European Medical Device Regulation: Collaboration to Drive Innovation

by Monica Tocchi, MD, PhD

ABSTRACT

Europe, the second largest global medtech market, is enduring a major overhaul as two brand new regulations for medical devices and in-vitro diagnostics will soon replace previous legislation. By May 26, 2020, more complex rules will impact the daily work of manufacturers, health professionals as well as the public, creating new opportunities for collaboration to drive innovation. Complying with the new Medical Device Regulation seems overwhelming and many don't know where to start. This paper discusses the key changes and best practices for a successful transition to the new legislative framework.

THE ACTORS

In the new European Medical Devices Regulation (MDR) 745/2017 [1], **Economic Operators** are defined as *"a manufacturer, authorized representative, importer or distributor"*, lumped together under the acronym of MAID. **Health Institution** means an *"organization with the primary purpose of the care or treatment of patients or the promotion of public health"*. In addition, **User** means *"any healthcare professional or lay person who uses a device"*, while a **Lay Person** is *"an individual who does not have formal education in a relevant field of healthcare or medical discipline; in vitro use, software, material or other similar or related article intended for human beings, for one or more of the specific medical purpose(s)."*

For all stakeholders, it is imperative to get ready for the regulatory framework as soon as possible. MDR is complex legislation and manufacturers and economic operators need to analyze various factors that impact their practice. Updates and new obligations span every aspect of the medical device lifecycle, from development and clinical evaluation to market access, surveillance and vigilance. Indeed, economic operators and health institutions in Europe are expected to comply with the applicable requirements of the MDR by the application date of May 26, 2020.

A proactive approach is needed to understand the requirements applicable to different devices and entities to avoid setbacks in healthcare delivery and business liability.

The new MDR intent is to reinforce the scrutiny of notified bodies and supervision of competent authorities, whilst also introducing provisions as to transparency, compliance and traceability throughout the supply chain for medical devices (Figure 1). Today, supply chain qualification and collaboration is a game-changing differentiator.

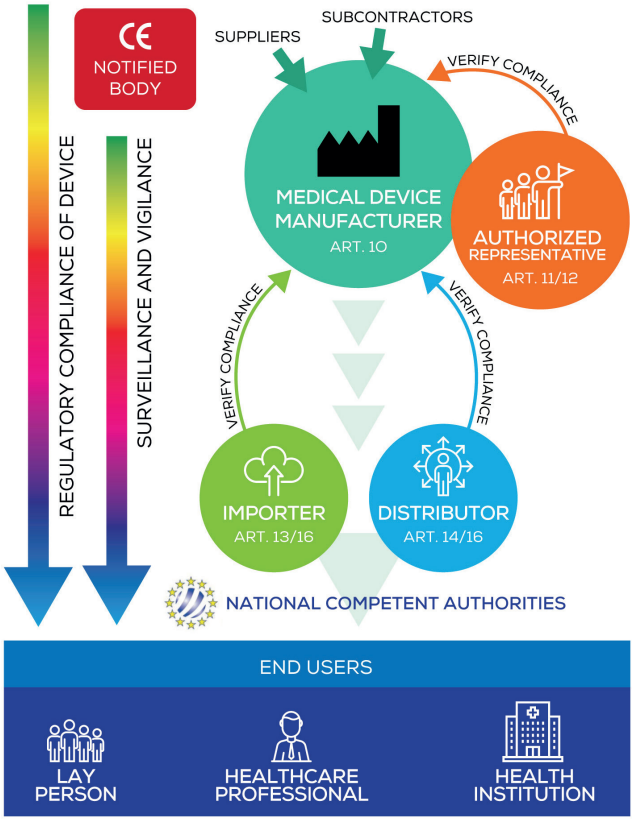


Figure 1. Supply chain and cooperation of economic operators (MAID) under the MDR

Creating open lines of communication, establishing programs for engagement and regulatory training are key elements to the MDR transition. This paper discusses the importance of mastering the MDR requirements and presents Meditrial's regulatory compliance approach for a successful transition.

Dr. Monica Tocchi

Founder and Chief Medical Officer, Meditrial

Dr. Tocchi is a cardiologist and regulatory expert involved in writing standards on clinical trials (ISO 14155), cardiac valve replacement and repair (ISO 5840; ISO 5910), cardiac occluders (ISO 22679) .

Meditrial is a trusted international consulting firm, Authorized Representative and certified provider of effective medical and regulatory trainings.
Meditrial is recognized as a leading CRO and digital health provider for medtech trials and applications for US approval and European CE marking.

THE MEDTECH MARKET

Perhaps no other sector of life sciences encounters as much transformation and opportunity as the medical device industry. Rapid growth is a result of technological advancements combined with the rising burden of population aging and chronic diseases. Based on the comprehensive study conducted by Fortune Business Insights, the global medical devices market size in 2018 was valued at $425.5 billion and is expected to reach $612.7 billion by 2025. [2]

Europe is the second largest medtech market after the US, with estimated value of €115 billion in 2017, representing 27% of the world market. [3] New regulatory requirements, fierce competition, and rapidly emerging technologies are creating new challenges for those operating in the sector. In particular, the stricter MDR requirements are driving up costs and increasing the risk of costly compliance failures. Startups and small companies experience difficulty navigating the complex approval processes. Also, established companies are exposed to third-party risk related to new obligations extended to suppliers and subcontractors. Industry therefore is facing the need to assess the impact of changes and prepare an action plan, defining the strategy for implementing appropriate upgrades, integrating new technologies and processes which are necessary to enable timely and effective compliance. Companies also need to ensure they have the right internal competencies required by the new MDR.

KEY CHANGES

The new MDR comprises 10 Chapters (Table 1) which include a total of 123 articles; and 17 Annexes (Table 2).
Compared to the previous Medical Device Directive, the MDR promotes a shift to a life-cycle approach, and brings Europe closer than ever before to the US regulatory framework [3].

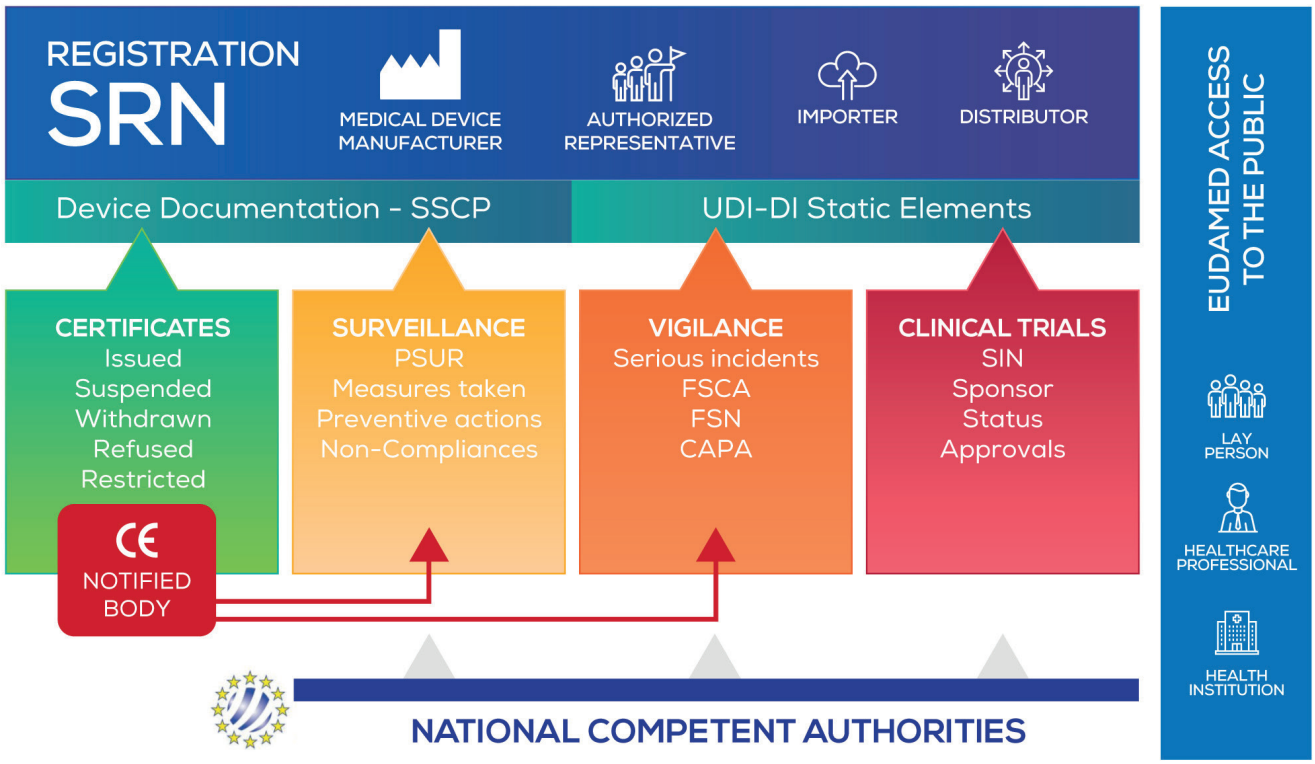
ABBREVIATIONS AND ACRONYMS

CER	Clinical Evaluation Report
DI	Device Identifier
IVDR	In vitro Diagnostic Device Regulation
GSPR	General Safety and Performance Requirements
MDR	Medical Devices Regulation
MDD	Medical Device Directive
NB	Notified Body
PI	Product Identifier
PMCF	Post Market Clinical Follow-Up
PRRC	Person Responsible for Regulatory Compliance
MAID	Manufacturer, Autohrized Representative, Importer, Distributor (Economic Operators)
SIN	Single Identification Number (for clinical trials)
SPR	Safety and Performance Requirement
SRN	Single Identification Number (for Economic Operators)
SSCP	Summary of Safety and Clinical Performance
UDI	Unique Device Identifiers

EUDAMED

The philosophy of the MDR is based on a central repository of information to lay the foundation for collaboration, transparency and interaction of all parties, namely the new European databank for medical devices and in vitro diagnostic devices (Figure 2) [4]. The EUDAMED databank has been in existence for many years but was only accessible by the European Commission and the National Competent Authorities (NCAs).
With the MDR, EUDAMED-2 expands to contain more extensive data and allow access to many more groups including the European Commission, NCAs, Notified Bodies, MAID, Sponsors and the public.

Figure 2. Functioning of EUDAMED-2, European Databank according to the MDR and IVDR



EUDAMED-2 will allow economic operators to register their organization and devices, upload relevant documentation, apply for clinical investigations and performance studies, and upload post-market surveillance documentation. It is forecast that 70,000 organizations will register, with an estimate of more than 300,000 users. The European Commission has recently set up a new webpage to share information on EUDAMED implementation [4]. Economic operators should regularly check this page to keep updated and be ready to o plan an appropriate data upload and transfer strategy.

Unique Device Identification

The new Regulations introduce a system of unique device identifiers (UDIs) to facilitate the traceability of devices, significantly enhancing the effectiveness of the post-market safety-related activities and allowing better monitoring by competent authorities. The UDI system should also improve purchasing, and waste disposal policies, and stock-management by health institutions and other economic operators.

Devices will be allocated a device identifier (DI) and production series or batches will be identified with a production identifier (PI). The basic UDI-DI must also be referenced in the declaration of conformity.In the US, FDA rules require medical device labelers to submit data to the Global Unique Device Identification Database (GUDID) for the highest-risk medical devices.

Although the US and European authorities are aiming for a globally harmonized and pursue a consistent approach based on the use of standardized nomenclature, variations still exist. MedTech Europe released a document that highlights the differences between the US UDI and EU UDI system requirements [5].

Compliance requirements

The MDR integrates requirements on authorized representation, clinical evaluation, vigilance, and post-market clinical follow-up. Details on new obligations to be met by manufacturers can be found in MDR Article 10.
As an example, the terminology of the MDR has changed. There are no more “essential requirements” as per MDD; under MDR, these are now safety and performance requirements (SPR).

The compliance of all marketed devices with the SPR presented in MDR Annex I has to be reassessed, with reference to current standards and state of the art. Along with these are increased requirements for clinical data. Previously a literature review and reliance on data of similar devices may have been sufficient, but some companies will now need data from clinical studies. In fact, equivalence is now more rigorously interpreted and only applicable in a limited number of cases. The qualification requirements for auditing and criteria for notified body (NB) reviews have increased, emphasizing clinical data and clinical evaluations. The UK competent authority has created an interactive introductory guide to the MDR and IVDR, that can be consulted for additional information [5].

COMPLIANCE CHAMPIONS

One of the first steps for compliance, is to have a designated person responsible for regulatory compliance (PRRC).
This person must have a relevant degree or sufficient work experience to understand and meet the requirements of the standard. In addition, the PRCC must also designated by outsourced suppliers: importers and distributors are deeply affected by the new regulation, leading to the need to address respective responsibilities regarding verification of compliance, cooperation in complaint handling and field

Table 1. MDR CHAPTERS

CHAPTER I	Scope and definitions
CHAPTER II	Making available on the market and putting into service of devices, obligations of economic operators, reprocessing, CE marking, free movement
CHAPTER III	Identification and traceability of devices, registration of devices and of economic operators, summary of safety and clinical performance, European database on medical devices
CHAPTER IV	Notified Bodies
CHAPTER V	Classification and conformity assessment
CHAPTER VI	Clinical evaluation and clinical investigations
CHAPTER VII	Post-market surveillance, vigilance and market surveillance
CHAPTER VIII	Cooperation between member states, medical device coordination group, expert laboratories, expert panels and device registers
CHAPTER IX	Confidentiality, data protection, funding and penalties
CHAPTER X	Final provisions

Table 2. MDR ANNEXES

I	General safety and performance requirements.
II	Technical documentation.
III	Technical documentation on post market surveillance.
IV	EU declaration of conformity.
V	CE marking of conformity.
VI	Information to be submitted upon the registration of devices and economic operators in accordance with Articles 29 par 4 and 31, core data elements to be provided to the UDI database, the UDI system.
VII	Requirements to be met by notified bodies
VIII	Classification rules.
IX	Conformity assessment on a quality management system and on assessment of technical documentation
X	Conformity assessment based on type- examination.
XI	Conformity assessment based on product conformity verification.
XII	Certificates issued by a notified body.
XIII	Procedure for custom-made devices.
XIV	Clinical evaluation and post- market clinical follow-up.
XV	Clinical investigations.
XVI	List of groups of products without an intended medical purpose referred to in Article 1 par 2.
XVII	Correlation table.

safety corrective actions and cooperating with manufacturers and Competent Authorities in device traceability.

A small company may not have a properly experienced and qualified regulatory person on-staff. Given the shortage of expert resources, it is urgent for any company to identify the right resources to fulfill this critical role, and ensure the right qualifications of the champion for each of the key suppliers or economic operators.

IMPACT ON MANUFACTURERS

As under the current regulatory regime, manufacturers of medical devices take prime responsibility for getting a CE mark certification for the European market. Now, companies need to manage the necessary upgrades to get new products CE- marked or old products re-certified under the new Regulation.

Conformity assessment procedures are more complex, and equivalence with other devices will be more rigorously interpreted, reducing reliance on evidence from the market and leading to the need for more clinical investigations.

Clinical data and Clinical Evaluation Report (CER) will face heavy scrutiny and require recurring updates. Manufacturers must also fulfill increased post-market surveillance requirements, perform Post-Market Clinical Follow-up (PMCF) studies when required to address residual risks, and deliver Period Safety Update Reports (Class IIa devices and above).

IMPORTERS, DISTRIBUTORS AND AUTHORIZED REPRESENTATIVES

Manufacturers outside the EU market should have a contract with an authorized representative inside the EU, whereas designating an importer or distributor is optional. The Regulations clarify the respective responsibilities of these economic operators (Figure 1), that are now for the first time involved in the evaluation of compliance and are exposed to direct liability for product nonconformities.

The Regulations also clarify the distinction between vigilance and post-market surveillance, pointing to the involvement of the entire supply chain. Reporting serious incidents and conducting safety-related corrective actions requires direct and efficient cooperation between healthcare professionals, health institutions, manufacturers, economic operators and national competent authorities for medical devices.

Selection of the Authorized Representative is a fundamental choice for non-EU companies, but it can also be a valuable option for small and medium-size European companies who seek support and advice for compliance. An Authorized Representative firm with expertise in regulatory affairs can facilitate fulfilling many of the MDR obligations, such as registration in Eudamed, assistance with FSCA and incident reporting, and compliance support. Under the MDR, the Authorized representative will take on more risk and liability, as the firm will be held jointly and severally liable for defective medical devices. As such, Manufacturers can expect that their representative will monitor compliance more thoroughly.

HEALTHCARE PROFESSIONALS AND HEALTH INSTITUTIONS

Healthcare professionals need to be aware that the Regulations are more stringent than the previous Directives. During the transition from Directives to Regulations and for a few years afterward (until 2025), some products certified under the Directives and products certified under the new Regulations will coexist on the market. Both will have equal status under the law, and no discrimination in public tenders may take place.

The Regulations require manufacturers to implement post-market surveillance follow-up plans. This could lead to the need for health institutions to provide more information about their experience with their medical devices. Health institutions could prepare for this by thinking about convenient ways to gather information about their experience with medical devices.

In addition, with each implantable device, the manufacturer will have to deliver implant card-carrying-appropriate information. This card, including the patient's identity, shall be supplied to each patient fitted with an implant. Health institutions shall allow rapid access to the information contained on the implant card to any patient fitted with a device, unless the type of implant is exempt from this obligation (currently this includes for example staples and dental hardware).

Finally, if a health institution itself is sponsoring or the healthcare professional is taking part in a clinical investigation or a performance study, the institution needs to be aware of enhanced MDR obligations.

TIMELINES

MDR will take effect on May 26, 2020. Exclusion to the deadline of May 2020 is the implementation of UDI (Unique Device Identification), for classes IIa and IIb – May 26th, 2023 and classes I and III – May 26th, 2026.

The EUDAMED launch is expected to be delayed by about 2 years, i.e. May 2022 [4]. As such, Member States are discussing temporary solutions to be adopted for the application of the related Article 123 paragraph d, until EUDAMED becomes operational. However, the MDR date of application is not affected by the EUDAMED delay, and manufacturers are expected to comply with the preparation and exchange of all required reports using the existing systems as far as possible.

For clinical investigations new requirements, the application date is May 2020, although the MDR coordinated assessment procedure which allows the centralized approval of a multinational clinical trial by a single coordinating Member State, will only be implemented from May 26, 2017.

QUALITY SYSTEM UPGRADE

Even when a manufacturer has products on the European market, and CE certificates have been renewed to enable continued commercialization under the "old" regulation, the manufacturer must to evaluate the impact of the

MDR and update the quality system, to meet the new requirements by May 2020. All audits after this date will be to the MDR standard. As such, companies must conduct a quality system assessment and identify areas impacted by the changes. Importantly, the upgrade requires that interconnections are created among all quality documents, records, product information, and risk management. In other words, the documentation and quality records and products' documentation need to be a seamless system of data and information.

New or updated procedures are essential to comply with the extensive MDR requirements. Consultation with regulatory experts is more important than ever to figure out what applies to each company and how devices will be impacted. It is up to manufacturers to know the timelines and what to do to ensure products are compliant with MDR.

Some distributors and importers may never have had a quality system before. Under this regulation, every importer or distributor and the authorized representative will need to develop one. The manufacturer, therefore, need to be proactive, ensuring and documenting that suppliers are aware of the new regulations and are compliant.

CONCLUSION

The EU MDR deeply impacts economic operators and health institutions alike, creating the need to adopt a structured cross-functional approach in order to change together and adjust to the new scenario. The level of time and effort needed for defining the strategy and planning the implementation of the new regulations is not to be underestimated. Expanded collaborations and broader partnerships are vital in this highly competitive and specialized industry to drive medtech innovation in Europe in the age of the MDR.

As industry seeks access to global markets and harmonized requirements are still a future goal, a winning strategy relies on the ability of organizations to build robust international alliances and guarantee effective stakeholder supervision based on high staff competence and strong project management capabilities. Especially for small and mid-sized companies, the balance between in-house capabilities and outsourced support, as well as the implementation of modern digital software to aid R&D and quality management, are paramount for market success.

TIPS TO GET READY

If you are involved with the MDR transition strategy, gap assessments, or simply getting up to speed quickly on the MDR requirements, start by learning the regulation firsthand by identifying suitable training for key people in your organization. The knowledge gained will allow you to asses the impact on your organization and the appropriate next steps to meet the new requirements for all members of the supply chain, health institutions and healthcare professionals.

Rely on regulatory experts, who have assisted multiple medical device companies with QA/RA compliance, to address all of your questions and help you organize a specific transition strategy for your company based on your product range, certification cycle, and markets you serve. Gain the competence needed to interact effectively with your Notified Body. Expert consulting groups may provide a headstart and accelerate your transition, reducing business risk and enabling success.

For example, Meditrial, a trusted consulting company and European representative. offers clear and effective training courses and consulting services designed to illustrate to economic operators and health professionals what are the new rules for in-house devices, custom-made devices, and clinical investigations. Meditrial also provides strategic advice and support for regulatory compliance and quality management system upgrade including digital tranformative options.

REFERENCES

1. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC.
2. Medical Devices Market Size, Share and Industry Analysis by Type, End User and Regional Forecast, 2019 - 2025 Fortune Business Insights, April 2019.
3. The European Medical Technology Market in Figures. Medtech Europe Report 2019
4. EU Commission EUDAMED 2 webpage https://ec.europa.eu/growth/sectors/medical-devices/new-regulations/eudamed_en-
5. UDI System in the US and in the EU, Mapping of the differences. Medtech Europe, January 2019
6. MHRA An Introductory guide to the MDR and IVDR https://www.gov.uk/guidance/

Monica Tocchi MD, PhD
Founder, Chief Medical Officer

Meditrial Europe Ltd.
Birmensdorferstrasse 198
8003 Zürich, Switzerland
Ph. +41 4178498 84 - Fax. +41 4178498 85

Meditrial USA Inc.
19W 34Th Street
Suite 1018 - New York, NY 10001
Ph. +1 646 741 9156 - Fax. +1 646 741 9156

What is your opinion on the proposed new Medical Device Regulation? Stay intouch!
@meditrial-europe