Available online on 15 Dec, 2023 at https://ijdra.com/index.php/journal

International Journal of Drug Regulatory Affairs

Published by Diva Enterprises Pvt. Ltd., New Delhi
Associated with RAPS & Delhi Pharmaceutical Sciences & Research University

Review Article

Open Access

Regulatory Skeleton of Medical Devices in the European Union

Soundarya Reddy Kalva[a,*] , Sahitya Reddy Kalva[b], Haripriya[c]

[a]11430 Hayloft ln, Glen Allen, Virginia, USA, 23060: +1 (804) 874-5928;
[b]Kaseya Software Company, Ground Floor, Tower B, Prestige Shantiniketan,Mahadevpura, Whitefield.
[C]50832, Sevilla Circle, Novi MI, 48374, USA;

Abstract

'Medical device' means any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s). Medical devices make an essential contribution to healthcare in the Europe for the benefit of European citizens. These products must undergo a conformity assessment to demonstrate that they meet legal requirements to ensure they are safe and perform as intended. The European Medicines Agency (EMA) is responsible for the scientific evaluation of a product through centralized marketing authorisation applications (MAA). In order to commercialize medical devices in the European Union, a (European Conformity) CE Mark certificate is needed.

Keywords: Medical Device, European Commission, MDR, Centralized Procedure, European Medicines Agency

Article Info: Received 18 Oct 2023; Review Completed 02 Dec 2023; Accepted 06 Dec 2023

Cite this article as:
Kalva SR , Kalva SR, Haripriya. Regulatory Skeleton of Medical Devices in the European Union. Int J Drug Reg Affairs [Internet]. 2023 Dec 15 [cited 2023 Dec 15]; 11(4):34-38. Available from: http://ijdra.com/index.php/journal/article/view/630

DOI: 10.22270/ijdra.v11i4.630
*Corresponding author

1. Introduction

Medical devices are products or equipment intended generally for a medical use and is regulated at Member State level. (1) The European Community has formally adopted several Directives that apply to the Europe Medical Devices Registration. This means that any company, interested in selling a product in one of the European Community countries, must comply with the requirements of the applicable Directive and must mark its product with the CE symbol according to those requirements. From 26 May 2021 the Medical Device Regulation (MDR) 2017/745 which entered into force on 25 May 2017 will become mandatory and will replace the Medical Device Directive and the Active Implantable Medical Device Directive (those will no longer be an option to obtain CE marking). Regarding the In Vitro Diagnostic Regulation (IVDR) 2017/746 the date of entry into force was also 25 May 2017 and it will become mandatory on 26 May 2022. (2) In order to commercialize medical devices in the European Union, a CE Mark certificate is needed. (3)

Overview of CE Marking Process

The below steps illustrate the European CE medical device approval process. (3)

(Medical Device Regulation (MDR) 2017/745 Chapter's and Annex's will apply)

Step 1: To obtain CE Marking certification, you must comply with Medical Device Regulation

(MDR) 2017/745.

Step 2: Appoint a Person Responsible for regulatory compliance. Determine classification of your device using Annex VIII (Classification Criteria) of the MDR - Class I (self-certified); Class I (sterile, measuring, or reusable surgical instrument); Class IIa, Class IIb, or Class III.

Step 3: For all devices except Class I (self-certified), implement a Quality Management System (QMS) in accordance with the MDR. Most companies apply the EN ISO 13485 standard to achieve compliance. Plan with suppliers about unannounced Notified Body audits.

For Class I (self-certified), you must implement a QMS, though Notified Body intervention is not required.

Step 4: In accordance with Annex II and III, prepare a CE Technical File or Design Dossier (Class III) providing information about your device and its intended use plus testing reports, Clinical Evaluation Report (CER), risk management file, IFU, labeling and more. Obtain a Unique Device Identifier (UDI) for your device.

Clinical studies are generally required for implantable and Class III devices. Existing clinical data may be acceptable. Clinical trials in Europe must be pre-approved by a European Competent Authority.

Step 5: If you do not have a location in Europe, appoint an Authorized Representative (EC REP) located in the EU who is qualified to handle regulatory issues. Place your EC REP name and address on device label. Obtain a Single Registration Number from the regulators.

Step 6: For all devices except Class I (self-certified), your QMS and Technical File or Design Dossier must be audited by a Notified Body (a third party accredited by European authorities to audit medical device companies and products).

Step 7: For all devices except Class I (self-certified), you will be issued a European CE Marking Certificate for your device and an ISO 13485 certificate for your facility following successful completion of your Notified Body audit.

Step 8: Prepare a Declaration of Conformity in accordance with Annex IV, a legally binding document prepared by the manufacturer stating that the device is in compliance with the applicable European requirements. You may now affix the CE Marking.

Step 9: Register the device and its Unique Device Identifier (UDI) in the European database on medical devices (EUDAMED) database. UDI must be on label and associated with the regulatory documents.

Step 10: For Class I (self-certified), annual NB audits are not required. However, CER, Technical File, and PMS activities must be kept updated.

For all other classes, you will be audited each year by a Notified Body to ensure ongoing compliance with the MDR. Failure to pass the audit will invalidate your CE Marking certificate. You must perform Clinical Evaluation, PMS, and PMCF activities to maintain certification.

2. Device Classification & Conformity Assessment Routes:

Medical devices in the EU must undergo a conformity assessment to demonstrate that they meet legal requirements to ensure they are safe and perform as intended. EU Member States can designate accredited notified bodies to conduct conformity assessments.

According to the European framework, there are four classes of medical devices: Class I, IIa, IIb and III. If your medical device is in any other class apart from clsas I, you will have to provide the Notified body with proof that your product fulfils the General Safety and Performance requirements of the respective MDR 2017/745 Regulations.

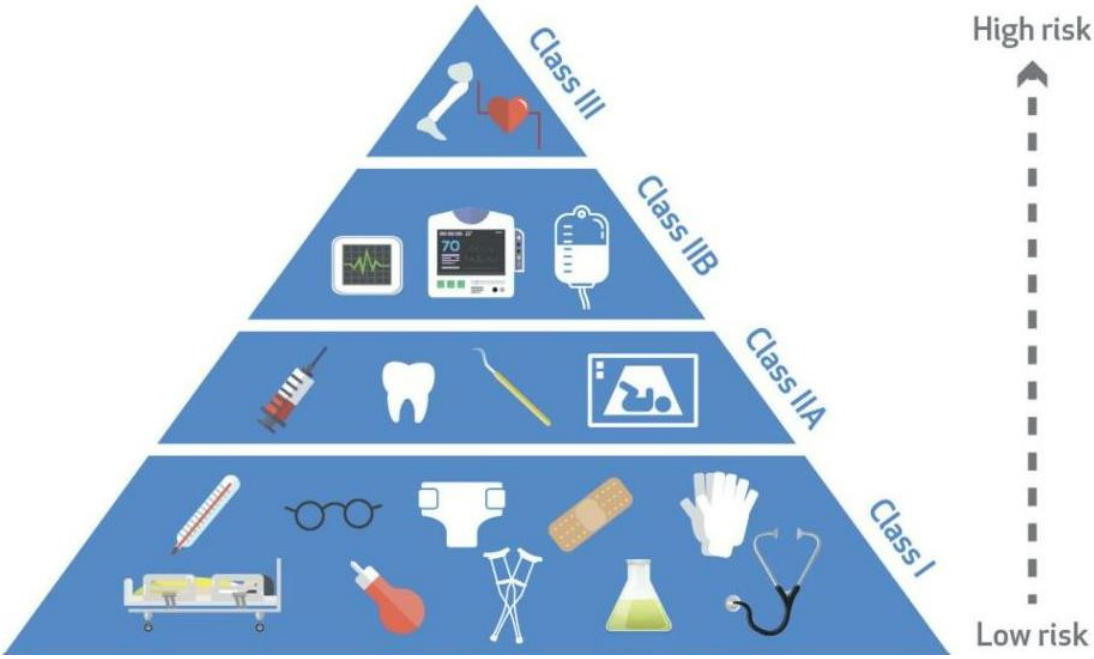

Figure 1. Classification of Medical Devices (with examples)

Class I Medical Devices

Medical devices class I have the lowest perceived risk. The manufacturers of such devices can choose one out of three possible CE marking routes. In this regard, they should consider the following: if the medical device is sterile, e.g., a personal protection kit; if the medical device has measuring functions, e.g., stethoscope; and, if it's not sterile, nor measuring, e.g., corrective glasses. If your product is class I, and it's not a sterile or measuring device, then all you need to do is to self-certificate it, and formally declare its compliance with the applicable requirements of the MDR via a written statement. If it is a sterile or a measuring medical device, then you will need a Notified body assessment.

Class IIa Medical Devices

Medical devices of class IIa could be such as surgical gloves, hearing aids, diagnostic ultrasound machines, etc. They usually constitute low to medium risk. Patients should use them for a short-term period, any less than 30 days. If you are a manufacturer of a class IIa medical device, you will have to back up your declaration of

compliance with a Notified body assessment. Only then, you will be allowed to place your product on the market. There are four possible routes to CE mark your product, split into two groups given the product's type, i.e., if it is sterile or not.

Table 1. CE marking routes of Class I Medical Devices. (4)

Sterile Medical Devices	Measuring Medical Devices	Other Medical Devices
1. Preparing technical documentation to support the Declaration of Conformity. 2. Notified body assessment of the products' manufacturing aspects related to securing and maintaining sterile conditions. 3. Placing the registration number of the notified body alongside the CE mark. 4. Affixing the CE mark to the product and storing the declaration of conformity and supporting evidence of the Competent Authority inspection. 5. Placing medical devices on the market.	1. Preparing technical documentation to support the Declaration of Conformity 2. Notified body conformity assessment of the product with the metrological requirements. 3. Compiling a Declaration of Conformity. 4. Registration with the Competent Authority 5. Affixing the CE mark to the product and storing the Declaration of Conformity and supporting evidence of the Competent Authority inspection. 6. Placing medical devices on the market.	1. Preparing technical documentation to support the Declaration of Conformity. 2. Compiling a Declaration of Conformity. 3. Registration with the Competent Authority. 4. Affixing the CE mark to the product and storing the Declaration of Conformity and supporting evidence of the Competent Authority inspection. 5. Placing medical devices on the market.

Table 2. CE marking routes of Class IIa Medical Devices. (4)

All Medical Devices		Only Non-Sterile Medical Devices	
Route 1	**Route 2**	**Route 1**	**Route 2**
1. Full quality assurance audit by a notified body 2. Creation a Declaration on Conformity 3. Affixing the CE mark and notified body number on the product. 4. Placing the medical device on the market	1. Preparing technical documentation of conformity. 2. Production quality assurance audit by a notified body 3. Creating a Declaration of conformity. 4. Affixing the CE mark and notified body number on the product. 5. Placing the medical on the market.	1. Preparing technical documentation to support the declaration of conformity. 2. Inspection quality assurance audit by a notified body (not including design and manufacturing) 3. Declaration of Conformity. 4. Affixing the CE mark and notified body number on the product. 5. Placing medical devices on the market.	1. Preparing technical documentation to support the declaration of conformity. 2. A notified body needs to verify every batch, 3. Creating a Declaration of Conformity. 4. Affixing the CE mark and notified body number on the product. 5. Placing medical devices on the market.

Class IIb Medical Devices

Here, we can include medical devices such as long-term corrective contact lenses, surgical lasers, defibrillators, and others. They are medium to high-risk devices, and patients may use them for a period longer than 30 days. In case your product is in class IIb, similar to the procedures in class IIa, you will need a Notified body to assess your technical documentation for compliance with the MDR. The choice of a specific CE marking route will depend again on the type of your product.

Class III Medical Devices

These are the highest risk possible devices, and permanent monitoring is required during their lifetime. There are specialized institutions responsible for conducting the products' monitoring. Such devices are, for instance, cardiovascular catheters, aneurysm clips, hip-joint implants, prosthetic heart valves, and others. Here, and also in class II, the conformity assessment of the medical devices may include an audit of the technical documentation and a quality system/product inspection, and to be focused on one or more aspects of the device design and production.

Table 3. CE marking routes of Class IIb Medical Devices. (4)

All Medical Devices		Only Non-Sterile Products	
Route 1	**Route 2**	**Route 1**	**Route 2**
1. Full quality assurance audit by a notified body.	1. Type examination by a notified body.	1. Type examination by a notified body.	1. Type examination by a notified body.

2. Creating a Declaration of Conformity. 3. Affixing the CE mark and notified body number on the product. 4. Placing medical devices on the market.	2. Production quality assurance audit by a notified body 3. Creating a Declaration of Conformity 4. Affixing the CE mark and notified body number on the product. 5. Placing medical devices on the market.	2. A notified body Inspection quality assurance audit (not including design and manufacturing) 3. Declaration of Conformity 4. Affixing the CE mark and notified body number on the product. 5. Placing medical devices on the market.	2. A notified body needs to verify every device/batch. 3. Creating a Declaration of Conformity 4. Affixing the CE mark and notified body number on the product. 5. Placing medical devices on the market.

Table 4. CE marking routes of class III Medical Devices. (4)

All Medical Devices			Only Non-Sterile Products
Route 1	**Route 2**	**Route 3**	**Route 1**
1. Full quality assurance audit by a notified body. 2. Creating a Declaration of Conformity. 3. Affixing the CE mark and notified body number on the product. 4. Placing medical devices on the market.	1. Design dossier examination by a notified body. 2. Creating a Declaration of Conformity 3. Affixing the CE mark and notified body number on the product. 4. Placing medical devices on the market.	1. Type examination by a notified body. 2. Production quality assurance audit by a notified body (not including design). 3. Declaration of Conformity 4. Affixing the CE mark and notified body number on the product. 5. Placing medical devices on the market.	1. Type examination by a notified body. 2. A notified body needs to verify every device/batch. 3. Creating a Declaration of Conformity 4. Affixing the CE mark and notified body number on the product. 5. Placing medical devices on the market.

3. Post Market Surveillance (PMS)

Post Market Surveillance (PMS) is a collection of processes and activities used to monitor the performance of a medical device immediately upon commercialization of the device. Ensuring adequate medical input into the risk management process during product development will help manufacturers characterize possible product safety issues. It is important to note that the requirements for PMS should be directly proportional to the risk associated with the device based on its intended use. (5)

PMS could be 'reactive' – responding after an event; of which there are many types ranging from complaints to those involving serious injury or in an extreme case where a serious injury or death has occurred known as 'Vigilance'. These activities can be considered 'passive' as they are largely data collection activities. On the other hand, PMS could be 'proactive' – endeavours meant to anticipate and curtail events before they occur; there are many types such as user surveys, manufacturer-sponsored clinical registry studies, Post Market clinical Follow-up (PMCF) studies. In 'proactive' PMS activities, information is actively sought to gain insight and data into the real-world performance of the device. A PMS plan must be provided as part of the assessment for CE mark certification and should be based on available clinical data and an assessment of residual risks.

Table 5. Examples of PMS data and their respective action types

Proactive	Reactive
➢ Customer Surveys	➢ Customer complaints
➢ Post CE mark clinical trials, including PMCF	➢ Unsolicited user feedback (other than complaints)
➢ Manufacturer sponsored device tracking/implant registries	➢ Maintenance/Service reports
➢ Expert user groups (focus groups)	➢ In-house testing (routine)
	➢ Failure analysis
	➢ Social media
	➢ Literature reviews
	➢ Regional or national device registries (non-manufacturer sponsored trials)

4. Outlook on Technical Documentation as per MDR (6)

(a) Annex II – Technical Documentation:

1. Device Description & Specification, Including Variants & Accessories

1.1. Device Description & Specification

1.2. Reference to previous and similar generations of the devices

2. Information to be supplied by the Manufacturer
3. Design and Manufacturing Information
4. General Safety and Performance Requirements
5. Benefit-Risk Analysis and Risk Management
6. Product Verification and Validation

6.1. Pre-clinical and clinical data

6.2. Additional information required in specific cases

(b) Annex III – Technical Documentation on Post Market Surveillance

1. The post-market Surveillance Plan
2. The PSUR (Periodic Safety Update Report)
3. PMS Report

5. Conclusion

Medical device' means any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purposes(s). In the European Union (EU) they must undergo a conformity assessment to demonstrate they meet legal requirements to ensure they are safe and perform as intended. They are regulated at EU Member State level, but the European Medicines Agency (EMA) is involved in the regulatory process. The EU MDR defines common specifications as "a set of technical and/or clinical requirements, other than a standard, that provides a means of complying with the legal obligations applicable to a device, process or system".

Acknowledgement

We would like to express our sincere gratitude to IJDRA Journal for publishing our work.

Financial Disclosure statement: The author received no specific funding for this work.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

References

1. Europe. European Medicines Agency, Human regulatory, Medical devices: Overview. Europe [Internet]. EMA; 1995-2020 [cited 2023 Aug 13]. Available from: https://www.ema.europa.eu/en/human-regulatory/overview/medical-devices
2. KOBRIDGE-Europe Medical Device Registration [Internet]. Korea: Medical Device Registration; 2020 [cited 2023 Aug 13]. Available from: https://kobridgeconsulting.com/europe-medical-device-registration
3. EMERGO, by UL. Global: Europe CE Marking Regulatory Process for Medical Devices [Internet].EMERGO; 2019 [cited 2023 Aug 13]. Available from: https://www.emergobyul.com/resources/europe-process chart#:~:text=In%20order%20to%20commercialize%20medical,they%20apply%20to%20your%20product
4. Max Stralin. CE check Support. Classification of Medical Devices and their Routes to CE Marking [Internet]. 2020 Jan [cited 2023 Aug 13]. Available from: https://support.ce-check.eu/hc/en-us/articles/360008712879-Classification-Of-Medical-Devices-And-Their-Routes-To-CE-Marking
5. British Standards Institute. Ibim Tariah Technical Expert: BSI Americas Rebecca Pine, Medical Devices Consultant. Effective Post-market Surveillance: BSI/UK/440/ST/0614/en/HL [Internet]. [cited 2023 Aug 13]. Available from: https://bsigroup.com
6. EUROPA, EUR-Lex-02017R0745-20170505EN. Regulation (EU) 2017/745 of the European Parliament and of the Council: EU [Internet]. eur-lex; 2020 Apr 24 [cited 2023 Aug 13]. Available from: https://eur-lex.europa.eu/eli/reg/2017/745/2017-05-05