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A REVIEW OF THE NEW EUROPEAN MEDICAL DEVICE REGULATIONS

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ABSTRACT

On May 26th, 2021, the new European medical device regulation has come into force. The three existing MDDs (93/42/EEC, 98/79/EC, and 90/385/EEC) have been replaced with the newest European regulations on medical devices (2017/745) and in vitro diagnostic (IVD) medical devices (2017/746). With the implementation of Medical Device Regulation, MDR gives the reclassification rules for medical devices. To increase market traceability and transparency, the EU has implemented a unique device identification (UDI) system and a European database (EUDAMED). Throughout the device's life cycle, the post-market surveillance paperwork is required to be updated following MDR. The new MDR will have multiple impacts, one of which is that it will slow down innovation in the medical device sector. Since the new MDR requires significantly tighter clinical data and a continuous process of clinical review, the development and introduction of new medical devices to the market might become more difficult and expensive as a result of the increased regulations. The objective of this review is to give a description of some of the key features of the new EU Medical Device Regulation and to demonstrate how they will impact manufacturers, innovators, and healthcare professionals.

KEYWORDS: Unique Device Identifier; Innovation; EUDAMED; Clinical evaluation; Medical Device Software.

INTRODUCTION

The EU 2017/745 Medical Device Regulation (MDR), which took effect in 2021, and the EU 2017/746 In Vitro Diagnostic Regulation (IVDR), which took effect in 2022, both provide new regulatory frameworks for the authorization of MDs. was introduced by the European

Parliament and the Council of the European Union(EU) in May 2017.[1] With the introduction of the new MDR, the standards for post-market surveillance, medical device traceability, and more stringent pre-market testing for entry to the European market have been dramatically raised. Additionally, new guidelines for the risk categorization of medical devices result in the reclassification of devices that were formerly in a lower-risk category into a higher-risk category.[2]

The EU also believes that the new MDR regulation's advantages exceeds any potential short-term negative effects and predicts that it will improve patient safety by the following points[3]

- After May 2024, existing devices that are not approved under the new legislation won't be manufactured.
- Improvements in the quality of medical devices and follow-up of incidents.
- The approval and release of new devices will take more time.
- There may be an increase in the price of new devices.[4]
- The regulation establishes a centralized European database for medical devices that are supervised by national agencies to make it easier to monitor and verify medical devices and, as a result, there will beenhanced collaboration between EU Member States.[3]

The Medical Device Regulation (EU) 745/2017 (MDR) has replaced the Medical Device Directives (MDD),which had been in effect since 1990s.[5] Before 2017, medical devices were marketed on the EU single market in accordance with the Council Directives.[6] Medical Device (93/42/EEC[7]), for active implantable medical devices (90/385/EEC[8]), and In Vitro Diagnostic Medical Devices (98/79/EEC), which are referred to as the Medical Device Directives (MDD) collectively.[6]

A "Conformité Européenne (CE) marking" was required by these directives for medical device makers to have access to the whole EU market for their goods.[1] A manufacturer must recognize and adhere to the relevant essential standards to meet the requirements for CE marking.[9] For the entrance into the European market, MDs must have a European Conformity (Conformité Européene [CE]) label obtained by an organization recognized by a Member State, referred to as a "Notified bodies.[8]"

When evaluating products for CE marking, NBs work with manufacturers of devices to make sure that all general safety and performance standards are satisfied. Device approval is given when these conditions are satisfied, and the CE mark is displayed.[10],[11] The European Union

(EU) MDR 2017/745 is a thorough regulatory framework that spells out the requirements for medical device manufacturers to sell their products in the EU. Increasing productivity, enhancing product quality, and improving the QMS are all advantages of adopting ISO 13485.[12]

To lower the health risks for patients, the MDR was established to make sure that all MD permitted for sale on the European market consistently meet strict safety and quality standards. Along with the primary goals toguarantee an elevated standard of consumer safety, and harmony, and enhance the European marketplace forMD, the EU also works to support innovation and assure the viability of the EU's medical device industry. The MDR tries to do this by establishing tougher standards for MD, such as improved clinical data testing, more stringent requirements for producers' quality management systems, and more supply chain transparency.[13]

New Medical Device Regulation

A set of regulations known as the European Medical Device Regulation (MDR) governs the manufacture and marketing of medical devices in Europe.[14] In 2017, the updated European Union (EU) regulatory framework for medical devices was released. On May 25, 2017, the three old MDDs—93/42/EEC, 98/79/EEC, and 90/385/EEC—were repealed in favor of the new European Regulations 2017/745 on MDs and 2017/746 on in vitro diagnostic (IVD) MDs. For medical devices and IVD medical devices, the new regulations will take effect in May 2021 and May 2022, respectively. A regulation is a piece of EU legislation that simultaneouslybecomes enforceable in all member states.[15]

The new regulations like MDR/IVDR improve traceability, transparency, and patient safety, which aids in raising the caliber and dependability of MDs in Europe. Patient safety is the focus of the new medical deviceregulations (MDR/IVDR), which apply to all medical devices sold on the EU market. Regulations, as opposed to previous Directives, are immediately applied to national legislation, decreasing inconsistencies across the EU.[16],[17]

Due to the MDR's requirement for evaluation and recertification of previously authorized devices, the move from MDD to MDR has effects beyond those for products that are still in development. For each item in theirproduct line, manufacturers must now create dossiers that adhere to the new MDR standard. Any product thathas been marketed for a long time and has a clear track record of performance is included in this, regardless of risk. The ensuing increase

in effort for both device makers and NBs, along with a decrease in certified NBs,has increased the difficulties for device developers to obtain meaningful evaluation and knowledge of what would be necessary for recertification.[10]

Unlike directives, which must be incorporated into national legislation, regulations take effect immediately in all EU member states. This implies that if new medical devices are to be marketed and sold after the four-yeartransition period, on May 26, 2021, they must comply with the MDR. However, earlier-issued certificates of conformity (necessary to put a medical device on the market) granted under the MDD will only be valid for as long as it says on the certificate (depending on the kind of the certificate, Article 120 of the MDR), which is no later than May 27, 2022, or May 24, 2024[18]). The whole transition of medical device regulation is shown in Figure 1.[19],[20]

According to the European Commission, the new law would engage specialists in high-risk gadgets, implyingtighter oversight and an enhanced pre-market apparatus. Additionally, the fundamental goal of Regulation (EU) 2017/745, which is to promote stronger consumer safety and health protection, presents a challenge to originators and manufacturers, who are primarily small and medium-sized businesses. This is because small- to medium-sized organizations (SMEs) rather than big businesses do most of the creative research in the medical device market. When it comes to development, SMEs are more vulnerable than large corporations since the associated administrative costs might be so expensive that they may force the firm to exit the market.[21]–[23]

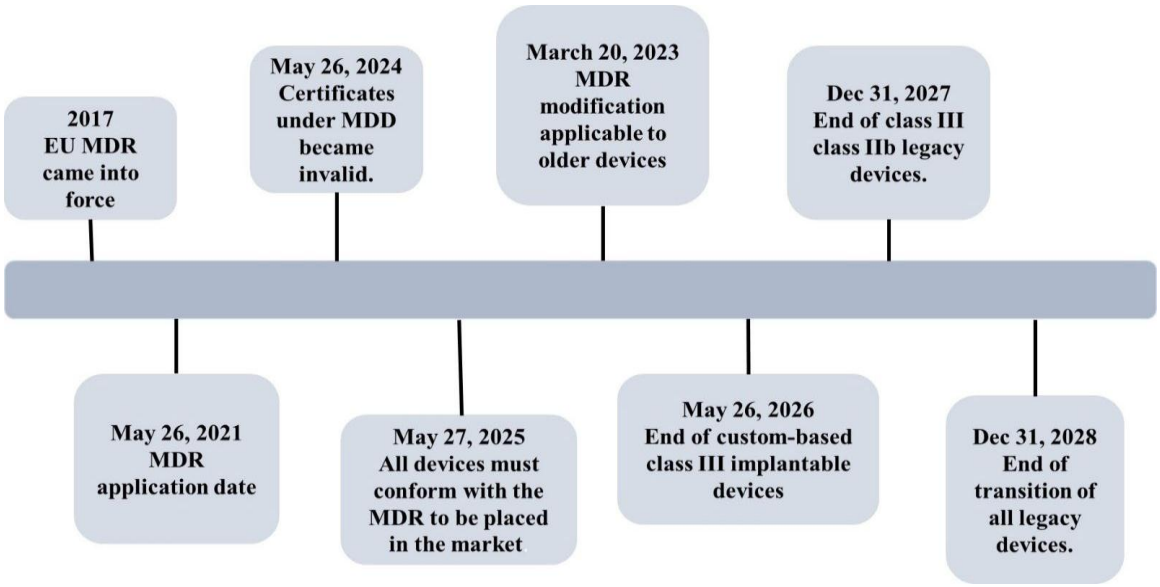

Figure 1: The transition timeline of MDR.

The European Parliament and the Council of the European Union enacted Regulation (EU) 2017/746 on in vitro diagnostic MDs on April 5, 2017, and it became effective on May 26. The original IVDR stipulated thatall standards for an in vitro diagnostic medical device must be fully completed by May 26, 2022, following a five-year transition period.[24] The EU In-vitro Diagnostic Device Regulation (IVDR) pursues post-market surveillance and transparent risk- and purpose-based certification of diagnostic devices. The IVDR controls the development, production, and usage of devices, but not the provision of medical services utilizing those technologies.[25] The EU (IVDR) intends to provide open, risk- and purpose-based diagnostic device certification as well as post-market monitoring. The IVDR regulates the development, manufacturing, and utilization of devices but not the delivery of healthcare services based on such technology.[14]

The post-market surveillance responsibilities of the manufacturer are another illustration of a risk-based strategy in the IVDR. According to Article 78, the PMS system is specifically matched to the device's risk class. Class C and D IVDs are subject to a more stringent requirement, which calls for a Periodic Safety Update Report ('PSUR') with more in-depth content under Article 81(1). Class A and B IVDs are required to submit a post-market surveillance report under Article 80, which has some latitude in terms of content and frequency of updating. The competent authority and the notified body (the "NB") must both receive the PSUR for class D IVDs as required by Article 81.[26],[13]

New features of the regulatory system

The European Union Medical Device Regulation (EU MDR), which establishes guidelines for the authorization of medical devices for human use in the European Union, aims to increase patient safety.[27],[28]

According to risk, devices are divided into four classes. The standards are reinforced if a manufacturer wishes to apply for approval of a new medical device by proving that it is equivalent to a product that is currently available on the market. This will make it more difficult for "me too" devices to obtain clearance based on information from other devices.[29],[30]

A Second important development is to enhance transparency under MDR. A summary of safety and clinical performance (SSCP) for high-risk devices must be published and updated annually in accordance with the MDR. The European Union's database of medical devices

(EUDAMED) will host SSCP records. This database, which was previously only accessible to regulators, can now be available to the public and is a crucial component of the new system but its completion has been delayed and the clinical module with access for healthcare professionals and patients will be the last to be produced, perhaps not until 2029.

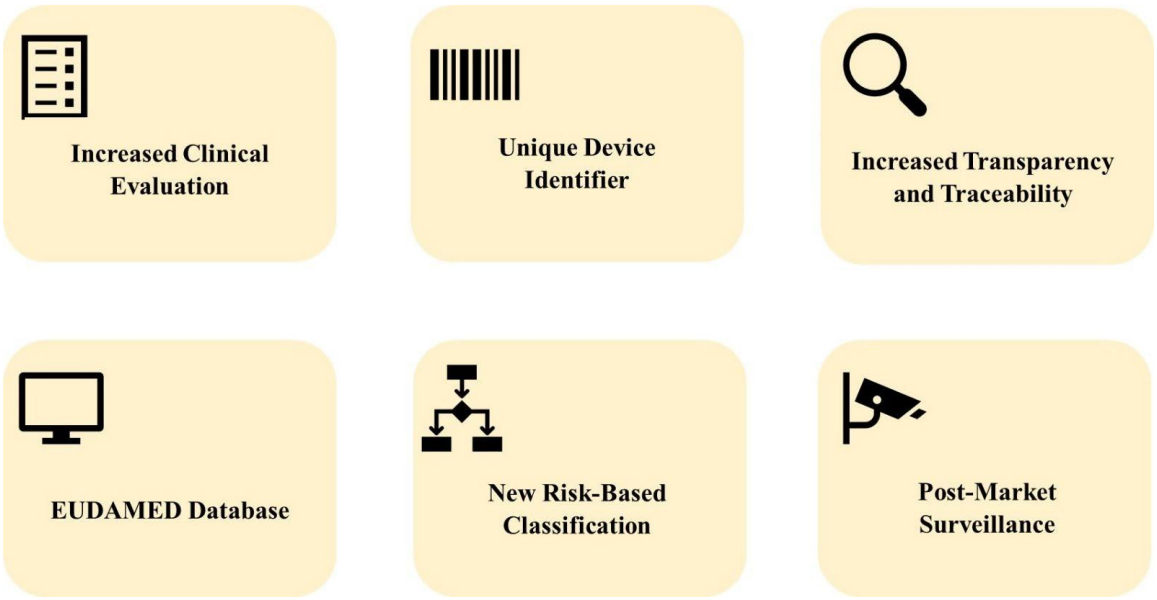

Figure 2: The Major changes in the MDR.

Thirdly, each medical device needs to be recognized using a system known as a unique device identification (UDI) to be held accountable.[29]

Fourthly, the standards for post-market surveillance will be raised. The new European Regulation on Medical Devices requires post-marketing surveillance for the safety and effectiveness of innovative devices. To facilitate the collection and adjudication of adverse device events in clinical practice, rigorous vigilance mechanisms should be in place. High-risk device adverse device occurrences are reported to manufacturers as well as regulatory organizations. Even seemingly insignificant instances might become more significant when combined with other reports.[28] The Key changes are mentioned below in Figure 2.[30]–[32]

Clinical Investigation and Clinical Evaluation

The MDR stipulates in Article 61.1 on clinical examination that "confirmation of conformity shall be based on clinical data providing sufficient clinical evidence." According to MDR Article 2.44, clinical assessment is "a systematic and planned process to continuously generate, collect, analyze, and assess the clinical data pertaining to a device in order to verify the safety and performance, including clinical benefits, of the device.[33]"

The clinical investigation design is connected to the device's risk category. The risk class of the device is related to the clinical trial design. Prior to the introduction of MDR 2017/745, clinical data were frequently not required for moderate-risk devices; nevertheless, the demand for clinical data for many of these devices is now growing. The principal laws and recommendations that are relevant to clinical research in Europe are included in Table 1.[34],[35]

Since the MDR is already in effect, Class III and implantable medical devices will specifically undergo a more thorough clinical examination (MDR Article 61.4). The investigational device's intended use as well as the suggested manner of usage must be taken into consideration throughout the review. It must be planned such that the outcomes are both legitimate from a scientific standpoint and regarding therapeutic applications. To carry out these processes, a new individual known as the sponsor, who developed in the MDR, conducts a series of clinical studies for the manufacturers in a highly rigorous manner and submits a report with all relevant information.[32][36]

According to MDR Article 61.5, any manufacturer seeking approval for their product based on the idea that it is equivalent to an already-available product must now show that it has a written agreement with the manufacturer of the competing product that gives it complete accessibility to all that company's documentation and clinical data. Technical, biological, and clinical characteristics must be met before equivalence can be taken into consideration (MDR Annex XIV, section 3); for instance, the new device should have a similar design to the predicate device, be made from the same materials that encounter human tissues and be used for the same clinical condition. Based on equivalence, it is predicted that these actions may result in the approvalof fewer high-risk devices.[33]

A theoretical and scientific framework for clinical evaluation and CI is created by emphasizing (i) "the confirmation of conformity" with respect to the safety and performance considering the "intended use" of the MD and (ii) the requirement basing the clinical assessment on an in-depth examination of the most recent research with regard to the safety, the performance of the MD, and a critical evaluation of "all available" CIs. The MDR simultaneously fixes expressly the "general requirements regarding CIs conducted to demonstrate the conformity of devices" (Article 62). The MDR also creates a balance between CI design and behavior that reflects the protection of "the rights, safety, dignity, and well-being of the subjects" as participants in CI.[37]The Clinical Investigation Plan (CIP) lays forth

the foundations, goals, project, and suggested analysis, monitoring, methodology, conduct, and record of clinical study in ISO 14155: 2011. Before beginning a clinical trial, the medical device's risk assessment must be completed. For clinical patients, the prospective risk and anticipated benefit must be weighed against one another. The clinical study strategy must also includea description of the device's anticipated drawbacks. Throughout the whole process of the clinical trial, there shouldn't be any unacceptable hazards. If not, the EC may suspend it or even terminate it. The steps to performa medical device's clinical research are provided in[38] Figure 3.

The assessment of the benefit/risk ratio's acceptability completes the evaluation. Benefits must clearly surpass dangers in this final analysis of risk, burden, and reward. It is important to highlight the various requirementsfor the clinical data required for the approval of MDs under the regulatory framework of medical devices in their quality, safety, and performance/efficacy aspects. As previously stated, it is anticipated that the MDR will offer some clarification about the clinical evidence used in the licensing of MDs in the EU through the need for public disclosure of data obtained in clinical research.[39],[40]

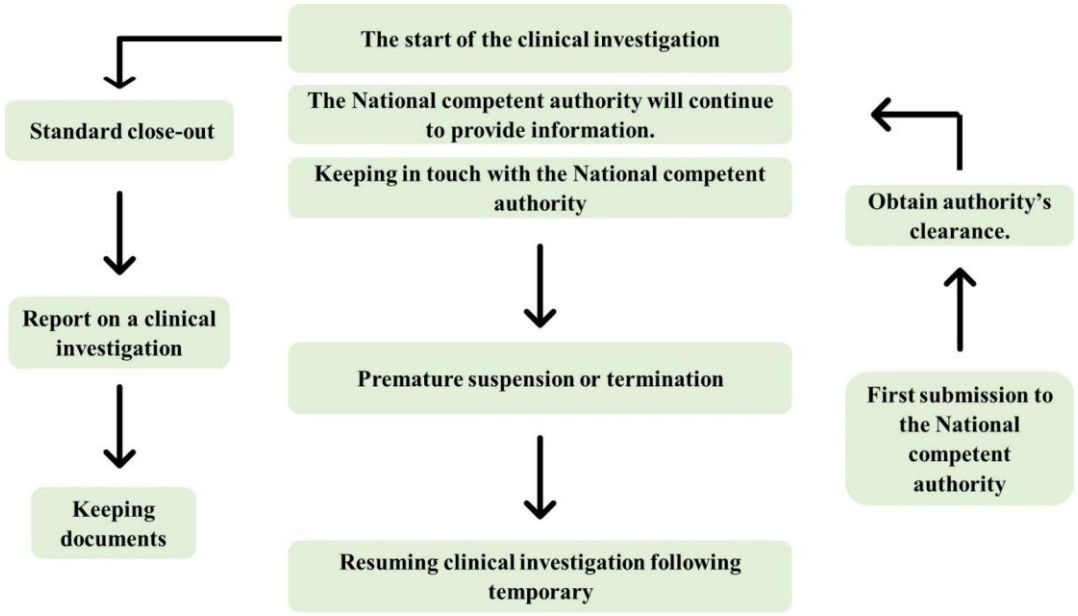

Figure 3: Flow chart of conducting a clinical evaluation of a medical device.

Safety should be provided together with any undesirable side effects and persistent risks found during the clinical trial management procedure. Several factors, including but not limited to those listed below, might influence the range of clinical data needed:

- Regulation classification and equipment type.

- Risks associated with using items. Examples: Procedure-related risks
- Current medical standards and the availability of alternative treatments.
- The anticipated lifespan of the device.
- Clinical evidence and clinical practice
- Modern technology and relevant earlier experiments
- Ethics-related matters[38]

The UDI and EUDAMED application in the medical device sectorThe UDI System

In the medical device sector, transparency and tracking have increasingly received significant attention to increase user and patient safety, medical device quality, and the efficiency of post-market operations.[41] The International Medical Device Regulators Forum (IMDRF) took up the worldwide Harmonization Task Force's(GHTF) 2011 work, which led to the publishing of a roadmap for the UDI's worldwide harmonization in December 2013.[42] In addition, the EU Commission has mandated that the member countries implement UDI systems. In accordance with this publication, member countries are provided early applications, and the key UDI provisions should be implemented.[43]

Three guidelines were released by the Medical Device Coordination Group (MDCG) on April 9, 2018, and are available on the website of the European Commission. These recommendations emphasize the medical device terminology, the design of the UDI database, and the definitions, descriptions, and formats of the UDIcore elements., are intended to make it easier to implement the new Regulation's UDI requirements. Refocusing on the upcoming European UDI, Article 2 of the new European Medical Device Regulation (MDR) (EU) 2017/745 defines it as a string of numeric or alphanumeric characters that enables the unmistakable identification of a specific device on the market by registering it in the UDI Database. There aretwo components to the UDI: device identifier (DI), UDI-DI, unique code specific to the device's model, whichserves as the primary key for records in the UDI database, and the production identifier (PI), or UDI-PI, which identifies the unit of the manufactured device and, if appropriate, the packed devices as described in Annex VI Part C. Every time there is a modification that can cause confusion in device identification or traceability, a new UDI-DI should be introduced. For instance, modifications to the device's trade name, brand name, model, number of devices included in a box, and the necessity for disinfection prior to use necessitate the creation of a new UDI-DI.[41]

The EUDAMED

The European Database on Medical Devices also called (EUDAMED)[44] is a secure, web-based site that enforces market monitoring and transparency by serving as a conduit for information sharing between national competent authorities and the European Commission. The requirement for an electronic UDI system as a crucial component of EUDAMED (referred to in Clause 24a of the new Regulation) stems from the EuropeanCommission's firm belief that a UDI system harmonized across Europe is the best way to ensure the efficient traceability of medical devices in the EU. The device and its UDI must be registered in the EUDAMED database, and the UDI must be displayed on the label in order to facilitate market surveillance and vigilance and to contribute to patient safety.[41]

The European legislator was keen to ensure that all the information in EUDAMED was accessible to the CAs of the Member-States and the Commission in the new legislation, whereas the earlier two editions of EUDAMED were only available to the Member-State CAs and the European Commission. In contrast, only the information pertinent to their usage will be available to the public, sponsors, and economic operators who have been alerted. Along with healthcare providers and institutions, the public also includes patients.[42] It will make it simpler for patients to obtain device data, which might result in better-informed treatment planning or outcomes, but it may also mean more paperwork for dentists as they must record information on the devices that were used during a procedure.[45] It will have access to information on marketing, certifications, economic operators, clinical research, the overview of the safety and performance characteristics of the device, and the most recent iterations of the safety notifications.[42] However, there areseveral challenges in implementing the database, such as the short implementation time frames and the stakeholders' lack of knowledge of the database itself.[46]

The Scope of medical device software in MDR regulation

This section aims to define what software falls under the scope of the MD regulations. To be categorized as medical device software, a product must first meet the requirements for both software as defined by this guidance and a medical device as defined by Article 2(1) of Regulation (EU) 2017/745 - MDR. The product must also meet the requirements set out in Article 2(2) of Regulation (EU) 2017/746 - IVDR for an in vitro diagnostic medical device to qualify as software.

Other Community and/or national laws may be relevant where a specific product does not

meet the definitionof an MD or is not covered by the MDR.

Regulations (EU) 2017/745 - MDR or Regulations (EU) 2017/746 – IVDR software that is not MDSW but isintended by the manufacturer to be an accessory for a medical device or an in vitro diagnostic medical device, even if it does not meet the criteria for either category. The software can be used to directly regulate a medicaldevice's (hardware) operation (for example, radiation treatment software), to deliver prompt decision-triggering data (for example, blood glucose meter software), or to help healthcare personnel (for example, ECG interpretation software).

The revised guideline on software as MDs is titled "Guidance on Qualification and Classification of Software in Regulation (EU) 2017/745 - MDR and Regulation (EU) 2017/746 - IVDR" and is known as MDCG 2019-11. Regardless of whether the software is independent or driving or influencing the usage of a medical device Software is described as software designed to be used alone or in conjunction with other tools for a certain purpose as indicated in the definition of a "medical device" in the MDR or IVDR. Manufacturers are responsible for ensuring that all legal criteria for marketing and conformity testing have been met. This also means that any claims linked to the intended medical purpose of their MDSW must be backed by clinical data, as stated in Article 7 of MDR and IVDR. If not, the software would not be compliant with the rules and hence might not be given the CE mark for a medical device or make the stated claims. Decision-making procedures to help Medical Device Software (MDSW) qualification[47] are mentioned in Figure 4.

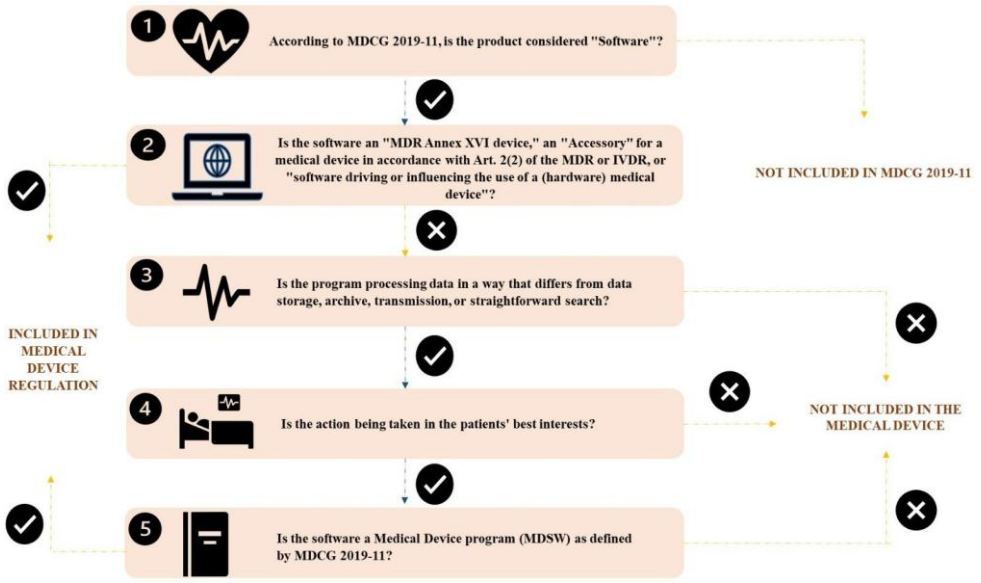

Figure 4: Conventional representation of medical devices as software.

The number of medical devices that employ software in some capacity, such as surgical robots, pacemakers, automated insulin dispensers, and a wide range of other devices, is at an all-time high. Although this is neither unknown nor unusual in the EU, many producers, caregivers, and consumers might not be aware of the MDR. All MDs in the EU will have to abide by it starting in late May 2021. When it comes to MDs, the usage of software is highly unique because of its absence of a physical presence. If it is a component of a device (an accessory) or if it is required for it to operate, it may materialize physically. However, it can also exist independently and still be an MD.[48]

Implementation of post-marketing surveillance on MDR regulation

To oversee manufacturers in maintaining the quality and effectiveness of MDs, PMS offers efficient vigilance should be used to guarantee the efficacy and safety of the commercially available and ongoing inspection. As soon as a medical device (MD) is put on the market, manufacturers should evaluate it to see if there are any design, technical, or performance problems. They should also get advice from the notified organizations to guarantee the item meets quality standards and lowers risk. The manufacturer should adhere to Good Manufacturing Practices (GMP) and QMS (ISO 13485). The producers, importers, and distributors must provide reports on grievances, side effects, safety concerns, and efficacy restrictions, as well as any incidentsinvolving injuries and fatalities brought on by the MD.[49]

The review of regional and national law recommends that authorized regulatory agencies, maintain the medical device and drug registers to achieve a successful MD PMS. The law mandates that upon import and market placement, producers and distributors must register their items in the registry. National regulatory agencies do the initial registration and take the findings of the initial product conformity evaluation performed by unaffiliated third-party entities in this procedure. This registration is a requirement for the national marketplacement of MD, and the market placement itself is a requirement for any other PMS strategies that come after MD. There are many medical device registries in some nations that have established various PMS plans.[50]

The new EU Medical Device Regulation 2017/745 (MDR) mandates companies to submit periodic safety update reports (PSUR) and post-market surveillance reports (PMSR). By increasing product quality and patient safety, the production of these reports will boost the post-market surveillance and vigilance system for medical devices. The PSUR is a summary of the findings and recommendations from the PMS data obtained via the PMS activities

described in the PMS strategy (Article 84). The PMSR is a smaller, more condensed document than the PSUR containing information that is identical to it but with fewer criteria.

The Medical Device Coordination Group's (MDCG) guidance documents, which are created in cooperation with several stakeholders, are intended to promote improved document harmonization in the medical device sector and a shared understanding of the law. The European Commission (EC) has been working on a guide to help manufacturers create PSURs that are MDR-compliant for several years. The first PSURs for class IIb (including implantable) and class III devices are due on May 26, 2022, which is somewhat alarming. It offersmore details on the CAPAs that should be included in the PSUR, how the devices should be grouped, the PMS requirements for medical devices that are still covered by Medical Device Directives, the time period during which a PSUR is necessary (i.e., device lifetime), the data collection periods, subsequent updates to the PSUR, and finally regulatory aspects (such as timelines and submission to the European Database for Medical Devices [EUDAMED] and in the absence of EUDAMED).

The regulation also includes six annexes that provide additional information, such as a content checklist, details on requirements, data reporting, data assessment, and terminology, as well as a PSUR form to be completed for EUDAMED submissions. Certainly, the MDR increases patient safety. Undoubtedly, among itsmost helpful tools to show cohesion between vigilance, PMS, clinical evaluation, risk processes, and regulatory bodies are the PSUR and PMSR. They are therefore essential for identifying changes in the benefit-risk profile.[51]

Current challenges with implementation

The Medical Device Regulation (MDR) 2017/745 is a revolutionary piece of legislation designed to fully regulate the high-tech commercial sector of medical devices in the European Union. Even six years after its publication on April 5, 2017, the reasons, viability, and effects are still highly debated.

Moving to the MDR, changing to the MDR presented several practical difficulties. The absence of notified bodies, which manufacturers must rely upon to reach the market for the majority of medium- to high-risk classproducts, is the first barrier that is frequently bemoaned within the sector. Only 38 notified bodies had obtained the accreditation required to carry out the conformity assessment review of medical devices in accordance with the new Regulation as of April 2023, nearly two years after the MDR became fully applicable in May 2021.

Under the Directive, there were more than 51 notified bodies, even without considering the 11 notified bodies based in the United Kingdom that withdrew on December 31, 2020, because of Brexit. The second barrier is included in the quantity of certifications. The number of certifications granted by notified organizations under the MDD that are still valid between 2022 and 2024 is shown in Figure 5A.

The third piece of the dilemma is the lengthy waiting period for certifications, in addition to the fact that there are fewer notified organizations and fewer certificates are provided. More than half of notified bodies recognized in the medical device industry take more than a year to release a product, and more than a tenth require two years or longer, according to a survey by Team-NB Figure 5B).[52]

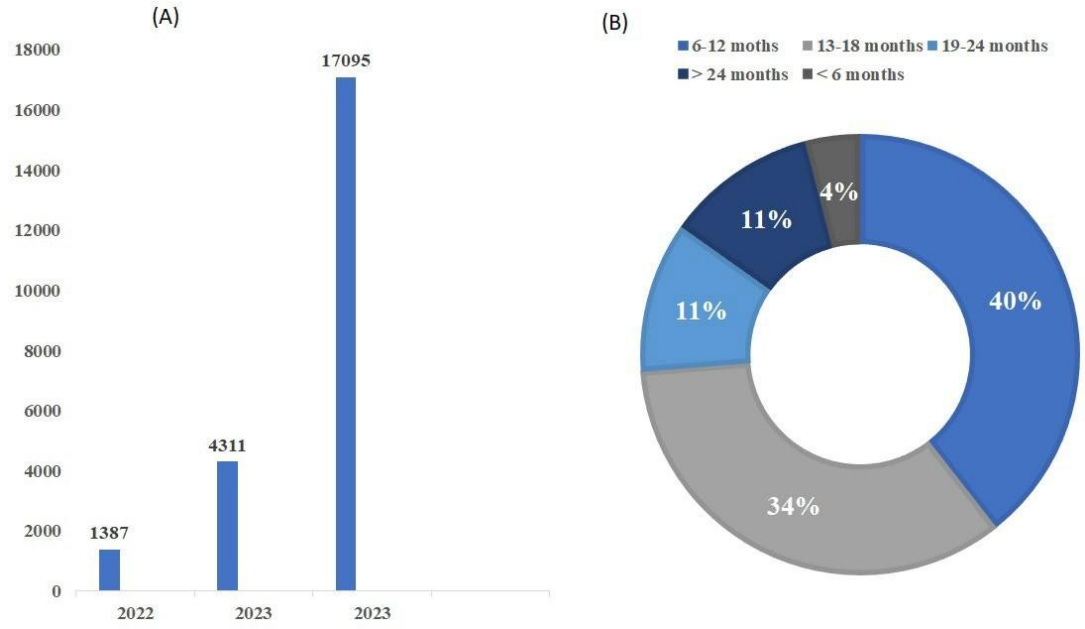

Figure 5: A) Number of MDD certifications in force, and B) Average time to issue an MDR certificate.

1. Innovation

Today, both developed and emerging economies are driven by innovation. Making decisions on new products is crucial to the development and success of any business, particularly in the rapidly evolving medical device sector. The complicated effects of legislative changes on innovation are presently being seen in the European medical device sector. Regulation (EU) 2017/745 of the European Parliament and of the Council on Medical Devices (MDR), Small and medium-sized businesses, even micro-enterprises, make up most of the medical device industry in Europe.[22]

Due to their narrow product focus, these businesses typically lack the profit margin to cover all the expenses associated with MDR compliance. SMEs should expect to spend between EUR 1-4 million or EUR 7-28 million to launch a new class III MD, depending on whether the device must meet the requirements of the centralized pre-market licensing procedure.[22]

The lack of clear records and methodologies for the creation of medical devices, as well as the lack of a formal system for tracking the expenses of routine tasks, are typical in the day-to-day operations of many businesses. In terms of the attitudes of the companies themselves, there is a clear sense of concern for potential future developments, worries about additional costs, dissatisfaction with the standards for puttingthe product on the market in the European Union, and even considerations of leaving the market and focusing on products other than medical devices. Massive, powerful businesses usually adjust well, embracing the changes and focusing their efforts on meeting the new standards.

Since there aren't enough notified bodies in the European Union, and other nations don't even have any notifiedbodies at all, it may be claimed that certain countries' conditions don't match up with the new legislation. The number of applications for the current notified bodies will also presumably increase as a result, which will result in a heavier burden and perhaps a delay in the release of new technology to the market. The approval procedure, including how long it takes and where it is available, poses a danger to the preparation of businesses for the regulatory shift. It will be feasible to analyze the effects of MDR 2017/745 on the medical device industry and its innovative activities in a few more years with the same economic metrics and various measures that have previously been employed to assess the impact of regulation.[22]

2. The legacy period to address transitional challenges

The grace period provided a transition time to devices authorized under the previous Directives, known as "legacy devices," is an actual step towards easing the transition hurdles to MDR. 'Legacy devices' are those that were given a transition time, and they are governed by MDR Art. 120.

In a nutshell, legacy devices are those that had a valid MDD or AIMDD certificate and were in use or on the market before the MDR took effect on May 26, 2021, or devices that were subject to an up-classification withthe MDR but did not require pre-market certification under the directive.[52]

The latest extension of the transition time under the MDR should continue to guarantee both the availability of MD in Europe and the sustainability of the healthcare system. At this initial stage, following the MDR's introduction, which included stricter pre- and post-market criteria for clinical data, it is hard to say whether the MDR will result in fewer safety concerns in the EU. It is unclear whether there will be an increase in premarket clinical investigations for novel devices because of this significant tightening of the possibility to demonstrate equivalence or if manufacturers will choose to first enter other markets with less stringent regulations and collect clinical data there before applying for the CE mark in the EU.

There is concern that the strict MDR standards might prevent manufacturers from releasing innovative medicaldevices in Europe since they could choose to focus on other markets first. Currently, most manufacturers are concentrating on moving their medical equipment from the[53] MDD and AIMDD[54] Hence, it is too soon to tell if the MDR will result in fewer inventions in Europe.

When specific data on implantable and high-risk medical devices becomes available to the public, such as in the Summary of Safety and Performance report or the EUDAMED database, which is anticipated to be fully operational by 2024, it is anticipated that physicians and patients will gain from the increased transparency inthe EU. Modern medical devices will always be available in the EU thanks to the prolongation of the transition period between the MDD and the AIMDD, and all parties involved should have enough time to complete the transfer procedure.[53]

3. Recognizing the new legal requirements

The many new requirements of the MDR have not yet been clearly defined, therefore it is difficult to comply with them. It might be challenging to understand the rule itself, thus templates and guidelines are being createdto assist researchers in their presentations to ethical committees and regulators. It is possible to find documents like the MDCG 2021: Regulation (EU) 2017/745 - Questions and Answers regarding clinical investigation by the Medical Devices Coordination Group Document and a template for an application to a Medical Research Ethics Committee (MREC) in the Netherlands for non-CE-marked medical devices. The information is dispersed, and each nation is generating instructions for its researchers and businesses to adopt MDR in their environment. Even the authorities are getting guidance materials, such as the MREC guide for reviewing clinical research using medical devices. However, there isn't a clear manual on how to carry out a clinical

assessment to complete a certification procedure. The MDR framework and the new guidelines for study submission continue to provide difficulties for clinical researchers, which might impede and prolong the process of performing a clinical trial.[55]

4. More rigorous testing for manufacturers

Pharmaceuticals and medical devices are two of the industries with the highest regulations. A medical devicemust not cause unintended side effects or significant health difficulties for the end user, regardless of the kindof device or its intended usage. A medical device's producer must prove to its notified body (N.B.) that the product is safe, effective, works as intended, and does not unexpectedly injure a patient when being used normally before it can be sold in Europe. Creating a clinical evaluation report (CER) with recorded clinical data to back up claims about the safety and effectiveness of a product is one-way manufacturers may show safety. This important file was delivered to their notified body in support of their request for a C.E. for marketing permission.

Manufacturers will face significant difficulties because of the stricter clinical evaluation requirements imposed by the new MDR, as discussed by commentators, once the notified bodies have access to the CER and the device's safety for use and ability to carry out its intended function are confirmed by the other components of the regulatory submission.

These difficulties are particularly connected to the increased need for clinical data compared to the MDD/AIMDD, which is needed to establish device efficacy and safety as well as to support an acceptable benefit-risk ratio.

Prior to the MDR, manufacturers would have relied on proving similarity to a product that was already on themarket to support their regulatory clearance request, lessening the need for clinical evidence. The MDR, however, adds far more stringent criteria for proving equivalency. Device manufacturers cannot utilize an equivalency case and must instead offer clinical data to support their C.E. marking application if they are unable to gather enough information to demonstrate conformance to the new standard.

Therefore, manufacturers of some high-risk and legacy devices that are no longer dependent on proving equivalence must conduct clinical trials to obtain adequate clinical evidence. The technical paperwork for thedevice, including the CER, is submitted to the N.B. to prove the equipment's performance and safety before itcan be sold on the European market and get the

C.E. mark. The C.E. mark is applied to the device if the notified bodies evaluate the scientific information and determine that the equipment is secure and operates in line with the manufacturer's intended usage declaration.[56]

CONCLUSION

With the objective of bringing safer and more effective medical products to market, the MDR transforms medical device regulation in Europe. This leads to improved devices and higher patient safety. Additionally, EUDAMED will have access to a collection of data, including the findings of clinical trials, and this will help to increase the transparency of the marketing of medical devices. Standards can be used to ensure physical and functional compatibility, product quality, compatibility and accessibility, security, protection of human health and the environment, and usability in connection to a medical device's software. The current legislation is undoubtedly not as straightforward and stringent as it might be, but it does appear to be a sensiblemove in the right direction. The coming years will show if adjustments are needed to stop harmful technologyfrom entering the market.

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Authors Contribution

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Conflict of interest

The authors disclose no potential conflict of interest.

REFERENCES

1. S. M. Ben-Menahem, R. Nistor-Gallo, G. Macia, G. von Krogh, and J. Goldhahn, "How the new European regulation on medical devices will affect innovation," *Nat. Biomed. Eng.*, 2020; 4(6): 585–590.

2. F.-S. K.-B. Tang, M. Bukowski, T. Schmitz-Rode, and R. Farkas, “Guidance for Clinical Evaluation under the Medical Device Regulation through Automated Scoping Searches,” *Appl. Sci.*, Jan. 2023; 13(13): 13, doi: 10.3390/app13137639.
3. A. Nüssler, “The new European Medical Device Regulation: Friend or foe for hospitals andpatients?,” *Injury*, Jun. 2023; 110907, doi: 10.1016/j.injury.2023.110907.
4. “New regulation of medical devices in the EU: impact in dermatology.” Accessed: Oct. 10, 2023. [Online]. Available: https://onlinelibrary.wiley.com/doi/epdf/10.1111/jdv.17830?src=getftr
5. “The European Medical Device Regulation–What Biomedical Engineers Need to Know - PMC.” Accessed: Aug. 01, 2023. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9395138/
6. K. Vasiljeva, B. H. van Duren, and H. Pandit, “Changing Device Regulations in the European Union: Impact on Research, Innovation and Clinical Practice,” *Indian J. Orthop.*, Apr. 2020; 54(2): 123–129, doi: 10.1007/s43465-019-00013-5.
7. “(PDF) The European Medical Device Regulation 2017/745/EU: Changes and Impact on Stakeholders.” Accessed: Aug. 01, 2023. [Online]. Available: https://www.researchgate.net/publication/327337806_The_European_Medical_Device_Regulation_2017745 EU_Changes_and_Impact_on_Stakeholders
8. B. Olberg, S. Fuchs, D. Panteli, M. Perleth, and R. Busse, “Scientific Evidence in Health Technology Assessment Reports: An In-Depth Analysis of European Assessments on High-Risk Medical Devices,” *Value Health J. Int. Soc. Pharmacoeconomics Outcomes Res.*, Dec. 2017; 20(10): 1420–1426, doi: 10.1016/j.jval.2017.05.011.
9. R. Behan, A. Pandit, and M. Watson, “New EU medical device regulations: Impact on the MedTechsector,” *Med. Writ.*, Jun. 2017; 26: 20–24.
10. “The Impact of the Medical Device Directive to Medical Device Regulation Transition on Early Clinical Testing of Cardiovascular Devices - Journal of the Society for Cardiovascular Angiography & Interventions.” Accessed: Aug. 01, 2023. [Online]. Available: https://www.jscai.org/article/S2772- 9303(22)00392-1/fulltext
11. N. Martelli *et al.*, “New European Regulation for Medical Devices: What Is Changing?,” *Cardiovasc. Intervent. Radiol.*, Sep. 2019; 42(9): 1272–1278, doi: 10.1007/s00270-019-02247-0.
12. A. Sharma and G. Luthra, “Implementing a Risk-Based Approach to Quality Management System ISO-13485 Processes in Compliance with EUMDR 2017/745 for Medical Device Industry,” *J. Pharm. Res. Int.*, May 2023; 35: 8–19, doi:

10.9734/jpri/2023/v35i137365.

13. "Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU (Text with EEA relevance.) - EU monitor." Accessed: Aug. 31, 2023. [Online]. Available: https://www.eumonitor.eu/9353000/1/j9vvik7m1c3gyxp/vkdyxt59idzu
14. "wjpps | ABSTRACT," *World J. Pharm. Pharm. Sci.*, Accessed: Oct. 10, 2023. [Online]. Available:https://www.wjpps.com/Wjpps_controller/abstract_id/15402
15. P. Vermeersch and E. André, "How the European in vitro diagnostic regulation could negatively impact the European response to the next pandemic: an urgent call for action before May 2022," *Clin. Microbiol. Infect. Off. Publ. Eur. Soc. Clin. Microbiol. Infect. Dis.*, Aug. 2021; 27(8): 1074–1075, doi: 10.1016/j.cmi.2021.05.009.
16. E. Bianchini and C. C. Mayer, "Medical Device Regulation: Should We Care About It?," *Artery Res.*,2022; 28(2): 55–60, doi: 10.1007/s44200-022-00014-0.
17. R. P. D. Majety, "New Era in Medical Device Regulations in the European Union," 2021; 10.
18. E. Niemiec, "Will the EU Medical Device Regulation help to improve the safety and performance of medical AI devices?," *Digit. Health*, Mar. 2022; 8: 1–8, doi: 10.1177/20552076221089079.
19. "Consult our Medical Device Experts - You can book online!" Accessed: Dec. 19, 2023. [Online]. Available: https://outlook.office365.com/owa/calendar/ConsultourMedicalDevicesExpert@FreyrSolutions.com/bookin gs/
20. H. Lacalle, "'Legacy' medical devices and IVDs under EU legislation," Decomplix. Accessed: Dec. 19, 2023. [Online]. Available: https://decomplix.com/legacy-medical-devices-ivds-eu-legislation/
21. "MDR 2017/745 - New EU Regulation for Medical Devices: A Process Description for EHRManufacturers on How to Fulfill the Regulation." Accessed: Aug. 24, 2023. [Online]. Available: http://kth.diva-portal.org/smash/record.jsf?pid=diva2%3A1458462&dswid=8420
22. P. Maresova, "Impact of Regulatory Changes on Innovations in the Medical Device Industry," *Int. J. Health Policy Manag.*, Jun. 2022; 12: 7262, doi: 10.34172/ijhpm.2022.7262.
23. "Administrative Sciences | Free Full-Text | New Regulations on Medical Devices in

Europe: Are They an Opportunity for Growth?" Accessed: Oct. 10, 2023. [Online]. Available: https://www.mdpi.com/2076-3387/10/1/16

24. A. Kahles *et al.*, "Structure and content of the EU-IVDR," *Pathol. Heidelb. Ger.*, Feb. 2023; 1–13, doi: 10.1007/s00292-022-01176-z.
25. F. J. L. A. Vanstapel *et al.*, "ISO 15189 is a sufficient instrument to guarantee high-quality manufacture of laboratory developed tests for in-house-use conform requirements of the European In-Vitro- Diagnostics Regulation," *Clin. Chem. Lab. Med.*, Mar. 2023; 61(4l): 608–626, doi: 10.1515/cclm-2023-0045.
26. A. M. Hallersten, N. M. Decker, and Y. Huang, "Principles of ideal diagnostic regulation and the IVDR," *Clin. Chem. Lab. Med.*, Mar. 2023; 61(4): 599–607, doi: 10.1515/cclm-2022-1206.
27. P. S. Abraham, J. Gholmie, E. Seoane-Vazquez, and R. Rodriguez-Monguio, "PHP136 - PRE- Marketing Authorization Of New Medical Devices In The European Union And The United States," *ValueHealth*, May 2013; 16(3): A267, doi: 10.1016/j.jval.2013.03.1370.
28. E. Klar, "[Medical Device Regulation as current challenge for the legally safe introduction of new technologies]," *Chir. Z. Alle Geb. Oper. Medizen*, Oct. 2018; 89(10): 755–759, doi: 10.1007/s00104-018-0705-3.
29. R. A. Byrne, "Medical device regulation in Europe – what is changing and how can I become more involved?," EuroIntervention. Accessed: Sep. 22, 2023. [Online]. Available: https://eurointervention.pcronline.com/article/medical-device-regulation-in-europe-what-is-changing-and-how-can-i-become-more-involved
30. C. C. Mayer *et al.*, "Regulatory Requirements For Medical Devices And Vascular Ageing: An Overview," *Heart Lung Circ.*, Nov. 2021; 30(11): 1658–1666, doi: 10.1016/j.hlc.2021.06.517.
31. S. Rahi and A. Rana, *global updation in regulations of medical devices in EU*, 2021; 65. doi:10.47583/ijpsrr.2020.v65i02.010.
32. S. P. Y. Kanti, I. Csóka, L. Adalbert, and O. Jójárt-Laczkovich, "Analysis of the renewed European Medical Device Regulations in the frame of the non – EU regulatory landscape during the COVID facilitated change," *J. Pharm. Sci.*, Oct. 2022; 111(10): 2674–2686, doi: 10.1016/j.xphs.2022.07.011.
33. "Implementing the new European Regulations on medical devices—clinical responsibilities for evidence-based practice: a report from the Regulatory Affairs Committee of the European Society of Cardiology | European Heart Journal | Oxford Academic." Accessed: Aug. 01, 2023. [Online]. Available:

https://academic.oup.com/eurheartj/article/41/27/2589/5849536

34. H. P. Zenner and M. Božić, "Clinical Evaluation of Medical Devices in Europe," in *Personalized Medicine in Healthcare Systems: Legal, Medical and Economic Implications*, N. Bodiroga-Vukobrat, D.Rukavina, K. Pavelić, and G. G. Sander, Eds., in Europeanization and Globalization. , Cham: Springer International Publishing, 2019; 21–32. doi: 10.1007/978-3-030-16465-2_2.
35. C. DI DOMENICO, "Medical Device Regulation in the European Community: EU Medical DeviceRegulation (MDR) vs Medical Device Directive (93/42/EEC) and Active Implantable Device Directive (90/385/EEC)," 2019, Accessed: Oct. 10, 2023. [Online]. Available: https://tesi.univpm.it/bitstream/20.500.12075/4324/1/PDF_A_Tesi_DiDomenico.pdf
36. A. G. Fraser *et al.*, "Clinical evaluation of cardiovascular devices: principles, problems, and proposals for European regulatory reform: Report of a policy conference of the European Society ofCardiology," *Eur. Heart J.*, 2011; 32(13): 1673–1686.
37. Faculty of Social Sciences, University of Craiova, Romania, A. P. Olimid, D.-A. Olimid, and Department of Biology, University of Craiova, Romania, "Ethical review of patient safety and public healthin EU clinical trials legislation: impact of COVID-19 pandemic," *Rom. J. Morphol. Embryol.*, Aug. 2020; 61(1): 277–281, doi: 10.47162/RJME.61.1.34.
38. Manita, A. Deep, Vikram, A. C. Rana, and P. C. Sharma, "Regulation and Clinical Investigation of Medical Device in the European Union," *Appl. Clin. Res. Clin. Trials Regul. Aff.*, 6(3): 163–181.
39. F. Hulstaert *et al.*, "Pre-market clinical evaluations of innovative high-risk medical devices inEurope," *Int. J. Technol. Assess. Health Care*, Jul. 2012; 28(3): 278–284, doi: 10.1017/S0266462312000335.
40. F. Albuquerque de Almeida and M. Ricardo, "Different regulatory framework for medical devices and drugs in the European Union: Impact on clinical research and health technology assessments," *Int. J. Health Plann. Manage.*, 2023; 38(5): 1420–1434, doi: 10.1002/hpm.3671.
41. E. Bianchini, M. Francesconi, M. Testa, M. Tanase, and V. Gemignani, "Unique device identificationand traceability for medical software: A major challenge for manufacturers in an ever-evolving marketplace," *J. Biomed. Inform.*, May 2019; 93: 103150, doi: 10.1016/j.jbi.2019.103150.
42. D. Camus, D. Thiveaud, A. Josseran, and participants of GIENS XXXIV round table "Health Technologies," "New European medical device regulation: How the French

ecosystem should seize the opportunity of the EUDAMED and the UDI system, while overcoming the constraints thereof," *Therapie*, Feb. 2019; 74(1): 73–85, doi: 10.1016/j.therap.2018.12.001.

43. T. Bayrak and F. Özdiler Çopur, "Evaluation of the unique device identification system and an approach for medical device tracking," *Health Policy Technol.*, Jun. 2017; 6(2): 234–241, doi:10.1016/j.hlpt.2017.04.003.
44. A. Badnjevic, R. Magjarevic, E. Mrdjanovic, and L. G. Pokvic, "A novel method for conformity assessment testing of electrocardiographs for post-market surveillance purposes," *Technol. Health Care*, Jan. 2023; 31(1): 307–315, doi: 10.3233/THC-229006.
45. D. Mohn and M. Zehnder, "The medical device regulation (MDR) from a dental perspective," *Front. Dent. Med.*, 2023; 4, Accessed: Oct. 10, 2023. [Online]. Available: https://www.frontiersin.org/articles/10.3389/fdmed.2023.1155820
46. K. Shatrov and C. R. Blankart, "After the four-year transition period: Is the European Union's Medical Device Regulation of 2017 likely to achieve its main goals?," *Health Policy*, Dec. 2022; 126(12): 1233–1240, doi: 10.1016/j.healthpol.2022.09.012.
47. "European Commission, official website." Accessed: Oct. 10, 2023. [Online]. Available: https://commission.europa.eu/index_en
48. K. Ludvigsen, S. Nagaraja, and A. Daly, "When Is Software a Medical Device? Understanding and Determining the 'Intention' and Requirements for Software as a Medical Device in European Union Law,"*Eur. J. Risk Regul.*, Mar. 2022; 13(1): 78–93, doi: 10.1017/err.2021.45.
49. N. Jiang, J. E. Mück, and A. K. Yetisen, "The Regulation of Wearable Medical Devices," *TrendsBiotechnol.*, Feb. 2020; 38(2): 129–133, doi: 10.1016/j.tibtech.2019.06.004.
50. A. Badnjević, L. G. Pokvić, A. Deumić, and L. S. Bećirović, "Post-market surveillance of medical devices: A review," *Technol. Health Care Off. J. Eur. Soc. Eng. Med.*, 2022; 30(6): 1315–1329, doi: 10.3233/THC-220284.
51. K. E. Tecante and A. Sokija, "The periodic safety update report and post market surveillance reportunder the new EU Medical Device Regulation," *Med. Writ.*, Jun. 2022; 31: 50–55.
52. "Needs, Challenges, and Obstacles in the Implementation of the EU Medical Device Regulation," Lexology. Accessed: Aug. 27, 2023. [Online]. Available: https://www.lexology.com/pro/insideview/needs- challenges-and-obstacles-in-the-implementation-of-the-eu-medical-device-regulation
53. M. Fink and B. Akra, "Comparison of the international regulations for medical devices–

USA versusEurope," *Injury*, Jun. 2023; 110908, doi: 10.1016/j.injury.2023.110908.

54. F. Windisch, "Glossary of single-use devices and Reprocessing terms," 2023.
55. "The Challenges of Setting Up a Clinical Study with the New European Union Medical Device Regulation - PubMed." Accessed: Oct. 10, 2023. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/37235206/
56. "The Challenges for Manufacturers of the Increased Clinical Evaluation in the European Medical Device Regulations: A Quantitative Study | Therapeutic Innovation & Regulatory Science." Accessed: Oct. 10, 2023. [Online]. Available: https://link.springer.com/article/10.1007/s43441-023-00527-z