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RESEARCH ARTICLE

A Comparative Study of Medical Device Regulations in India: Before and After the Implementation of Medical Device Rules 2017

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ABSTRACT:
The medical device industry in India is one of the fastest growing commerce in the world as it is growing at a rate of 15.8% CAGR (Compound Annual Growth Rate) vis-à-vis a CAGR of 4.1% for the global medical device industry. Since 1940, medical devices were regulated as per Drug and Cosmetic Act 1940 and Rules 1945, CDSCO (Central Drug Standards Control Organization) regulated only a handful of medical devices through gazette notifications, these devices being called as notified devices. Many devices were classified as drugs in India. This system was not in consonance with the international standards and was rudimentary in character. Revamping the existing regulatory framework and creating harmonizes standards for all medical devices was the need of the hour. CDSCO, after thorough study overhauled the regulatory framework for medical devices in 2017 by passing Medical Device Rules and has brought it at par with international norms. It has also introduced various fiscal measures to promote research, development, manufacturing and import of medical devices in India. This review highlights the recent progress in Indian medical device regulation with the dawn of Medical Device Rules 2017 in the light of Drugs and Cosmetics Act 1940 and Rules 1945.

KEYWORDS: CDSCO, Notified Devices, Medical Device Rules 2017, International Regulations, Drugs and Cosmetics Act 1940 and Rules 1945.

INTRODUCTION:

Medical devices are now an important part of modern medical care. In some cases, the medical devices have improved the quality of medical care provided to the patients. But in some cases, substandard medical devices have caused havoc and severe health issues. The approach of ensuring the quality, safety and performance of medical devices largely depends on regulations a country is following.[1]. The Indian market is among the top twenty in the world by market size and fourth in Asia after Japan, China and South Korea[2]. The current market size of the medical device industry in India is estimated to be $7 billion and it is expected to reach $9.6 billion by 2022. As per the Department of Pharmaceuticals, the estimated retail market for medical device is between $9.3 billion to $10.8 billion.

But the per capita spent on medical device is significantly lower than other emerging markets. The industry in India is largely dependent on imports around 75%, with local manufacturers contributing to the lower end of the value chain[3].

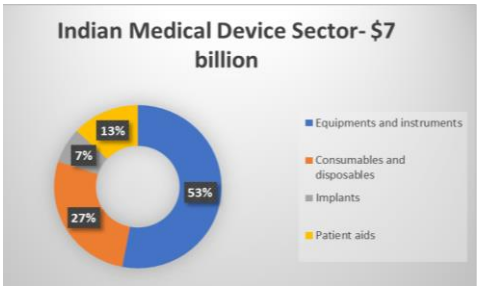

Figure 1- Indian Medical Device Sector
Source: SKP analysis 2018

The Indian medical device industry followed Drug and Cosmetic Act 1940 and Rules 1945 which is ambiguous, complex and lacking transparency till when Medical Device Rules 2017 was passed and came into effect from 1 January 2018. The MDR 2017 (Medical Device Rules 2017) is in conformity with the Global Harmonization

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Task Force (GHTF) framework and it was drafted with the intention to distinguish medical devices from pharmaceuticals for improved and well-defined regulations. The key highlights of the Rule are:

1. Redefining 'medical devices', making it more comprehensive and easier to understand.
2. Introduction of risk-based classification of medical devices.
3. Single window clearance i.e., online portal for applications for import, manufacture, sale or distribution and clinical investigation.
4. Establishment of product standards for medical devices.
5. Rationalization of timelines for obtaining licenses required to market medical devices.
6. Consolidation of registration certificate and import license into a single license.
7. New regulatory framework for clinical investigation of medical devices.

KEY HIGHLIGHTS OF MEDICAL DEVICE RULES 2017:

1. Definition of Medical Devices:

Under the 2017 Rules, medical devices mean:

1. Substances used for *in vitro* diagnosis and surgical dressings, surgical bandages, surgical staples, surgical sutures, ligatures, blood and blood component collection bag with or without anti-coagulant;
2. Substances including mechanical contraceptives (condoms, intrauterine devices, tubal rings), disinfectants and insecticides; and
3. Devices notified from time to time under sub-clause (iv), of clause (b) of section 3 of the Drugs and Cosmetics Act, 1940 (23 of 1940);
4. Substances used for in vitro diagnosis[4]

MDR 2017 gives a definition which covers most of the medical devices in a better way when compared to the D & C Act.

2. Introduction of risk-based classifications system:

In tune with the global practice and GHTF guidelines, the 2017 Rules has introduced a risk-based classification system for regulation of medical devices.

The classification is as follows:

Medical devices and *in vitro* diagnostic medical devices are classified based on risk into four classes:

Table 1: Classification of medical devices based on risk as per MDR 2017.

Associated Risk	Class of Device
Low risk	Class A
Low-Moderate risk	Class B
Moderate-High risk	Class C
High risk	Class D

The Central Licencing Authority has classified medical devices based on the intended use of the device and other parameters specified in the First Schedule of the MDR 2017.[4]

It is important to note that unlike other countries which give liberty to manufacturers/importers to classify their product for the purpose of registration, the 2017 Rules do not provide this liberty and the manufacturers/importers will have to follow the classification decided by DCGI (Drug Controller General of India).[4]

An example of the difference in regulation based on risk-based classification is as follows:

The application for import license for Class A or Class B medical devices from Unregulated Jurisdictions can be granted on the basis of a free sale certificate and either of published safety and performance data or clinical investigation in the country of origin. However, an application for import of Class C or Class D medical devices from Unregulated Jurisdictions can be granted only after its safety and effectiveness has been established through clinical investigation in India. Unregulated Jurisdictions are jurisdictions other than Australia, Canada, Japan, European Union Countries, or the United States of America.

Similarly, for applications for grant of license to manufacture - Class A medical devices do not require prior audit by third party [4] or official inspection; Class B medical devices require prior audit by third party but do not require official inspection, and; Class C or Class D medical devices require prior official inspection. The application for manufacture of Class A or Class B medical device will be assessed by the State licensing authority whereas the application for manufacture of Class C or Class D medical device will be assessed by DCGI.[4]

3. Single window clearance:

All applications for import, manufacture, sale or distribution and clinical investigation, whether to be assessed by the DCGI or State licensing authority, is to be made through a single online portal of the central government, https://cdscomdonline.gov.in/NewMedDev/Homepage. [6] [7]

4. Product standards for medical devices:

All medical devices are expected to conform to the following standards, in the same order of relevance:

1. A standard notified by central government for the medical device specifically or which has been laid down by the Bureau of Indian Standards (**"BIS"**); or

2. Where (a) is absent, to a standard laid down by International Organisation for Standardisation (**"ISO"**) or the International Electro Technical Commission (**"IEC"**), or by any other Pharmacopoeial standards; or
3. Where both (a) and (b) are absent, to the validated manufacturer's standards.[4]

5. Certainty and rationalization of timelines:

The government has brought certainty of timelines and has rationalized the time required for obtaining licenses required to market medical devices. Under the 2017 Rules, an applicant can be certain of the time within which its application will be decided and can also plan the time within which it can expect an audit or inspection to happen because timelines have been assigned to each regulatory function. Further, unlike the D&C Act (Drugs and Cosmetics Act 1940 and Rules 1945), the 2017 Rules do not give any scope to the regulators to extend the timeline for coming to a decision for any reason whatsoever. For instance, in case of license to manufacture Class C or Class D medical device, the scrutiny of the application is required to submitted within forty five (45) days of the date of the application, the inspection of the manufacturing site is required to be completed before sixty (60) days from the date of the application, the report of the inspection has to be forwarded to the applicant, and the decision on the application has to be communicated within forty five (45) days from date of receipt of the inspection report.[5] Similarly, a decision on application to import a medical device is required to be communicated within 9 months from the date of the application irrespective of whether the foreign manufacturing site is inspected or not. ()

The 2017 Rules have also introduced the concept of deemed approval in event of non-communication of a decision in application for approval to undertake major change in licensed particulars (the subject of major change in licensed particulars is discussed later in detail). If the appropriate licensing authority i.e. the DCGI or the State licensing authority is unable to communicate its decision on the aforesaid application within the stipulated timeline, i.e., forty-five (45) days for manufacture, sixty (60) days for import, then such approvals shall be deemed to have been granted.[8]

6. Perpetual licenses:

The licenses granted under the 2017 Rules shall remain valid in perpetuity, subject to payment of licence retention fee as specified in the Second Schedule before completion of the period of five years from the date of its issue, unless, it is suspended or cancelled by State Licensing Authority or the Central Licensing Authority, as the case may be. If the licence holder fails to pay the required licence retention fee on or before due date, the licence holder shall, in addition to the licence retention fee, be liable to pay a late fee calculated at the rate of two per cent. of the licence retention fee for every month or part thereof within one hundred and eighty days and in the event of non-payment of such fee during that period, the licence shall be deemed to have been cancelled.[4] While the license may be perpetual, if a licensed manufacturer has stopped manufacturing activity or closed the manufacturing site for a period of thirty days or more, it is obligated to inform the appropriate licensing authority.

7. Consolidation of import license and registration certificate:

Before the dawn of the MDR 2017 era, a manufacturer or his authorized agent who wishes to import a medical device into India, needs a registration certificate in Form 41 and import license in Form 10 on a mandatory basis [8].

But the MDR 2017 has eliminated the need for registration certificate for the registration of the foreign manufacturers, their products and its manufacturing facilities. The basic requirement to import a medical device to India is to obtain is to obtain an import license in Form MD-15 which is to be applied via an authorized agent in Form MD-14 along with the prescribed fee and documents. This has made the import process less complicated than before[4].

8. New regulatory framework for Clinical investigation:

The MDR 2017 has overturned the clinical trial milieu for an investigational medical device from a four-phase trial like those needed for drugs as per Schedule Y of D & C Act to a two-phase trial. The first phase is 'Pilot Clinical Investigation' – clinical investigation carried out for the first time in human participants. The second phase is called 'Pivotal Clinical Investigation' which is a confirmatory study conducted to gather evidence to support the safety and effectiveness of the investigational medical device.[8] In addition to this, the post-market surveillance has been made compulsory after gaining market approval for the device. Nevertheless, for obtaining import license for a medical device not having a predicate device in India, clinical investigation is not needed if a Free Sale Certificate has been issued by a competent authority from Australia, Canada, Japan, US or EU.[8] If a Free Sale Certificate is not available, then a pivotal clinical investigation is needed to be conducted in India to generate evidence of safety and effectiveness of the investigational medical device in Indian Population, except for Class A investigational devices. Furthermore, establishment of 'Subsequent Equality' to a predicate device is introduced in the new Rules. In the case of In-vitro Diagnostics,

'Clinical Performance Evaluation' which is a systematic investigation by which data is assessed and analyzed to establish or verify performance of the in vitro diagnostic medical device for its intended use is to be performed. No prior approval is required for conducting academic clinical trials.[4]

9. Notified bodies:

The MDR 2017 has introduced Notified Bodies (NB) in the Indian medical device scenario for third-part conformity assessment and certification[8]. A notified body is a body corporate or other legal entity registered under Rule 13 of the MDR 2017 as a body competent to carry the audit of manufacturing site, assessment and verification of specified category of medical devices for establishing conformity with standards.

Notified bodies are permitted to conduct audit of the manufacturing site of Class A and Class B medical devices after getting accredited by a National Accreditation Body and a registration certificate from the Central Licensing Authority. A Notified body having at least 2 years' experience can conduct audit of the manufacturing site of Class C and Class D medical devices, provided it has personnel with required qualification and experience.

The application for inspection of manufacturing site is allotted to the NB by the State Licensing Authority through the portal of Central Government. The NB is needed to have a Standard Operating Procedure (SOP) for identification, review and resolution of all cases of conflict of interest[4].

Key Differences Between Drug and Cosmetics Act 1945 and Medical Device Rules 2017:

Classification as per Drug and Cosmetics Act 1940 and Rules 1945:

Medical devices were classified as "drugs" under section (3)(b)(iv) of the Drug and Cosmetics Act 1940. [8]

Notified Devices as per the Act

- Disposable Hypodermic Syringes
- Disposable Perfusion Sets
- In vitro Diagnostic Devices for HIV, HBsAG and HCV
- Cardiac Stents
- Drug Eluting Stents
- Catheters
- Intra Ocular Lenses
- I.V. Cannulae
- Bone Cements
- Heart Valves
- Scalp Vein Set
- Orthopaedic Implants
- Internal Prosthetic Replacements [9]

Classification of medical devices as per MDR 2017:

Medical devices and *in vitro* diagnostic medical devices are classified based on the parameters specified in Part I of the First Schedule, based on the intended purpose of the device into four classes namely Class A, Class B, Class C and Class D with increase in the inherent risk. [4]. Refer Table 1.

Import of Medical Devices as per D&C Act:

- For the import of medical devices in India, Registration Certificate in Form 41 and Import License in Form 10 are required as per provisions of the Drugs and Cosmetic Act and Rules.
- For import of medical device, it is mandatory that the manufacturing site and medical devices are required to be registered with Indian drug regulatory agency.
- Any person/firm/enterprise etc. having wholesale license and/or manufacturing license issued under Drugs and Cosmetics Act, 1940 and Rules 1945 can be an applicant for Registration and import of medical devices into India.
- Registration was not required for import of non-notified medical devices in India. [11] [12]

Import of medical devices as per MDR 2017:

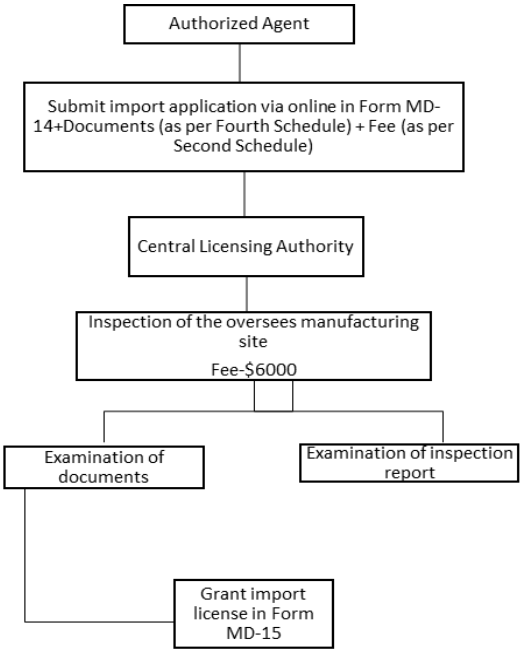

Fig. 1: Application for manufacture for import of Medical Devices to India

For the import of an investigational medical device or a new IVD medical device prior permission from the Central Licensing Authority is needed in Form MD-27 or in Form MD-29.

Validity of licence-License remains valid in perpetuity on paying the license retention fee every 5 years from the date of its issue, unless it has been cancelled or suspended.[4] [13]

Manufacturing of Medical Devices as per D&C Act:

- Application for the grant of license for manufacture of the notified devices is to be made in Form 27 to the State Licensing Authority, along with the prescribed fee.
- For the manufacture of new medical devices or those that do not have any benchmark certification, Expert Committees will examine in detail the information provided by the applicant for the assessment of the device and put forward the opinion regarding sustainability of the device to the competent authority.
- The State Licensing Authority after Joint Inspection and verification forward the license to CLAA for approval.
- The license is issued in Form 28 after due approval of CLAA.[11][12]

Manufacture of medical devices as per MDR 2017:

Application for manufacture for sale or for distribution of Class A or Class B medical device[4] [13].

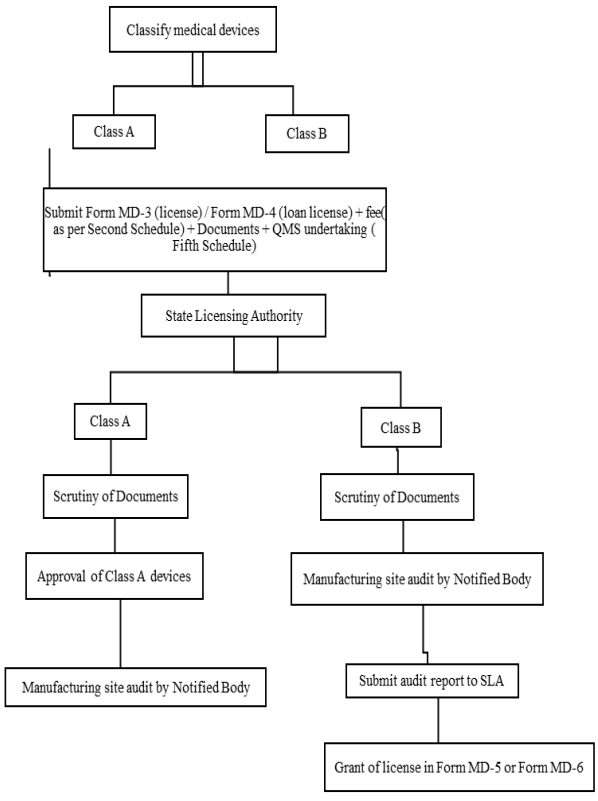

Fig. 2- Application for manufacture for sale or for distribution of Class A or Class B medical devices

Application for manufacture for sale or for distribution Class C or Class D devices

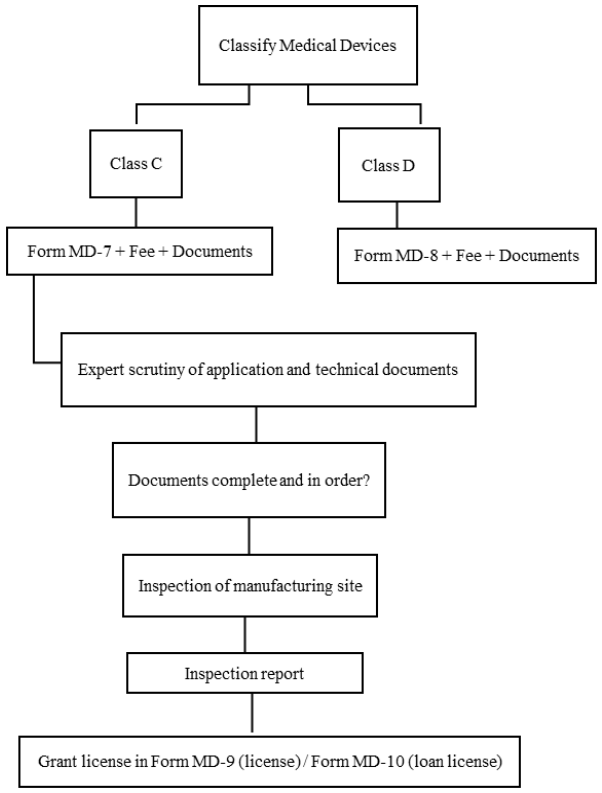

Fig. 3: Application for manufacture for sale or for distribution of Class C or Class D medical device[4][13]

Validity of licence-License remains valid in perpetuity on paying the license retention fee every 5 years from the date of its issue, unless it has been cancelled or suspended.

Clinical Evaluation of Medical Devices as per D&C:

Drug and Cosmetics Act 1940 and Rules 1945 does not state provisions for conducting clinical evaluations specifically for medical devices, but they were conducted just like clinical trials for drugs as stated in Rules 122A, 122D, 122DA 122DAA, 122DAB, 122DAC and 122DD of Part X-A.[11][12]

Clinical Evaluation of Medical Devices as per MDR 2017:

An application for the permission to conduct clinical investigation of an investigational medical device is to be made by the sponsor to the Central Licensing Authority in Form MD-22 along with the fee specified in Second Schedule and documents specified in Seventh Schedule. A clinical investigation of medical devices can be initiated only after approval has been obtained from the Ethics Committee, registered under rule 122DD of Drugs and Cosmetics Rules, 1945[14].

Fee to be paid to the Central Licensing Authority:

- Permission to conduct pilot clinical investigation- Rs.100000.00
- Permission to conduct pivotal clinical investigation- Rs.100000.00
- Documents to be submitted along with application form as per Seventh Schedule: -
- Design analysis data
- Biocompatibility and Animal Performance Study
- The agreement between the Sponsor and Principal and coordinating investigator (s).
- Appropriate insurance certificate, if any.
- Forms for reporting any adverse event and serious adverse event.
- Report of biocompatibility tests along with rationale for selecting these tests including a summary report and conclusion of the study.
- Results of the risk analysis.
- Animal Performance study data.
- Clinical Investigational Plan (CIP).
- Investigator's Brochure.
- Case Report Form.
- Informed Consent Form.
- Investigator's undertaking and Ethics Committee clearance.
- Pilot and Pivotal Clinical Investigation data including that, if any, carried out in other countries.
- Regulatory status and Restriction on use in other countries, if any, where marketed or approved.
- Proposed Instructions for use and labels.[4]

Table 2- Comparison of Drugs and Cosmetics Act 1940 and Rules 1945 Vs Medical device Rules 2017

Parameters	Drug and Cosmetics Act 1940, Rules 1945	Medical Device Rules 2017
Market overview	Outdated regulatory standards	Streamlined regulatory standards
	Largely unregulated; tough challenges were faced to place a medical device in market	Possibility of as strong, sustainable and regulated domestic market
	Lack of multi-national company investors	International standards, many multi-national companies are eyeing to set up facilities in India
Regulatory	Medical devices regulated as 'DRUGS'; no device-only regulation	Medical Device Rules 2017 is devoted only for medical devices
	Budding regulatory framework	Robust regulatory framework
	Classification-Notified devices-22, Non-notified devices	Classification-well defined; based on risk, into A, B, C and D (increasing risk)
	Only paper submission	Entire process from submission to grant of application is through online electronic platform
	No defined approval procedure, no list of required documents, no audits and no renewal requirements.	Defined approval procedure, list of documents per product classification, audits of manufacturing facility and renewal process.
Quality audit, registration and renewal.	Audits of facility required only for notified devices.	Quality audit of facility is required for all devices
	No third-party assessment required.	Third-party conformity assessment and certification through Govt. appointed Notified Bodies
	Registration certificate and approval valid for 3 years.	Perpetual validity id prescribed fee payed every 5 Years and license not revoked or cancelled.
	Application submitted in Form 40 and registration granted in Form 41 for all types of medical devices.	Different types of Forms based on class of medical devices.
Manufacture, distribution, sale, import and export.	Not well defined, regulated as drugs.	Well defined pathways for each class of medical devices.
	QMS not included	Mandatory to follow ISO 13485 and have QMS documented.
	CDSCO handled all activities	Import and clinical trials handled by CDSCO; Manufacturing handled by CLA
	Periodic renewal required	License valid for perpetuity unless suspended, cancelled or surrendered.
Labelling and shelf-life	No evidence required.	Must comply with new labelling provisions; Not to exceed 5 years from manufacturing date unless approved by CLA upon receiving sufficient evidence.

CONCLUSION:

The medical device industry is a vast sector, extending from the simple stethoscope, glucometers, and highly efficacious and complicated cardiac stents to surgical implants. With aging population, increase in non-communicable diseases, and a large underprivileged population, India needs cost-effective and population-specific medical devices[15][16]. By reviewing the Medical Device Rules 2017, it is evident that there are significant differences from Drug and Cosmetic Act 1940 and Rules 1945, for medical devices. Medical Device Rules 2017 has many requirements than previous version. Medical Device Rules 2017 provides an environment that fosters innovation and improves quality of medical devices[17]. It has definitely improved the ease of doing business in India and has ensured safety of high-risk devices. It is a

giant leap when Indian medical device legislation is concerned. Though the 2017 Rules have introduced a number of business-friendly provisions, one cannot help but regret that it was an opportunity lost to bring more change [18].

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CONFLICT OF INTEREST:

No.

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