The New European Medical Device Regulation – Balancing Innovation and Patient Safety

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Abstract

The European Union (EU) has introduced stricter provisions for medical devices, the new Medical Device Regulation (MDR). The MDR raises the bar for pre-market testing and post-market surveillance of most medical devices used in Europe This will have important consequences for manufacturers, researchers, clinicians, and patients.

The new MDR increases requirements for clinical trial testing for many devices before being able to be legally placed on the market, and it extends requirements for rigorous clinical surveillance of benefits and harms to the entire life cycle of devices.

New so-called “expert panels” are currently established by the European Commission to advise in the assessment of devices towards certification, and private companies (so-called “notified bodies”) are charged by the Commission to ensure that companies follow the requirements for device testing.

The MDR does not contain a grandfathering clause; all medical devices which are currently used in Europe must be re-certified under the stricter regulation. The re-certification deadline was originally in May 2024, and physician organizations and the device industry have expressed concern about a shortage of life-saving medical devices in Europe next year. The European Commission recently adopted a proposal to extend the deadline until 2027 and 2028, depending on the device’s risk class.

The medical device industry and their physician partners should use this extra time to gather additional evidence, such as from clinical trials and observational studies, which will be needed under the new, stricter rules to re-certify current devices and bring new innovations for patient care to market.

Introduction

Devices are an important and integral part of modern medicine, from intravenous lines over sutures, snares, scissors, and catheters to sophisticated devices which remain in the body for a long period of time, such as brain stimulators or cardiac pacemakers. Certain software which serve as decision aids for doctors, such as Artificial Intelligence (AI) tools to aid detection of early cancer on a mammogram are also regarded as medical devices by regulators like the US Food and Drug Administration (FDA) and the European Union (EU).

The regulation of medical devices has not been as strict as for drugs. Clinical testing requirements have been more relaxed, and approvals have often been granted with limited evidence for patient benefits and harms. Wide-reaching scandals with faulty medical devices in the early 2010's have shown that poor design and lack of testing of medical devices can result in severe patient harm; in the US with high failure rates of certain metal-on-metal hip implant, and in Europe with breast implants which turned out to contain potentially health-damaging containing silicon material which had not been tested for use in humans (1,2).

The EU has recently introduced a new Medical Device Regulation (MDR – 2017/745) mandating much stricter requirements for medical device pre-marketing testing, certification for use, and post-marketing surveillance in Europe (3). The MDR became effective on May 26, 2021 and is directly applicable in all EU Member States. It replaced the Medical Device Directive (MDD) and the Directive on active implantable medical devices (AIMD) (3).

Compared to the MDD, the new MDR extends requirements for medical devices in four important ways: Firstly, it increases the bar for clinical trial testing for many devices; secondly, it introduces new EU-designated independent "expert panels" for assessment of devices; thirdly, it extends requirements for clinical testing and surveillance to the entire life

cycle of medical devices, and fourthly, it increases responsibilities and influence of private companies called “notified bodies” for device assessment and certification.

While the new regulation may improve patient safety, the device industry is concerned that investment costs will dramatically increase to develop new devices and get them approved and marketed. Recently, European cardiology organizations have warned of an imminent device shortage in Europe, and the European Society of Gastrointestinal Endoscopy (ESGE) has published guidance for European endoscopists to deal with the stricter regulations (4,5). This paper explains the challenges and opportunities of the new European device regulation.

European and US standards

Both in the US and in the EU, medical devices are categorized into different categories based on risk—class I (low risk), class II (medium risk), and class III (highest risk). The EU MDR subclassifies class II devices further into class IIa (medium risk) and class IIb (higher risk). Importantly, the US Federal Food, Drug, and Cosmetic Act (FDCA) does not have a class II subclassification (Table 1).

For example, class I devices include bandages, handheld surgical instruments, and nonelectric wheelchairs. Class IIa devices include surgical clamps and computed tomography (CT) scanners, and Class IIb devices include infusion pumps for intravenous medications or bone fixation devices. Examples of class III devices are cardiac pacemakers or deep-brain stimulators.

Table 1 shows similarities and differences between the old and new EU regulations (MDD and MDR), and the US FDCA regulation for medical devices (3, 5). The new EU MDR

appears to be stricter than the requirements under the US FDCA. For example, the MDR's definition of a medical device (Art. 2) (3) is broader in scope than the medical device definition under the US FDCA (Section 201h) (6). Moreover, most medical devices in the US are cleared through the so-called 510(k) pathway (mainly Class II devices), which only requires demonstration that the device is "substantially equivalent" to an already marketed device (the "predicate") (5,6).

Under the MDR, AI software products that provide information for clinical decision-making (diagnostic or therapeutic) are also medical devices and will be classified at least as class IIa (MDR Rule 11 in Chapter III of Annex VIII). In addition, the EU currently prepares its own regulation on AI (the so-called "AI Act"). The AI Act aims to create even stricter rules, especially for high-risk AI systems (such as AI-assisted surgery), and covers topics such as transparency, cybersecurity, and data governance (7,8). The idea is that the AI Act will be applicable alongside the MDR.

The definition of medical devices are also broadened under MDR to include non-medical and cosmetic devices not previously regulated. Examples include products for cleaning, disinfection or sterilization of devices as well as contact lenses, liposuction equipment, or epilation lasers (3).

Grandfather rule

Importantly, the MDR does not contain a grandfathering clause. Originally, all medical devices certified under the old MDD must be recertified by the end of May 2024 (3,). However, after physician organizations and industry complained about the risk of shortage of

life-saving devices in Europe from June 2024, the European Commission in January 2023 adopted a proposal toextend the deadline for re-certification until 2027 and 2028, depending on the device's risk class. This will give the medical device industry and their partners some more time to set up systems to comply with the additional tasks for evidence on benefits and harms of medical devices.

Attention and uncertainty

National legislators and device manufacturers have been uncertain about how to interpret the new requirements, the pandemic diverted the interest and action of policymakers to other areas, and the EU needed time to establish new designations for notified bodies under the MDR. Therefore, the new MDR has not yet received much attention among stakeholders, and the transition to the new regulation has been slow.

Device manufacturers have started to realize the extent of the new regulation. They must establish infrastructures for proper device development under the new MDR. This will need strong liaison with clinicians, researchers, and hospitals to establish high-quality clinical trial environments for medical devices in Europe. Even with the extended deadline until 2027/2028, it will be challenging to facilitate systems and infrastructure to adhere to the new bars and avoid device shortages in Europe (9).

The new MDR has a broader medical device definition and contains more detailed rules (in total 22) determining device categories. Many products previously not considered devices are now regarded as medical devices and must comply with the MDR. Many currently used devices certified under the old MDD are reclassified into a higher class under the MDR, and

many manufacturers face stricter requirements, including undertaking new clinical investigations for already marketed products.

More clinical trials

Rigorous clinical testing is a requirement for many class II devices and all class III devices under the new regulation. The MDR explains that clinical testing shall be done in such a way that potential risks are justified when balanced against clinical benefits. This includes "reliability and robustness of the data generated in the clinical investigation, taking account of statistical approaches, design of the investigation and methodological aspects, including sample size, comparator and endpoints" (MDR Art. 71(3)(d)). Importantly, the MDR explicitly states that endpoints in device trials need to be "clinically relevant" for patients (MDR Section 3.6 in Chapter I, Annex XV).

New devices can still avoid clinical testing if equivalence can be established with a device already certified under the MDR. But the MDR is stricter than previous EU and current US legislation (table 1). Manufacturers now need to take into account not only technical and biological but also clinical characteristics to claim equivalence (MDR Section 3 in Part A of Annex XIV) (3).

It has been criticized that under the new MDR, not all results of clinical testing will be publicly available, while others have pointed out that publication of testing results will be improved under the MDR as compared to the old legislation (10). A step forward is that the EU established a new database which gathers information on medical devices (EudaMed;

European Database on Medical Devices). However, at the time being, full access to clinical testing data is limited to the manufacturer, the expert panel and the notified body (3,10).

Independent expert panels

The MDR introduces independent "expert panels" which play an important role in assessment of high-risk medical devices (3,11). The panels provide scientific advice in relation to the manufacturer's proposals for clinical investigation and clinical development strategy (MDR Art. 61(2)). The panels are also tasked to assess the results of the clinical evaluations of medical devices (11). Panel members are appointed by the European Commission based on clinical, scientific, or technical expertise and geographical diversity (MDR Art. 106(3)). The bar for membership is high and will exclude many experts in their respective medical fields; panel members must be impartial and not have any conflicts of interest with device companies or other stakeholders. The EU has so far set up twelve expert panels, with between three and more than 40 members, in areas such as circulatory system; respiratory system; gastroenterology; orthopaedics and traumatology neurology; endocrinology and diabetes; surgery and dentistry; obstetrics and gynaecology (11).

Notified bodies

The EU charges private entities called "notified bodies" with all handling of device assessment. Notified bodies are companies with technical expertise in assessment of device testing and clinical trials, which are designated by EU member states. Notified bodies were also part of the old MDD, but under MDR are required to undergo new assessment and re-approval. This has led to a significant reduction in notified body capacity. Currently, 38

companies are designated as notified bodies under the MDR, most in Germany and Italy with eight companies each (12).

Notified bodies are responsible for negotiations with the manufacturer about technical requirements, for communication with the designated expert panel about the required nature and extent of clinical testing of a device, including study design, clinical endpoints and sample size calculations, and to achieve conformity with the applicable MDR requirements (also called "CE marking"). The MDR does not regulate a formal authorization process of devices; once the manufacturer fulfils all requirements as set out by the notified body and the expert panel and is thus "in conformity," the manufacturer can affix the CE marking and place the device on the EU market.

The heavy reliance on notified bodies under the new MDR may lead to conflicts of interest because the notified bodies are acting both as business partners for device companies and are certifying devices on behalf of the lawmaker (13). This places notified bodies at both ends of the table and may blur proper judgment and oversight. Further, competition amongst notified bodies to attract business from industry may incline notified bodies to lower their bar for device testing, jeopardizing the goals of the new regulation (13). Currently, it is unknown how the new regulations will affect categorization of devices into risk classes at different notified bodies, and what standards different notified bodies will apply for device testing across and within device categories, such as for endpoints and sample sizes for clinical trials.

Post-marketing surveillance studies

The MDR extends device scrutiny by increased post-market surveillance requirements (MDR Chapter VII). Manufacturers are now obliged to establish systems to track the performance of

devices throughout their entire life cycle (MDR Art. 83). The MDR requires high-quality data and detailed planning of design and endpoints to be collected in post-marketing studies. The expert panels need to be consulted about planning, conduct, and results of post-marketing surveillance.

Implementation

It is too early to assess how the new MDR will affect categorization of new and old devices into risk classes with the new MDR. It is also currently unknown how strict the requirements for clinical trials will be interpreted, what trials will be required, and what endpoints assessed for which devices. However, requirements are increased within risk classes, and many devices will likely be classified in higher risk classes under MDR as compared to older regulation (7). Voices have already been raised that the new regulation may stifle innovation and delay marketing of new devices (14). Especially smaller device manufacturers and start-ups may be unable to handle the stricter rules for large-scale clinical testing (9).

The medical device industry is not used to strict requirements for clinical testing, and MDR implementation is time-consuming and costly. Some device companies have already reduced development of new devices or prioritize other markets where regulations are more relaxed (15). Only about 6,000 new medical devices have so far been certified under the MDR, a small number in light of the more than 500,000 medical devices currently used in Europe under the MDD and AIMD. More than 85% of devices certified under the MDD or AIMD have not undergone recertification (15).

An industry survey suggests that certification times with the involvement of notified bodies have already increased from 9 months on average before the new regulation to now more than 18 months (15). Further, there are currently long waiting times at notified bodies for manufacturer's assessment of devices (15). In addition to the increased requirements for device testing, this will further delay certification of devices in Europe.

A large part of European device innovation is currently done in small and medium size enterprises (SME). SMEs have difficulties to navigate in the complexity of MDR certification rules and with finding local notified bodies designated under the MDR (15). EU grant mechanisms have been encouraging collaborative research of academic institutions and European SMEs for medical device development and innovation. The new MDR may lead to a decline of such academic-industry research partnerships.

Implications for patients and healthcare systems

For decades, hospitals and clinical research groups have been central for clinical testing of new drugs by contract of pharmaceutical companies. With increased requirements for clinical testing, clinical environments will experience an increase in requests from device companies to perform device testing. Access to hospital databases for real-world studies, which is specifically encouraged in the new MDR, will need to be handled properly and expediently (3). This represents an opportunity for new scientific activity but will require new mechanisms and solutions for data sharing, patient consent, and patient privacy (14). Recently, a collaboration of the European Society of Cardiology and the European Federation of National Associations of Orthopaedics and Traumatology has been established with the goal to partner with industry to "review methodologies of clinical investigations, advise on

study designs, and develop recommendations for aggregating clinical data from registries and other real-world sources" (13).

Maybe the most important difference between the US law and the new EU law is the increased requirements for clinical trials testing under the new MDR. Under the MDR, device manufacturers are required to perform clinical trials with "clinically relevant" endpoints (Annex XV, chapter I;2.6) for all class III and many class IIb medical devices and file a detailed clinical evaluation report (called "CER"). CER reports must be reviewed by a notified body in conjunction with an independent expert panel, a resource-intensive, long-lasting process which involves several independent organizations and entities. In contrast, most medical devices in the US are 510(k)-cleared as Class II medical devices, and only some are categorized as high-risk (Class III) and require the strictest pathway which includes proper scientific evidence for the device's safety and effectiveness, including clinical investigations (so-called PMA (premarket approval)) (6). Also, requirements for expert panels more relaxed in the US (Table 1). Finally, the EU MDR has extensive clauses about penalties for non-compliance, which appear to be more severe than enforcement actions by the FDA for violations of the FDCA (Table 1).

Interpretation

The MDR may lead to certification of fewer devices in Europe; those which do not fulfil strict requirements for clinical benefit at acceptable harms. This will increase patient safety and may thus improve medical care. The MDR significantly raised bars for clinical testing and requirements for proof of clinical benefit for patient-important outcomes. The price to

pay is an increased level of bureaucracy, an increase in costs for the industry (17), and a possible shortage of devices when transition phases expire in 2027 and 2028.

The EU thinks the price, which comes with the new regulation, is worth the extra patient protection. Indeed, in the past, serious patient harm has occurred due to poor oversight of medical devices, such as the scandal with breast implants in the early 2010s (2). The new MDR aims at improving patient safety and may reduce risk. The new regulation also aims at preventing marketing of devices, which are not necessarily harmful but have limited or no clinical benefit for patients. This will reduce healthcare costs and thus enable better prioritization in European healthcare toward effective and safe procedures and interventions.

It remains to be seen if the new MDR will lead to increases in device costs for hospitals and patients, or if it will mainly reduce revenue margins for the device industry. If European device companies and payers of medical services are ready to pay more for safer and more effective devices is unknown. At its best, the regulation has the potential to significantly increase patient safety and reduce patient harm. At its worst, it may hinder innovation and stifle investments in the device industry and decrease innovation and entrepreneurship.

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Table 1: Regulatory requirements for medical devices in the old EU Medical Device Directive (MDD – 93/42/EEC), the new EU Medical Device Regulation (MDR – 2017/745), and the US Federal Food, Drug, and Cosmetic Act (FDCA)

	Classification of devices according to patient risk	Assessment and certification/ marketing authorization	Independent expert panels required	Obligation to report design, testing, manufacturing, labeling.	Level of clinical trial testing for clinical benefits and harms for moderate or high-risk devices	Self-declaration sufficient for low-risk devices	Life-cycle clinical surveillance	Penalties for non-compliance
EU MDD (repealed by EU MDR)	Four classes: I, IIa, IIb, III (from low to high risk)	Private companies ("notified bodies")	No	Yes	Low	Yes	No	Few
EU MDR	Four classes: I, IIa, IIb, III (from low to high risk)	Private companies ("notified bodies")	Yes	Yes	High	Yes	Yes	Many
US FDCA	Three classes: I, II, III (from low to high risk)	FDA	No*	Yes	Moderate**	Yes (if 510(k) exempt)	No	Fewer

* FDACA provisions expert panels (Art. 513, FDCA), but there is no formal requirement. FDCA panels do not have the same strict conflict-of-interest policy as in EU-MDR, and FDA panels shall include a representative of interests of the device manufacturing industry, which is not the case in EU MDR independent expert panels.

** US FDCA has so-called 510(k) pathway (mainly Class II devices), only requiring demonstration of a device as “substantially equivalent” to an already marketed device. EU MDR does not have such a pathway for approval.

Data from: 3, 5