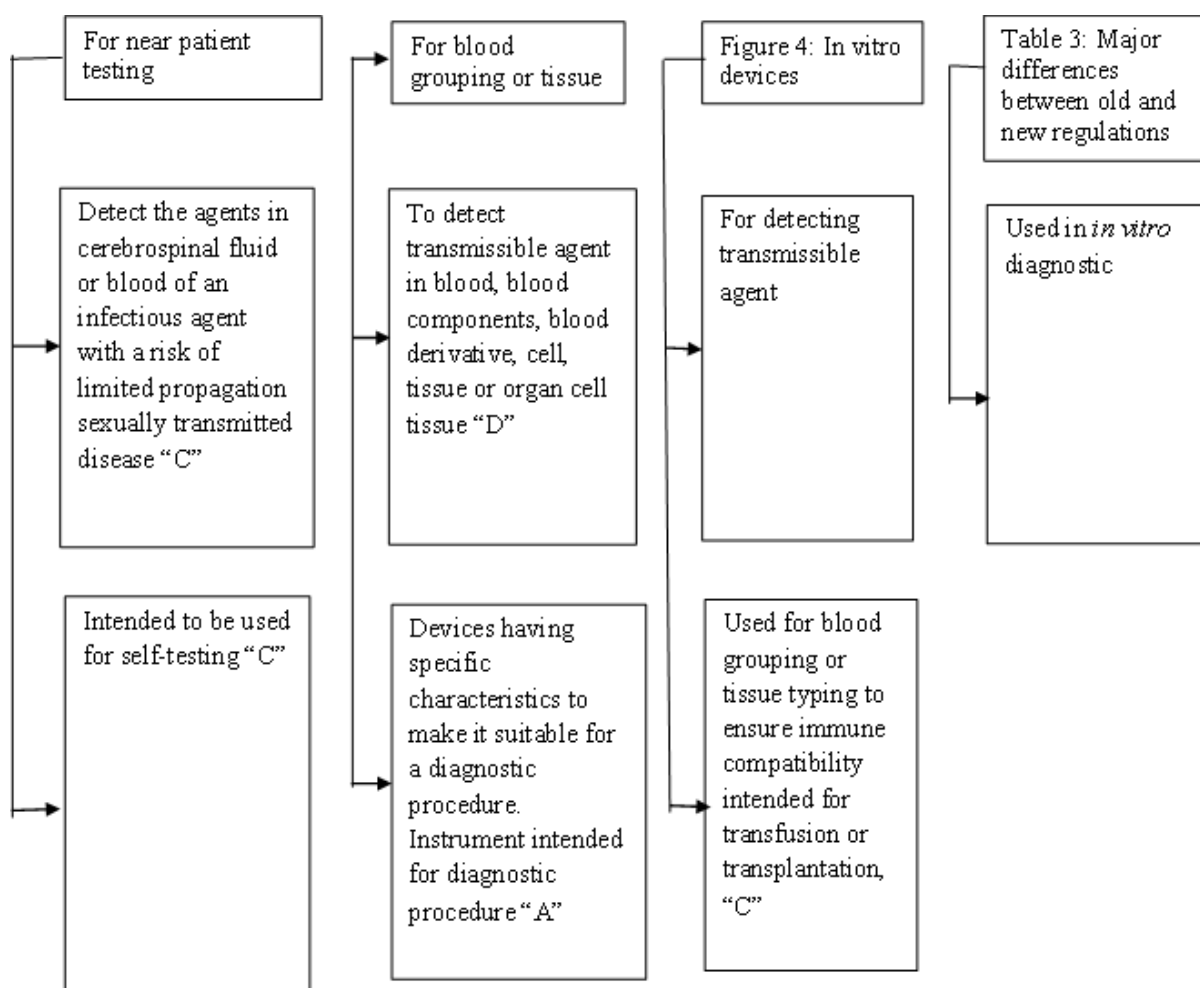


Figure 2: Invasive medical devices classification.

Class A: Dental impression materials, tubes used for pumping the stomach, impression trays, enema devices, examination gloves, urinary catheters intended for transient use, dressings for nose bleeds, materials for manufacturing dentures.

Class B: Urinary catheters, tracheal tubes, orthodontic materials, removable dental prosthesis.

Class C: Tracheal cannula, urinary catheters intended for long term use, short term corrective contact lenses, tracheal tubes, stents, vaginal pessaries, indwelling urinary catheters intended for short term use, orthodontic wires, fixed dental prostheses, fissures sealants, tracheostomy or tracheal tubes connected to a ventilator, blood oxygen analyzers placed under the eyelid.

It also contains the **essential principles for safety and guidelines**^[34] and describe three types of standards:

Basic/ horizontal standards: It indicated fundamental concepts for general safety and performance to the manufacturer such as risk management, clinical investigation, quality management system.

Group standards/ semi-horizontal standards: It is related to family of similar products or processes with reference to basic standards, such as standards for sterile medical devices, stability of IVDs, electrically powered medical devices.

Product/ vertical standards: It is related to essential safety and performance aspects of specific products or processes with reference to basic and group standards such as standards for infusion pumps and for self- testing blood glucose meters.

Essential principles for safety and guidelines specify that the devices should be designed, manufactured and packaged in a way that:

- Integrity and function should not be disturbed at any cost without comprising patient safety and health and having high benefit/ risk ratio.
- Risks must be minimized by the manufacturer and residual risks should be informed to users.
- Transportation and storage conditions (such as temperature and humidity) should be having a minimum impact on the safety of users and person involved in transportation without compromising its efficacy.
- It should not support microbial growth and infection.
- Sterile devices should be manufactured in a controlled environment in a non- reusable pack and should be maintained in the sterile state till their use.
- Drugs incorporated in medical devices and the devices both should meet their safety, quality and performance criteria and it should be verified.

- Medical devices with substances of biological origin should be subjected to veterinary controls and surveillance if their origin is from animal tissue, cells or substance (veterinary must ensure that the animal is free from Transmissible spongiform encephalopathies (TSE) and Bovine spongiform encephalopathy (BSE) whereas medical devices incorporating cells, tissues and derivatives of microbial or recombinant origin should be tested and validated for their sources, processing technology and preservation . Same testing and validation should be performed for medical devices incorporating human non-viable cells and tissue.
- Devices should be free from radiation and if not possible, the radiation (intended, unintended or ionizing) from devices level should be minimized which should be warned to the user. One should be familiar on the way of use of such devices, nature of radiation emitted and steps to eliminate any risk.
- Devices with software or software that are devices in themselves must be validated with incorporation of development, lifecycle, risk management, verification and validation principles.

Product standards: The medical devices should comply with the standards laid down by bureau of Indian standards under section 3 of the bureau of Indian standards act, 1985 (63 of 1985). Where no such standard has been laid the device should comply to the standard laid down by the International standard organization (ISO) or International electro technical commission (IEC).

Details the various authorities, Officers and bodies appointed by the government have been listed in chapter 3. The various authorities appointed by the government are:

Central licensing authority (CLA) is the govt body responsible for granting licenses for import, manufacturing, clinical investigation and approval of medical devices and in vitro diagnostics by working in coordination with state licensing authorities. Both the state and central authorities can exercise its power by appointing an officer not below the rank of Assistant Drug controller who can exercise the powers of State and central licensing authority respectively.

National accreditation body function is to conform assessment activities for accreditation of notified bodies and laying down standards along with preparing norms for such accreditations.

Notified bodies are accredited institute/ organization or a corporate body registered with Central licensing authority that is competent to carry out the audit of manufacturing sites of Class A and Class B medical devices.

Documents required for registration as notified body (according to third schedule) are:

Details of body, organization profile, accreditation certificate, Standard operating procedures (SOPs) List, Technical personnel list etc.

The various registered notified bodies are^[35]:

M/s Intertek India Pvt. Ltd

M/s TUV Rheinland India Pvt. Ltd

M/s TUV Sud South Asia Pvt. Ltd.

Medical Device testing Officers and Medical Device officers are appointed as Government analyst and Inspectors respectively.

Some Central medical device testing laboratories have been established by the government.

For testing and evaluation of the listed medical devices the following laboratories have been established.^[36,37]

- The central Drugs Testing Laboratory, Mumbai for Intra Uterine Devices (IUD) and Falope rings.
- The Regional Drugs Testing Laboratory, RDTL, Guwahati for Disposable Hypodermic syringes, Disposables Hypodermic Needle, Disposable Perfusion Sets.
- The Central Drugs Laboratory, Kolkata for surgical dressings, Surgical cottons, Surgical bandages and Disinfectant.
- The Central Drugs testing laboratory, Chennai for Condoms.
- The National Institute of Biologicals, Noida for In vitro Diagnostics for HIV, Hepatitis B surface antigen and Hepatitis C Virus, Blood Grouping sera, Glucose Test strip, Fully Automated Analyzer Based Glucose Reagent.

INTRODUCTION OF ONLINE “SUGAM” PORTAL

An online portal named as “SUGAM” has been created by the CDSCO which acts as a single window for all application relating to import, manufacture, sale, distribution and clinical investigation which have to be assessed by the DCGI or state licensing authority. The portal

also contains video tutorials, notes to submit application, real time tracking of applications and provide timely alert and notifications.

Table 2: Various forms in Medical devices rules 2017.^[38]

FORM	APPLIED BY AND PURPOSE	CERTIFICATE ISSUED IN FORM	Fees (in INR) except where dollar have been specified
MD 1	Accredited Notified body to get registered with the Central Licensing Authority	MD 2	25000 (retention fees same)
MD 3 MD 4	Any person who intends to manufacture a Class A/ Class B medical device including in vitro diagnostic medical device for grant of license loan license to manufacture for sale or for distribution to the State Licensing Authority.	MD 5 MD 6	5000 for one site and 500 for each distinct medical device (retention fees same)
MD 7 MD 8	Any person who intends to manufacture a Class C/ Class D medical device, application shall be made to the Central Licensing authority for license loan license to manufacture for sale or for distribution, as the case may be	MD 9 MD 10	50000 for each site and 500 for each distinct medical device (retention fees same)
MD 11	Maintenance of audit or inspection book by license holder to enable the notified body or Medical device officer to record his observation and non-conformity	_____	_____
MD 12	Any person to get test license for manufacturing of small quantity of Class A/B/C/D of medical devices for the purpose of clinical investigations, test, evaluation, examination, demonstration or training to the Central Licensing Authority	MD 13	500
MD 14	For import license to Central Licensing authority by an authorized agent (having license to manufacture for sale or distribution or wholesale license for sale or distribution)	MD 15	Class A: \$1000 for one site and \$50 for each distinct device Class B: \$2000 for one site and \$1000 for each distinct medical device Class C and D: \$3000 for one site and \$1500 for each distinct device
MD 16	Test license for import for test, evaluation, clinical investigations to central licensing authority	MD 17	\$100

MD 18	Import of investigational medical device by Government hospital or statutory medical institution for treatment of patient	MD 19	500
MD 20	Import of medical device for personal use	MD 21	_____
MD 22	To Central Licensing Authority by Sponsor for grant of permission to conduct clinical investigation of a medical device	MD 23	100000 for Pilot and Pivotal investigation each 25000 for clinical performance evaluation
MD 24	By sponsor for grant of permission to conduct, clinical performance evaluation of new in vitro diagnostic device to the Central Licensing Authority	MD 25	25000
MD 26	Permission to import or manufacture medical device which does not have its predicate device to the Central Licensing Authority by an authorized agent	MD 27	50000
MD 28	Permission to import or manufacture new in vitro diagnostic medical device which does not have its predicate device to the Central Licensing Authority	MD 29	25000
MD 30	For sending a sample of medical device for Test or evaluation of to the Director of central medical device testing laboratory in a sealed packet with a memorandum	RESULT OF TEST in MD 31	_____
MD 32	Generation of report after completion of test or evaluation by the Medical Device Testing Officer to Medical Device Officer	_____	_____
MD 33	By a purchaser for test or evaluation of a medical device or portion of medical device	_____	_____
MD 34	Order not to dispose of stock by a Medical Device Office	_____	_____
MD 35	Receipt for seized medical devices, record, register, documents or any other material objects by a Medical Device Officer	_____	_____
MD 36	Purpose for which samples have been taken by a Medical Device Officer	_____	_____
MD 37	By medical device officer for receipt of samples of medical devices where fair price tendered are refused by the person from whom the samples have been taken purposes of test or	_____	_____

	evaluation has been refused by the person from whom such sample has been taken		
MD 38	Procedure for dispatch of sample to medical device testing officer by the Medical Device Officer for test or evaluation	_____	_____
MD 39	Application for registration of medical device testing laboratory on behalf of a manufacturer to the Central Licensing Authority	MD 40	20000 (same fees for retention)

Various norms for manufacturing and sale for distribution of medical devices under Class A/B/C/D. Applicant must submit list containing device description, use of device, accessories, material of construction, working principle, novel technology, labels, package inserts, site master file, firm details, conformity check, fifth schedule compliance undertaking, summary of any reported adverse drug reaction (ADR) in India or other countries.

Import of medical devices by companies, govt hospitals, for testing or for one's own use is covered in chapter 5. Application is filed by an authorized agent to central licensing authority in form MD 14. After inspection of manufacturing sites situated abroad, a report is generated within a period of nine months and the application is accepted or rejected; in which case the applicant can re-appeal within a period of 45 days on which decision have to be made within a period of ninety days from the appeal.

Devices which are already certified by the regulatory agencies of Australia, Canada, Japan, European Union or United States of America need not to be clinically investigated where devices imported from any other countries need to be investigated in India. The licenses issued for import are valid for a period of 5 years and can be reapplied within 90 days after expiry.

Provisions related to labelling of medical devices are covered in Chapter 6. Labelling should be done in a way so that buyers can easily identify the device and should contain correct information about the weight, number of units, volume of device, batch no/serial no. or lot no. It also states that it is mandatory for companies to assign a unique identification number to each approved device after January 01, 2022. It also states that shelf life should not be more than 60 months. Devices whose total shelf-life is 90 days or 90 days-1 year should be

having minimum 40% or 50% shelf life respectively; devices with less than this shelf life cannot be imported.

Clinical investigation and clinical performances evaluation of devices and IVD is covered in chapter 7, it states that a pilot investigation should be carried out. Medical devices for use in other countries don't need any permission. It is also stated that reasons should be given in written within 90 days for denying clinical investigation permission.

Clinical investigation should involve the use of good clinical practices (GCP) guidelines and registered in clinical trial registry. Annual status report submission, reporting ADR within a period of 14 days from occurrence, compensation to the victims of injury in trials, maintenance of record for 07 years are other aspects of the following chapter.

Regulations of import of devices which doesn't have any predicate device is covered in chapter 8. It states that the clinical studies need not to be done for Class A medical devices and in situations where they are intended for use in life threatening, medical emergencies and urgent conditions.

The role and duties of medical device officer, medical device testing officer and notified body is described in chapter 9 it along with procedures for carrying out inspection, maintaining of records of inspection and testing of medical devices sample.

Chapter 10 lists out all the facilities such as adequate space, availability of animals, list of instruments required for registration of medical device testing laboratory. The license obtained is valid for a period of 5 years.

Premises where the test or evaluation shall be carried out shall be:

- Well lighted and properly ventilated.
- Air- conditioned so as to maintain the accuracy and functioning of laboratory instruments or to enable the performance of special tests such as sterility tests, microbiological tests etc.
- The applicant shall provide adequate space having regard to the nature and number of samples of medical devices proposed to be tested and evaluated.

If it is intended to carry out tests requiring the use of animals, the applicant shall provide for an animal house and comply with the following requirements:

- The animal house shall be adequate in area, well lighted and properly ventilate, air conditioned, hygienic surroundings and necessary provisions made for removal of excreta and foul smell.
- Suitable arrangements for preparation of animal feed.
- Suitable arrangements for quarantining of all animals.
- Animals shall be periodically examined for their physical fitness.
- Isolation of sick animals as well as animals under test.
- Compliance with the requirements of the Prevention of Cruelty to Animals Act, 1960
- Proper arrangements for disposal of the carcasses of animals in a manner as not to cause hazard to public health.

Reviewed in 45 days

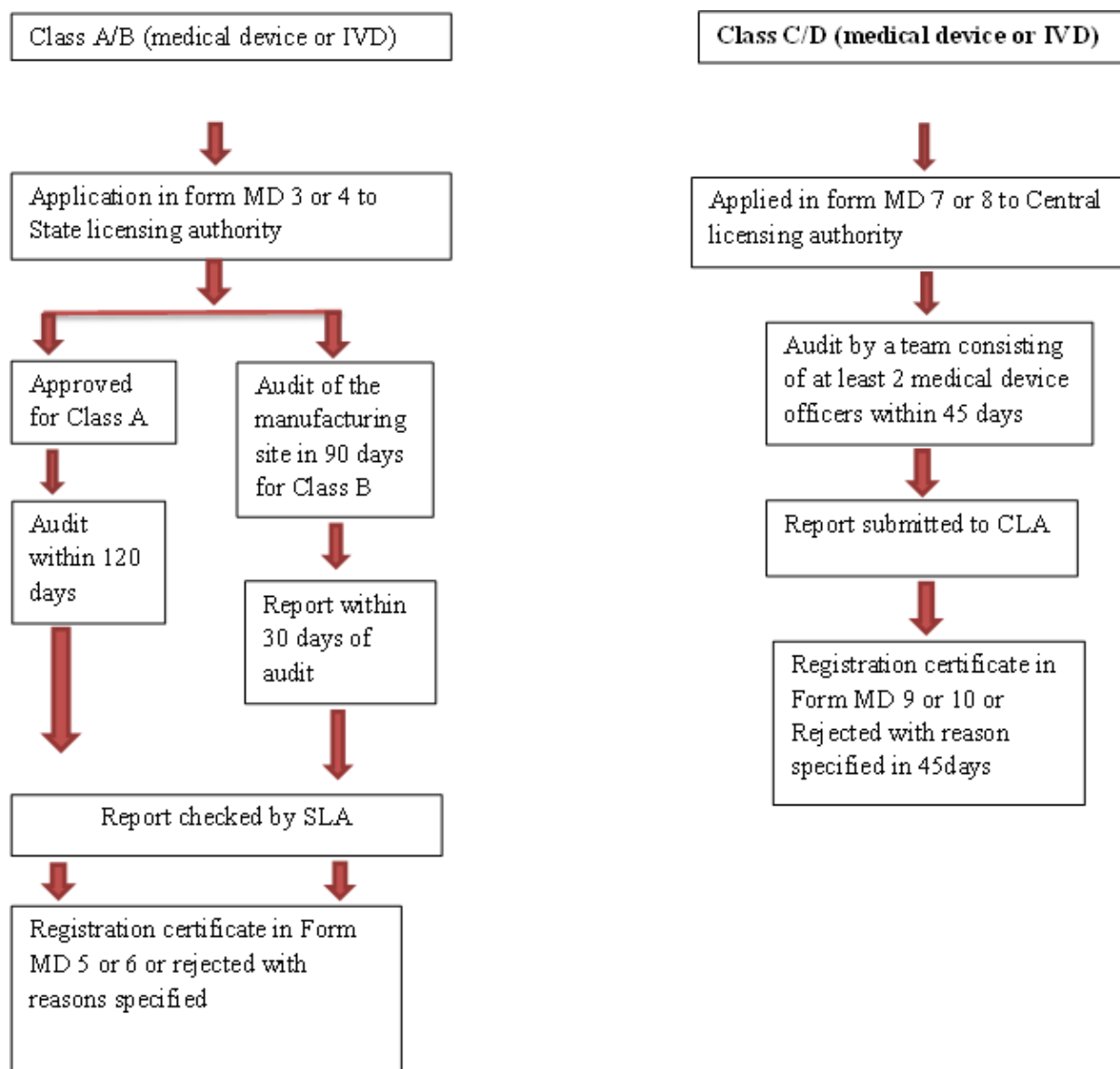


Figure 3: Medical device registration process.

Chapter 11 states that the license to sell drugs under Drugs and Cosmetics Act, 1940 should be valid for sale of medical devices.

Chapter 12 deals with miscellaneous issues such as payment of fees, digitalization of form etc.

IN VITRO DIAGNOSTICS (IVDs)

Medical devices rules 2017 states that IVDs are substances intended to be used outside human or animal bodies for the diagnosis of any disease or disorder in human beings or animals.

Table 3: Major differences between old and new regulations.

	IVD under drugs and cosmetics act 1940^[39]	IVD under medical devices rule 2017^[40]
Class	IVD were classified as Drugs	IVD are classified separately as devices, not as drugs
Definition	It was stated that they are a type of medical devices used to perform natural tests on samples taken from human body or animals such as blood, urine and tissues in order to detect an infection, diagnosis of a specific medical condition, prevention of disease or disorder, modifying a disease or to monitor a drug therapy	It states that IVDs are substances intended to be used outside human or animal bodies for the diagnosis of any disease or disorder in human beings or animals
Governing authority	Medical Devices & Diagnostics Division , Central Drugs Standard Control Organization (CDSCO), Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India FDA Bhavan	Drugs Controller General (India) , Central Drugs Standard Control Authority (CDSCO), Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India, FDA Bhavan
Classification	Classified as “Notified” and “Non-Notified” Notified IVD kits/ reagents: In Vitro Diagnostic Devices for HIV, HBV, HCV and In- vitro blood grouping sera come under the Class of Notified IVD kits/ reagents. Non- notified IVD kits/ reagents: All IVD kits and reagents excluding those listed under notified category come under the category of non-notified IVDs	According to type of risk they possess, as: Low risk - Class A Low moderate risk- Class B Moderate high risk- Class C High risk- Class D

Application	Form 25 for non-notified and Form 27 for notified device	MD 3,4 for Class A & B MD 7,8 for Class C & D
Fees	_____	Manufacturing site: USD 1000\$ for class A and B, 3000 for class C and D Product fees: INR 10 for class A and B, INR 1000 for C and D
Time required for issuing of certificate	03 months	03 months
IMPORT POLICY		
Application for import	Form 40	Form 14
Documents required for manufacturing/import^[41]	<p>Registration Certificate in Form 41 and Import License in Form 10</p> <p>NOC from department of Animal Husbandry, Dairying and Fisheries (DADF), Government of India, Krishi Bhavan, New Delhi in respect of products intended for veterinary purpose^[42]</p> <p>Expert Opinion/ Technical recommendation from DG, ICMR, New Delhi for the product intended for influenza</p> <p>For import of Notified IVD kits/reagents, the manufacturing site and products (IVD kits/reagents) are required to be registered with Indian Drug Regulatory Authority</p> <p>Only Import License in Form 10 is required as per provisions of the Drugs & Cosmetic Act & Rules.</p>	Import license in Form 15 and applicant have to submit the documents as per Fourth schedule Part I, Part II and Part II
Who can apply for import	A person/firm/enterprise etc. holding a valid wholesale license or manufacturing license issued under D & C Act, 1940 and Rules 1945	An authorized agent holding license to manufacture or wholesale license issued under MDR, 2017
Fees required for import	USD 5000\$ for inspection, 1500 \$ for registration, 1000\$ for a single device and 1000\$ for each additional device, USD \$100 for import license	Import license for Class A or Class B IVD device One site \$1000 and for each distinct IVD device \$10 Class C or Class IVD device: one site; \$3000 and for each distinct in vitro diagnostic medical device. \$500
Time required for issuing of certificate	Within 09 months	Within 09 months
Validity of certificate	03 years from date of issue	05 years

IN VITRO DIAGNOSTIC DEVICES

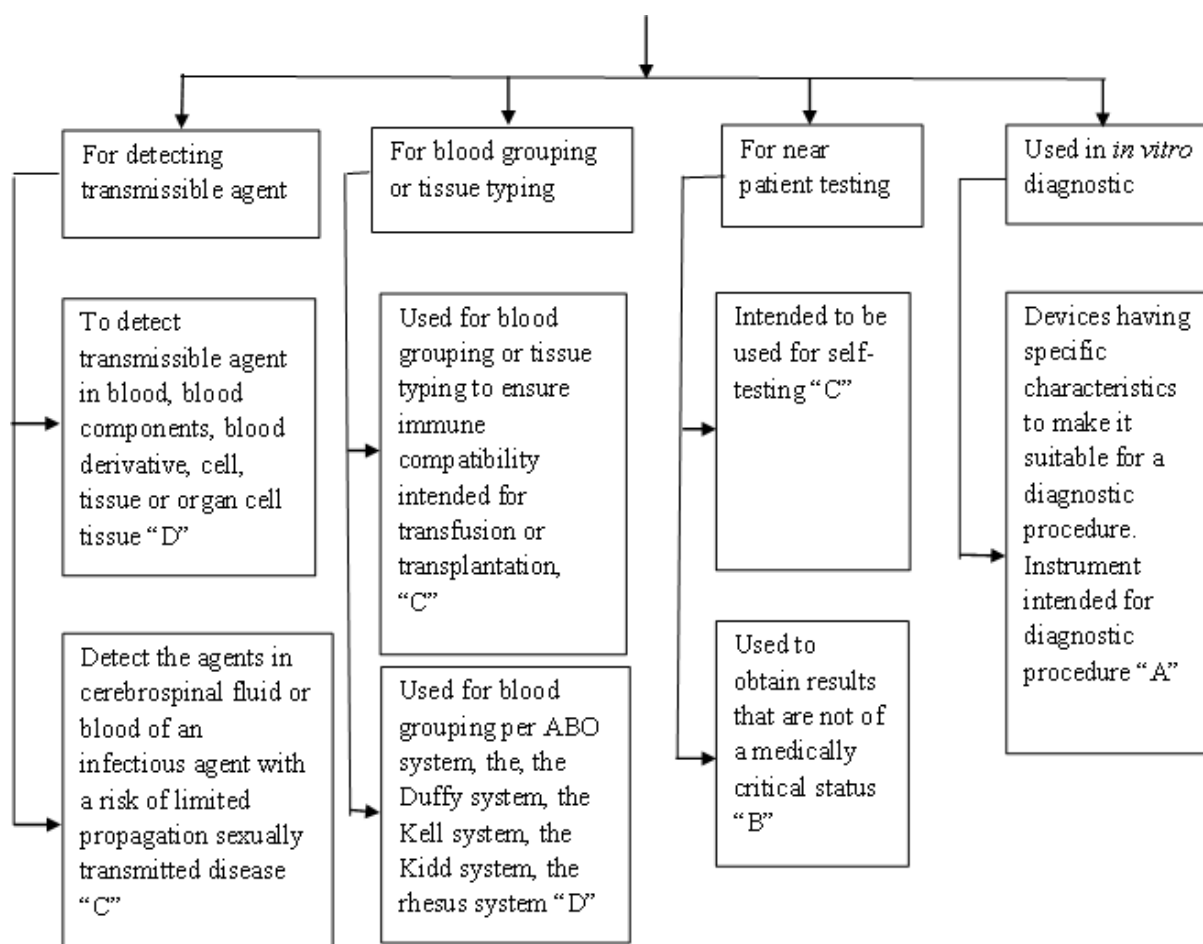


Figure 4: In vitro devices classification.

Class A: Clinical chemistry analyzer, prepared selective culture media.

Class B: Vitamin B12, Pregnancy self-testing, anti-nuclear antibody, urine test strips.

Class C: Blood glucose self-testing, Human Leukocyte Antigens (HLA) typing, Prostate-Specific Antigen (PSA) screening, rubella.

Class D: Human Immunodeficiency Virus (HIV) blood donor screening, HIV blood.

Challenges

Making medical devices available to all is a major challenge before the government as there have been high trade margins on some medical devices with “illegal profiteering”. The government counteracted it by capping prices of some high-end heart stents at around \$450, compared to \$3,000 charged earlier. But India’s National Pharmaceutical Pricing Authority (NPPA) has been pushing for more price controls. State government such as the Maharashtra

government has also submitted a report to the Central Health Ministry advocating the addition of 18 new medical apparatus in the Drug Price Control Orders (DPCO) in a similar attempt to rein in their prices.^[43] The list includes catheter, orthopedic implants, stents, intraocular cataract lenses, disposable syringe, IV fluid set, urine bag etc. There is also an international pressure by the USA. The United States trade representative (USTR) is currently reviewing India's eligibility under its Generalized System of Preferences (GSP), which allows duty-free imports of certain goods. India was the largest GSP beneficiary at \$5.6 billion according to the USTR.^[44,45]

Encourage local producers over imports is also a serious issue which the government is facing. The Association of Indian Medical Device industry has expressed disappointment^[46] over the Draft Medical Devices Preferential Market Access (PMA) Policy which has been issued by Department of Pharmaceuticals (DoP) and described it as a clear case of a lost opportunity to promote indigenous manufacturing of medical devices to boost 'Make in India' initiative. Further, the Draft PMA policy in its present form does not provide preferential pricing to Indian manufacturers, no incentives on maintaining and improving quality, indigenous development and no redressal / penal provisions against use of exclusionary 3rd country regulatory approval mandatory clauses, such as US- FDA.

Medical devices incorporating software and standalone medical device software are not covered in the new rules. It should be ensured that software and any software-driven functions are reliable and perform as intended for use and proper measures should be adopted to eliminate the subsequent risks. Well-defined software validation guidelines for post market surveillance, continued risk management and software performance verification should be included. Permissible lower and upper limits and safety guidelines are also missing from the new rules. Limits for parameters like validation, calibration, etc. should be defined for devices. Procedure for identification and correction of shortcomings in the device during a performance or clinical evaluation or risk to the environment because of device use or disposal should be introduced.

CONCLUSION

India has struggled with an ambiguous and archaic regulatory framework for the medical devices sector. The government of India have definitely taken a tremendous step with the release of medical devices bill 2017. From allowing 100% FDI to bringing medical devices under separate norms, every step of the government is applaudable.^[47,48] Introduction of

changes such as risk-based classification system, application of regulatory standards, proper manufacture licensing requirements, shelf life restrictions, quality management system and more focused clinical regulations were lacking from a long time in the regulations and have been certainly removed by the bill. Furthermore, the entire process has become hassle free through the online SUGAM procedure. The medical devices bill 2017 appears to provide an environment conducive to fostering innovation while at the same time improving product quality and the availability of medical devices in India as well as globally. The approach for ease in doing business has been certainly improved by the clear-cut demarcation of the rules. Clinical trial of the devices was a major issue which have been resolved by specific guidelines for the compensation of subjects who participate in a clinical investigation or clinical performance evaluation. Participation of third party assessment and certification for Class A (low risk) and Class B (low moderate risk) devices in the rules, is a feature of regulatory mechanism in the US and Europe, is a sure mark of maturity of the Indian standards system, which was lagging behind developing countries like China and Brazil. Moreover, compliance with the GHTF will ensure high quality products of international standard. help the new regulations will help Indian manufacturers become globally competitive and enable them to attract foreign investment to funnel their growth.

By potentially bringing more devices under its ambit, the new Medical Device Rules will bring in a huge wave of relief to consumers, protecting their right of access to high quality and safe products. The bill has many unique features to support the growth of the medical device sector in India. With new rules in place, the medical devices sector can catalyze the 'Make in India' platform to leapfrog into a stable, affordable and most importantly, patient safety-compliant future.

Therefore, it is expected that many new innovative products and MNCs will enter the Indian market. The streamlined regulations are expected to attract investors from around the world and because of the streamlined rules and improved government oversight, the quality and range of products and services will improve to better serve the citizens of India.

As the fastest growing healthcare market in the world, the government can further take several measures to boost the growth such as tackling high import duties. An autonomous body can be set up that tracks individual instances where a particular device has failed or led to detrimental consequences on life or property. Lastly, as an important measure to encourage compliance to safety standards among stakeholders in the industry, the government could

provide incentive schemes for the industry to adopt safety norms through cross subsidies in procurement policies.

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