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Research Article

Gap Assessment on New Medical Device Rules in India and EU

Nitika Agrahari*, Cs Lakshameesha, Divakar Goli, and Neha Chauhan Awadhesh

Drug Regulatory Affairs, Acharya & BM Reddy College of Pharmacy, India

***Corresponding author**

Nitika Agrahari, Drug Regulatory Affairs, Acharya & BM Reddy College of Pharmacy, Bengaluru-560107, Karnataka, India, Tel: 918003838674; Email: nikky4745@gmail.com

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- CDSCO

Abstract

Medical Device is an emerging market. The specific areas of application and extent of usage of medical devices is ever increasing throughout the world and becoming more and more sophisticated with every passing year. Regulations of Medical Devices vary from country to country. European Medical Agency (EMA) regulates medical devices in EU while the Central Drug Standard Control Organization (CDSCO) is its counterpart in India. Recently introduced guidelines and various amendments provide adequate guidance for the manufacturers, distributors and competent authorities to manage various activities and regulatory processes in an efficient manner. They perform a gap analysis of various regulatory frameworks of their business interests in order to thoroughly understand the inputs required for regulatory approvals across geographic territories. This research highlights comparative study of current regulations in India and EU, pertaining to applications for medical device registration certificates and medical device manufacturing/importation licenses. The recommendations are to be expected to implemented and regulated properly with effective outcome.

INTRODUCTION

Medical device is any instrument, implement, device, appliance, machine, implant, reagent for *in-vitro* use, material, software or other similar or related article, intended by the manufacturer to be used in combination or alone, for human beings, wherein the software required by its manufacturer is intended to be used exclusively for therapeutic/diagnostic purpose and vital for its proper application for one or more of the specific medical purpose(s) of:

a) Diagnosis, monitoring, preventing, alleviation or treatment of disease,

b) Examination, modification, support or replacement of the physiology processor anatomy,

c) Life sustaining or supporting or system,

d) Conception control [1].

India

In June 2005, CDSCO in India produced Medical Device guidelines and in Jan2017, MOH notified through GSR. 78 (E) the separate guideline for "Medical Devices Rules, 2017" which came into force from 1st Jan 2018. Before implementing the Medical Device rules of the Medical Device Rules, 'notified medical devices' were considered as pharmaceutical drugs in India according to the Drug and Cosmetic Act, 1940. Hence, it was necessary to have separate guidelines for pharmaceutical drugs and medical devices [2].

Classification

In line with world rules and regulations, there are new rules which are introduced based on the risk the new rules for classification.

Medical Devices are classified by CDSCO and it will periodically publish the classified medical devices on website. To classify the medical devices the importers and manufactures should follow the below mentioned classification list (Table 1).

If the medical device classification is in higher grade especially in GHFT countries here also it will be considered as higher grade medical devices.

European Union

On 25 May 2017 the latest MD Regulation (EU) 2017/745 and IVD Regulation (EU) 2017/746 come into effect. This replaces the 3 Directives which is existing beginning from May 2020 (for MDs) and from mid-2022 (for IVDs). The producers were granted this transitional phase to conform to the current MD

Table 1: Classification of Medical Devices [3].

CLASS	RISK LEVEL
CLASS A	Low
CLASS B	Low-moderate
CLASS C	Moderate-high
CLASS D	High

/ IVD regulations. Until the time as NBs have been assigned to certify against both the newly introduced regulations, all the MDs must meet the important/essential requirements set out in the directives [4] (Table 2).

Table 2: Classification of Medical Device as per EUMDR [5].

Classes	Risk Description	Example
Class I- sterile	Reusable sterile surgical instruments	Sterile gloves. Dressings, others.
Class I- measuring	Provided sterile and/or has a measurement function (low/medium risk);	Volumetric urine bag
Class I- basic	Provided non-sterile or will not have measurement feature (low risk)	Non-Sterile Gloves
Class IIa	medium risk	Suction equipment, Surgical Blades.
Class IIb	Medium to high risk	Radiotherapy equipment, orthopedic implants
Class III	High-risk	Drug-eluting cardiac stents, Absorbable Sutures, AIMD

OBJECTIVES

- To review regulatory framework for import registration.
- Potential Impact of Medical Devices Regulation, 2017/745
- To compare the detail regulations of Medical Device in EU and India to address compliance.

METHODOLOGY

The research carried out with the collected data by analyzing the terms of the below parameters:

1. Internet using official web page
2. Overview of Regulatory Guidelines
3. Review and compilation of documents

RESULT AND DISCUSSION

Medical Device Registration and Import Regulations in India

Registration Procedure: In India, for the medica1 devices import, registration and import permits are essential. Therefore, an individual who is likely to import medical devices into India must obtain a certificate of registration and import permit. Both production and import license applications are dealing with thru an online portal, SUGAM— an online licensing program is part of the MoHFW.

SLA shall control the manufacturing authorization for products of Class A and B medical device, and the prerequisite for Class C and D licenses will be referred to the CLA. A Quality Assurance Report (QAR) of Class B, C and D goods must be published in accordance with manufacturing license; By comparison, a QAR for medical devices under Class A has to be issued within 4 months from the authorization date of the license for manufacture. In the event that products were not shipped into the nation before the date of the notification, the import is not authorized. The permission of the competent authority is needed for the importation of medical devices into India. Certain products that are already in use are placed introduced in the market for a certain period of time until the request made is denied or accepted [6].

Chapter 5 of the MDR 2017, deals with the import of medical devices for marketing and distributing in the Indian market. International manufacturers may select a competent Indian agent to carry out PMS operations and medical device delivery by holding the license. Any authorized agent who already had a license for manufacturing the medical devices for the purpose of distribution or sale may request for an import license shall be presented to the CLA for all classes of medical devices. Indeed, any wholesaler planning to produce medical devices for import must request for an import license. The mechanism for licensing is governed through MoHFW under central government. The ministry has an electronic database, from which the demand for an import license will be rendered. Use Form MD-14, the submission is submitted with the regional licensing authority.

As well, the individual is required to present several other documentation together with the verification form. First of all, the submission must have a cover letter in an appropriate template, and the application must have the correct details. In addition, the applicant may apply for a valid Indian medical device distributor wholesale/manufacturer permit. This is an essential condition for submitting a request. The purchaser always needs to present the submission with FSC. A certificate signifies the manufactured medical devices are openly available into the selling country's open market and are allowed for sale and trade globalization is said to be Free Sale Certification.

The supporting documentation often include standard certificates from international manufacturers guaranteeing good quality of the product being imported. A DMF that describes the importing medical device technological, health, and safety-related information and test data. The application should also include a PMF which describes specifics of the medical device's manufacturing process.

In India, there are many items requiring registration including spinal pins, heart valves, syringes, annuloplasty tubes, and needles, cardiac stents, cochlear implants, catheters, etc. Any business company that wants to license or import medical devices lawfully into India must abide by the rules laid down in the New Medical Device Regulation 2017 of CDSCO. In case, in India, there is no registered office of the organization, then the organization will need to appoint an "authorized agent" to manage the registration processes and other functions. An "authorized agent" is the one who have a very important role in the registration process and is also authorize for the follow-up actions. (7-8)

1. Business activity
2. PMS
3. Pre-certification (Figure 1).

Medical Devices import procedure in India: A list of documentation is required for importation of medical devic-

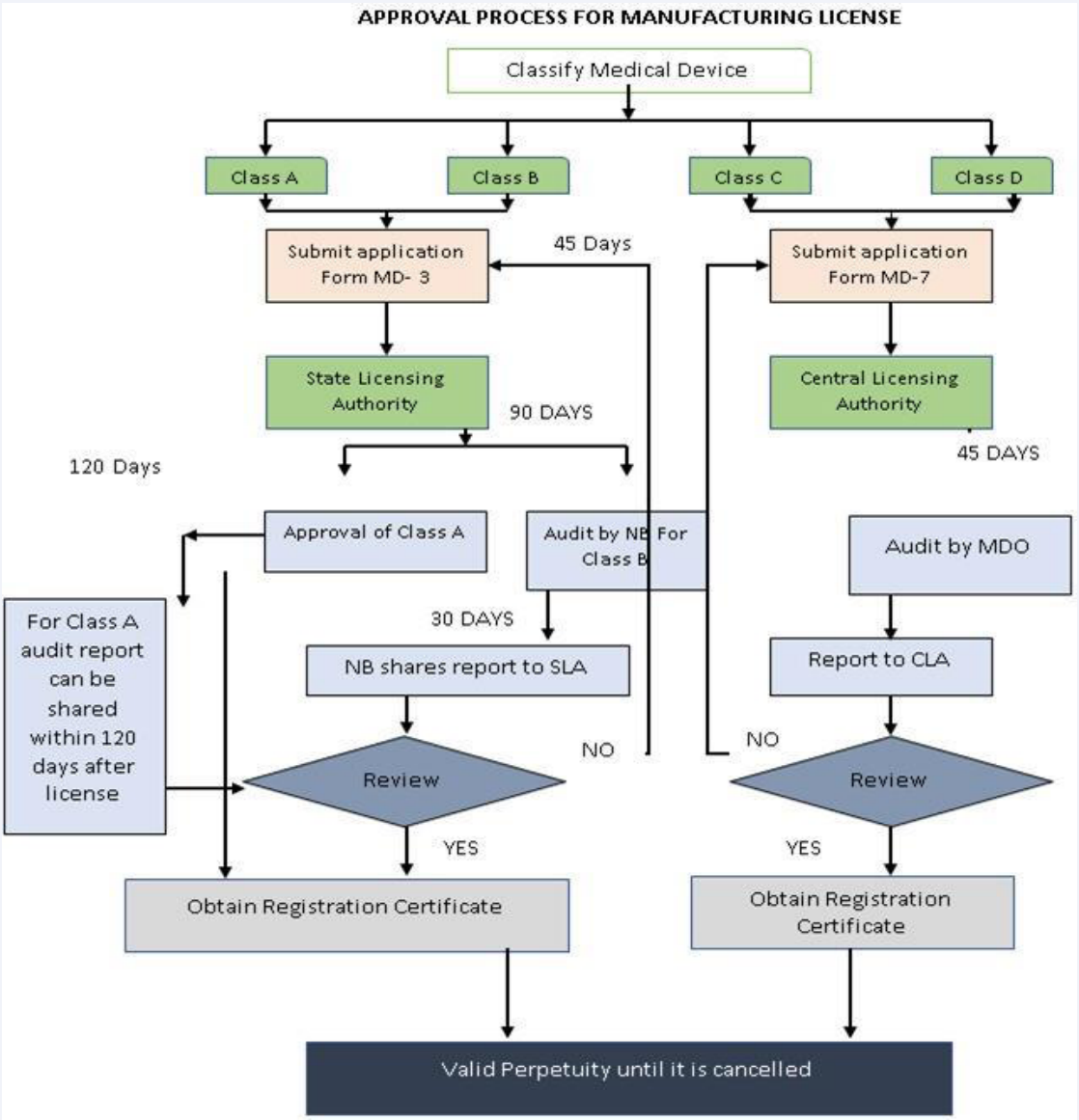

Figure 1 Process of Obtaining Registration [9,10].

es to be submitted with Form MD 14 (Table 3) (Figure 2).

Registration Certificates: The 2017 Rules also eliminated the need for a certificate of approval to recognize an international manufacturer its location and the goods. Presently we have to make two separate applications to import and marketing products in India (registration and import license). The international distributor shall designate an authorized agent in India after the start of the Rules 2017 and is applied to get import license to get imported and marketed devices into the nation. After 9 months the claimant will be issued an import permit.

In India, renewal process for certificates is far less rigorous when compared to other countries. For retaining certificate's permanent validity, the applicant should incur an annual renewal, maintenance charge of Rupees 20,000 (about $310) every 5 from years from the issuance date [12] (Table 4).

Potential Impact of Medical Devices Regulation, 2017/745: (Table 5 and 6).

CONCLUSION

The changes made by Medical Devices Rules 2017 are anticipated to allow more multinational companies (MNC) to build manufacturing facilities for medical devices in

- From this research project it is inferred that no such strict regulations and rules for the import, production, and selling of medical devices existed till 2017.
- The approved medical devices need to carry unique device identifiers by 2020. Medical devices licensed for manufacture, selling or delivery in India shall carry two different types of unique identifiers, beginning on January 1st, 2022 to ensure safety and effectiveness, the government is setting up research labs in the country to address shortcomings in medical device goods.

Table 3: List of Document to be Submitted with Form MD 14.

SL. No.	DOCUMENTS	SL. No.	DOCUMENTS
1.	Covering Letter	2.	Power of Attorney
3.	Wholesale License	4.	Free Sale Cert.
5.	Audit Report for past 3 years	6.	ISO 13485 Cert.
7.	Full Quality Assurance	8.	CE Design Certificate
9.	510K cert	10.	Decl. of Conformity
11.	Plant Master File • General Information • Personnel • Premises and Facilities • Equipment • Sanitation • Production • Quality Assurance • Storage • Documentation • Medical Device Complaints and Field Safety Corrective Action • Internal Audit • Contract Activities	12.	DMF- Executive Summary
13.	Subsequent Equivalence	14.	Labels and IFU
15.	Device Design and Manufacturing Process Flow Chart	16.	Essential Principles Checklist
17.	Risk Analysis and Control Summary	18.	Design Verification and Validation
19.	Bio-compatibility	20.	Medicinal Substances Data
21.	Biological Safety (TSE/BSE)	22.	Sterilization Validation Data
23.	Software Validation/ verification	24.	Animal Studies Preclinical Data
25.	Stability Validation Data	26.	Clinical Evidence
27.	Post Marketing Surveillance	28.	Batch Release certificate
29.	Notarized Copy of Overseas Manufacturing Site or establishment or plant registrations in Country of Origin issued by Competent Authority	30.	Constitution Details of Authorized Indian Agent
Approval process for Application through Online Sugam Portal [11].			

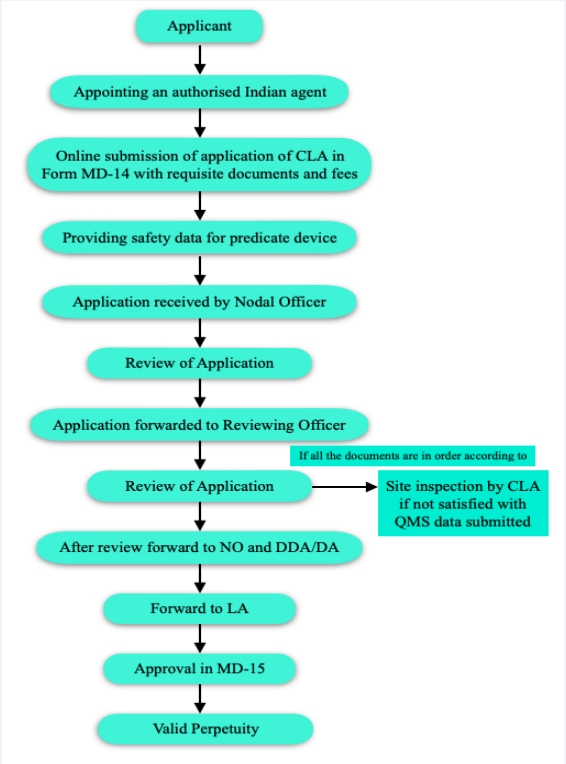

Figure 2 Application for Import License via SUGAM Portal every 5 from years from the issuance date [12].

Table 4: Timeline to obtain Manufacturing/ Import License for Medical Device.

Class/Timeline	Class A	Class B	Class C	Class D
Manufacturing License	45 Days	140 Days	150 Days	150 Days
Import License	Within 9 months			

Table 5: Potential Impact of Medical Devices Regulation, 2017/745 [13].

Parameter	Change	Potential impact
Scope of devices regulated	In new regulation include the some cosmetic devices and the devices using non-viable human tissues	Mainly impacted on the industrial regulators and increased training and the consultancy work increases for newly included devices
Validation of notified bodies	Mainly on the selection of notified body (NBs) with detailed criteria and the monitoring to notified body about requirements.	Shortage of the resourced validated notified bodies and strict requirements for present NBs and increased biocompatibility assessments and the higher costs and longer time periods for approval to manufacturer's
Device testing and inspection	Providing the more health safety and efficiency information details of high-risk devices and the supporting clinical investigation data and increased work for NBs for the providing data for EU reference laboratories which is validated for testing. The second look by the NBs for the biocompatibility for high risk devices, and authorization to conduct the confirmatory testing, NBs analysis of relevant laboratory results, and the unannounced inspection of premises by NBs of the high risk MD premises (e.g. Annually for class III devices)	The more importance on the test laboratory selection and increased release testing and must should be compliance to current standards and More need in biocompatibility /performance test training. Increased interpretation of requirements and standards and less tolerance for gaps in biocompatibility and enhance monitoring of controls on change.
Surveillance	Robust requirements and improved PMS, increased coordination in vigilance case analysis and reactions	Potential for higher expense for manufacturers and supplier Lawsuits.
Manufacturer staffing	The organization of a well-qualified person who will be responsible for regulatory compliance and increased manufacturer's Responsibility	Increased in demand of qualified personnel and increase the resource needed and costs increases
Comparison of Medical Device in EU and India [14,15]		

Table 6: Comparison of Medical Device Regulation in EU and India.

SL. No.	Point of Comparison	European Union	India
1.	Regulatory Authority	EMA and RA of member state	CDSCO
2.	Definition of Medical device	'medical device' means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes: • Diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease • Diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability • The investigation, replacement or modification of the anatomy or of a physiological or pathological process or state, • Providing information by means of *in vitro* examination of specimens derived from the human body, including organ, blood and tissue donations and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.	medical devices including software or an accessory, intended by its manufacturer to be used specifically for human beings or animals which does not achieve the primary intended action in or on human body or animals by any pharmacological or immunological or metabolic means but which may assist in its intended function by: • Diagnosis, prevention, monitoring, treatment or alleviation of any disease or disorder • Diagnosis, monitoring, treatment, alleviation or assistance for, any injury or disability • The investigation, replacement or modification or supporting anatomy or a physiological process • Supporting or sustaining life • Disinfection of medical devices, and • Control of conception

3.	Classification Categories	Class I	Class A
		Class II	Class B
		Class III	Class C
		Class IV	Class D
4.	Regulatory Pathway	Multiples Pathways	Market Authorization Application to Competent Authority
5.	Fees for available pathways	Fees for available pathways	Import License: For class A and B $ 1,000- Registration Fee $ 50- Premises Registration For class C and D $ 1,500- Registration Fee $ 3000- Premises Registration
6.	Quality Management Systems requirement	ISO 13485	ISO 13485:2016
7.	Technical Data Assessment performed by	EMA	CDSCO
8.	Requirement for establishment Registration	Responsible person registration	Premises Registration
9.	Regulation of Medical Device	EU MDR 2017/745	Medical Device Rule 2017
10.	Validity of License	The validity of CE marking is for Class I- Indefinite. Class IIa, IIb and III-3 years.	5 years from the date of approval, for Notified Devices.
11.	Requirement of document for import registration	• Single Administrative Document • Economic operator Registration and Identification • CE marked Certificate • EU declaration of Conformity • The manufacturer is identified and that an authorized representative. • Label and IFU • Unique Device Identifier • Biological Safety(TSE/BSE) • unique identification of devices • clinical investigations • vigilance and post-market surveillance • Regulatory certification • Product Validation and Verification Report • Audit Report • Clinical evaluation and PMCF • Correlation table • An assessment of conformity based on a quality management system and technical documentation • An assessment of conformity based on type examination • An assessment of conformity based on verification of product conformity • Certificates issued by NB • Custom-made devices procedures. • Summary of the Risk Analysis and Control • Device Design and Manufacturing Process Flow Chart • risk assessment of phthalates presence. • Infection and microbial contamination • Medicinal Substances Data • Devices construction and interaction with their environment • Pre-clinical and clinical data	• Covering Letter • Power of Attorney • Wholesale License • Free Sale Cert. • Audit Report for the past 3 years • ISO 13485 Cert. • Full Quality Assurance • CE Design Certificate • 510K cert • Decl. Of Conformity • Plant Master File • DMF- Executive Summary • Subsequent Equivalence • Labels and IFU • Device Design and Manufacturing Process Flow Chart • Essential Principles Checklist • Summary of Risk Analysis and control. • Design Verification and Validation • Biocompatibility • Medicinal Substances Data • Biological Safety(TSE/BSE) • Sterilization Validation Data • Software Validation/ verification • Animal Studies Preclinical Data • Stability Validation Data • Clinical Evidence • Post Marketing Surveillance • Batch Release certificate • Notarized Copy of Overseas Manufacturing Site or establishment or plant registrations in Country of Origin issued by Competent Authority • Constitution Details of Authorized Indian Agent

12	Labeling Requirements	(a) the name and address of the manufacturer or trade name (b) where appropriate, the word 'STERILE'; (c) Detail necessary to identify the device and its use for the user. (d) manufacturing date and expiry date; (e) EU representative being on both the label and not explicitly requiring that representative to be on the IFU. (f) the CMR/ endocrine disruptors over 0.1 percent by weight (g) Unique Device Identification (UDI) (h) Expiration date by using the word as 'using' or 'implanting'; (i) An indicator, where appropriate, of the date by which the device should be used, in safety, expressed as the year and month (j) Manufacturing year for active devices other than those referred to in (e). This indication may be included in the batch or serial number; (k) any special condition regarding storage and/or handling; (l) where applicable, method of sterilization; (m) any warnings and/or precautions which must be taken; (n) an indication that the device contains a derivative of human blood. (o) Where the device is a reprocessed single-use device, the number of reprocessing cycles performed and any limitation on the number of reprocessing cycles shall be indicated. (p) if the device is custom-made, using the term 'custom-made device' (q) the words 'exclusively for clinical examination' where the device is designed for clinical investigation; 'Overall qualitative structure' and 'quantitative knowledge on the key components responsible for performing the specific planned intervention' for devices made up of ingested or locally distributed compounds. (r) 'batch number previous to the word 'Lot or serial no.'	a) Medical device Name and description b) the details needed to identify the device and the use for the user. c) manufacturer name and address. d) Net quantity e) Manufacturing and expiry date (month and year) f) An indication that a medicinal or biological substance is present in the device, if required. g) Lot no. preceded by the word ''Lot'' or ''Batch no.'' also known as Production identifier h) Storage condition applicable to the device; i) To indicate, if a device is delivered as a sterile product, its sterile state and sterilization method. j) Warning or precaution; k) To label the device appropriately, if the device is intended for single use; l) ''Physician sample-Not to be sold'', if a medical device is intended to be distributed as free sample to a medical professional. m) Manufacturing license no. n) Unique Device Identification (UDI) o) Device identifier no. p) If a device is used for import, import license no. , name and address of the importer.
13.	Certificate of suitability	Mandatory	Not required
14.	TSE/BSE free statement	Mandatory only Once products containing components of biological origin	Not required
15.	CRO (Audits)	Audited by MHRA	CDSCO
16.	Reserve Sample	No such Requirement	No such Requirement
17.	Unique device Identification of the medical device (UDI)	'UDI system' shall composed of : (a) manufacture of a UDI may include: (i) manufacturer and device-specific UDI device identifier ('UDI-DI'), providing access to the information provided for Annex VI Part B; (ii) an UDI production identifier ('UDI-PI') identifying the device manufacturing unit and, where applicable, the packaged devices as set out in Part C of Annex VI; (B) place the UDI on the device package or label; (C) Installation of UDI by economic owners, healthcare institutions and healthcare practitioners, in compliance with the requirements laid down in paragraphs 8 and 9 of this Article; (D) Electronic 'UDI database' established in accordance with Article 28.	With impact from 1 January 2022, a medical product has been licensed for sale or delivery or import and export shall bear a UDI containing the device identifier and the identification of the production. Explanation.- To the end of this rule,- "Device identifier" implies the global trade items no.; (ii) "Production identifier" includes the serial number, lot or batch size, medical device type program, date of manufacture and/or expiry.
18.	Shelf life	5 years	The Medical Device's shelf-life shall not exceed 60 months from the expiration date.

Nonetheless, some analysts do believe that the strict regulations will contribute to delays in securing the approval of CE mark and leads to a significant decline in the number of groundbreaking CE marked MDs. The EU MDR is projected to dramatically alter MD manufacturers ' activities and even affect the structure of both their current and prospective portfolios.

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