WHITE PAPER

MEDICAL DEVICE

Strategic Planning for Compliance with the EU Medical Device Regulation

ABSTRACT

The EU Medical Device Regulation sets the stage for an arena where transparency, quality, and patient safety are paramount. Manufacturers must prepare and build compliance into their product development strategy to ensure a successful transition to this new regulatory environment.

Introduction

Medical devices play an increasingly critical role in the health and quality of life of millions of people worldwide. To reflect the substantial technological and scientific advances made by the medical device sector and to respond to the need for regulations that would significantly tighten the controls around medical devices, the European Commission published the EU Medical Devices Regulation (MDR) on May 5, 2017. These new, more rigorous regulations seek to set the standard for medical device regulation globally and impact the entire product development cycle, from concept to clinical trial conduct and post-marketing surveillance.[1]

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Key regulation changes under the EU MDR

The MDR replaces Directive 93/42/EEC regarding medical devices (MDD) and Directive 90/385/EEC regarding active implantable medical devices. The MDR will enter into full force in May 2020 and all CE Mark certifications issued before the implementation of this new regulation will automatically expire in May 2021.

With the looming deadline for compliance with the MDR, device manufacturers face a host of questions about how to prepare their products for compliance. Any manufacturer who intends to market their medical device in the EU member states – including manufacturers who already have devices on the market – must be compliant with the EU MDR. There are no grandfathering provisions with the regulation, and all currently approved devices must be re-certified in accordance with the new requirements.

Expanded definition of medical devices

Under the EU MDR, the definition of a medical device is any instrument, apparatus, appliance, software, implant, reagent, material, or other article intended to be used for any of the following medical purposes:[2]

+ Diagnosis, prevention, monitoring, prediction, prognosis, treatment, or alleviation of disease
+ Diagnosis, monitoring, treatment, alleviation of or compensation for an injury or disability
+ Investigation, replacement, or modification of the anatomy or of a physiological or pathological process or state
+ Providing data via *in vitro* examination of samples derived from a human body
+ Cleaning, disinfection, or sterilization of medical devices and devices for control or support of conception

The inclusion of devices that do not have medical-intended purposes and devices designed for the purpose of prediction of a disease or health condition represents a notable expansion of the previous definition of medical devices.

Compliance deadlines

The EU MDR went into force on May 25, 2017. Manufacturers who intend to bring a new product into the EU market on or after May 25, 2020 must be compliant with the EU MDR by May 25, 2020.

For existing products, manufacturers have the option of renewing MDD certifications that are about to expire to buy some time for compliance with the EU MDR. Re-certification under MDD will enable manufacturers to keep their products on the market until May 2024 or the re-certification expiration date, whichever comes sooner. However, manufacturers should keep in mind that their ability to recertify under MDD is dependent on certain circumstances related to their current MDD standing, including the absence of gaps in their compliance activities.

Reclassification of risk

The MDR reclassifies devices according to four risk classes, where risk is defined as the probability of occurrence of harm and the severity of that harm.[2] The MDR incorporates a variety of European guidance documents (MEDDEVs) and emphasizes the importance of clinical data, clinical evaluations, post-marketing surveillance, and post-marketing clinical follow-up.

Per MDR, medical devices are classified as Class I, Class IIa, Class IIb, and Class III according to 22 classification rules found in Annex VIII of the regulation. The specifics of these classification rules fall outside the scope of this white paper, but manufacturers are advised to thoroughly review and understand the rules and to update their technical documentation accordingly.

The MDR also includes a flexible list of devices that may not have a medically intended purpose but will nevertheless be regulated

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as medical devices (the Annex XV list). Currently, this list includes contact lenses, cosmetic implants, dermal fillers, and invasive laser equipment, as well as software used for any purpose covered by the definition of a medical device.

Increased need for clinical evidence

Regulations around systematic clinical evaluation of Class IIa and IIb medical devices have become more robust within the EU MDR. Manufacturers will need to prepare the clinical evaluation by considering the new wording in the regulations regarding when an equivalence approach is acceptable and under which circumstances it is possible to justify not conducting a clinical investigation.

The EU MDR is also more rigorous with regard to the provision of clinical evidence for Class III and implantable medical devices. In cases where they do not have sufficient clinical evidence to support claims of both the safety and performance of a particular device, manufacturers will need to conduct clinical investigations.

Updated labeling requirements

Under the EU MDR, Class I devices – particularly reusable medical devices – must be labeled with the number of a notified body. As current labels will no longer be acceptable, manufacturers should consider how changes to labeling will impact the process of getting finished products to market.

Understanding the new role of notified bodies

The EU MDR changes not only the responsibilities of manufacturers, but also the role of notified bodies. As manufacturers transition to EU MDR compliance, it is critical for them to understand the new role of notified bodies and to communicate with them proactively throughout the device certification process.

Shifts in the role of notified bodies

Under previous directives, medical devices were not subject to a pre-market authorization by a regulatory authority. Medium- and high-risk devices required a conformity assessment procedure involving a notified body. In the new MDR framework, an independent expert panel could be required to provide an opinion on a device before the final decision on certification is made. If that panel raises concerns about the level of clinical evidence or the benefit/risk ratio, the notified body is required to advise the manufacturer to address those concerns.

Under the EU MDR, notified bodies will also play a new role in enforcing regulation through unannounced audits of manufacturing processes. These audits may require manufacturers to amend their contracts with subcontractors and/or suppliers.

Recertification of notified bodies

One of the main objectives of the EU MDR was to evaluate the existing notified bodies and to determine which were qualified to carry out the requirements necessary for ensuring conformity. In order for these organizations to be able to issue MDR certificates for devices, they need to apply for re-certification according to the new MDR regulations and some may fail to meet the standards.

Reports indicate that 50 percent of EU notified bodies have not yet applied for MDR designation, indicating that the re-certification process is significantly behind schedule. As such, manufacturers should reach out to their respective notified bodies to better understand where they are in their designation process. In some cases, it may make sense for a manufacturer to leave their existing notified body and maintain compliance with one that has already been designated under the EU MDR.

Understanding the review timeline for conformity assessment

The reality is that not all current notified bodies will remain in business. Given this state of flux, manufacturers are advised to communicate with their respective notified bodies to clarify their intentions and timelines. Questions manufacturers may want to ask include:

1. How do you interpret the EU MDR as it relates to our product portfolio?
2. When will you be ready to review our technical documentation?
3. How long will it take for you to complete your review?

As some notified bodies need at least 12 months to review a file, proactive communication is critical for helping manufacturers understand the delays their R&D teams may encounter in bringing a new product to market.

A framework for EU MDR compliance

Compliance with the EU MDR is a significant undertaking that requires cross-functional collaboration. Following the six steps outlined below will help manufacturers ensure that they are fulfilling all the responsibilities required under the updated regulations.

1. Establishing a leadership team

Good leadership is essential for managing the transition to EU MDR compliance and creating an execution strategy which includes timelines and mechanisms for tracking progress on compliance activities. At a minimum, this leadership team should include representatives from regulatory affairs, quality assurance, medical and/or clinical affairs, marketing, manufacturing, biocompatibility, sterilization, R&D, and labeling. This leadership team must be actively engaged in communicating with the notified body, as well as establishing project harmonization amongst business units and product portfolios.

2. Identifying a person responsible for regulatory compliance

Under the EU MDR, manufacturers are required to identify a person responsible for regulatory compliance. This person should be a subject matter expert on the product portfolio and its safety and efficacy, and they should have the credibility to speak to those matters should questions be posed by regulatory authorities or the general public.

3. Conducting a gap analysis

One of the first questions for manufacturers to ask when conducting a gap analysis is whether their existing products are compliant with the current EU Medical Device Directive (MDD). If not, they will need to find a way to be compliant with the EU MDD as soon as possible in order to apply for re-certification. Or, in some cases, manufacturers may opt to remediate their files for existing products to be compliant with the new MDR rather than re-certifying.

A gap assessment can help manufacturers determine which compliance strategy is most appropriate for them. At a minimum, manufacturers should perform:

+ Technical gap analysis
+ Regulatory gap analysis
+ Clinical gap analysis

As a gap analysis is specific to the manufacturer, the therapeutic area, and the product or family of products, each gap analysis is unique. However, the objective of every gap analysis is the same: to identify areas of non-compliance and then remediate those areas to not only bring the product to compliance but also sustain that compliance.

4. Allocating resources to support compliance activity

The effort involved in compliance with the EU MDR is substantial, and it is critical to invest both budgetary and human resources in this activity. Work related to compliance with the new regulation is an added responsibility, likely one with which a manufacturer's current employees have little to no experience. For manufacturers who lack the necessary expertise, it is in their best interests to budget for and hire the right subject matter experts who can bring the company into MDR compliance and train employees to maintain that compliance.

5. Completing key compliance activities

Strategic planning for MDR compliance will need to include:

+ Development of an MDR project plan, which encompasses remediation/compliance activities, manufacturing and supply chain considerations, and labeling
+ Creation of a comprehensive list of products in the product portfolio, including their classifications and the cadence required for MDR compliance
+ Establishment of resource planning
+ Assessment of the rest-of-world (ROW) impact that may be a ripple effect of MDR compliance, including review and possible revision of global registrations outside of the EU

Figure 1. Minimum technical documentation requirements for compliance with the EU MDR

6. Seeking outside assistance

For assistance with strategic regulatory planning, manufacturers can hire consultants who have experience with EU MDR compliance activities. These consultants can assist with developing a robust strategy, conducting a gap assessment, communicating with the notified body on the manufacturer's behalf, and even creating pilot files. Pilot files are worst-case technical documents for a particular product or family of products, feedback on which is used to enhance and broaden compliance activities for the remainder of the product portfolio.

Potential benefits to device manufacturers

Due to the substantial increase in requirements and the resources necessary to comply with them, the new regulations will require significantly higher investment from manufacturers, but are expected to have the following positive impacts:[1]

+ **Simplified administrative procedures.** Registration of devices and operators will only need to be performed once at the EU level, rather than in all member states where the products are placed on the market
+ **Increased legal certainty.** Unlike the previous Directives, the MDR is directly applicable in all member states
+ **Increased credibility.** The new regulations aim to increase overall confidence in the medical device market among patients and healthcare professionals

Conclusion

The MDR sets the stage for a medical device development arena where transparency, quality, and patient safety are paramount. Device manufacturers who seek to gain access to the European market are charged with developing a solid understanding of the new rules and preparing for compliance. Given the broad scope and scale of the regulation, manufacturers must build compliance into their product development strategy to ensure a successful transition to this new regulatory environment.

References

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Nach Davé | RPh, MS, Vice President, Development Strategy

Mr. Nach Davé oversees the Premier Research regulatory affairs service offerings across its broad range of therapeutic focus areas, bringing to his position more than 20 years of experience in the pharmaceutical and contract research industries. He previously served the company as Director of Regulatory Affairs and rejoined Premier Research after two years as Senior Director of Regulatory Affairs at PRA Health Sciences. He has led clinical and regulatory affairs at Maxx Orthopedics, a developer of orthopedic medical devices, and has held roles in clinical operations, business development, strategic consulting, and medical affairs at companies such as Merck, Bristol-Myers Squibb, Aventis Pharmaceuticals and Mitsubishi Pharma America.

Mr. Davé holds a Master's degree in drug regulatory affairs from Long Island University and a Bachelor's degree in pharmacy from the Philadelphia College of Pharmacy and Sciences. He is a registered pharmacist in the state of New Jersey.

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