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A Review of the New European Medical Device Regulations

Natarajan Jawahar[1]*, Nimase Akshay Ashok[1], Bala Sai Soujith Nidamanuri[1], Senthil Venkatachalam[1] and Jubie Selvaraj[2]

[1]*Department of Pharmaceutics, JSS College of Pharmacy, JSS Academy of Higher Education & Research, Ooty, Nilgiris, Tamil Nadu, India*

[2]*Department of Pharmaceutical Chemistry, JSS College of Pharmacy, JSS Academy of Higher Education & Research, Ooty, Nilgiris, Tamil Nadu, India*

Abstract

Introduction: This article provides an overview of important new regulations and policies, including some new guidance's regarding research related to medical devices in the European Union. Also, the new timelines for submission documents. The medical device classification system has been updated to better represent the potential health concerns connected with the usage of modern high-end technologies in healthcare. Also express the major changeover that the new MDR brings to the medical devices industry, focusing on clinical investigations and clinical evaluations. The aim of this work is to give an overview of the new medical device regulations as well as the functions and activities under the European medical agency in terms of assessment, appraisal, and ongoing evaluation of medical devices. This modification ensures a high degree of safety and health via the medical device. In summary, medical device investigation protocols have been advised and authorized by competent authorities. Furthermore, the new MDR law says that the manufacturer is to be ready with a complete summary of their evidence for any high-risk devices. The alignment of the new EU MDR's evidentiary requirements is examined in this article.

Areas covered: This article discusses the guidelines and respective legislation, new content of medical devices, new features of medical devices, and new medical device clinical evaluation processes were reviewed and analysed. A systematic literature search of databases (Medline, PubMed, Google Scholar, European Medical Agency website), chosen journals, and websites turned up publications presenting novel MDR structures or the clinical evaluation and clinical investigation procedures of certain registries.

Expert commentary: This article scrutinizes the impact of new changes in medical device regulations for evaluation and conformity requirements as well as standards for new medical devices and shows that, although a high level of stability now occurs in needful requirements, there are still areas where there is a lack of methodological understanding.

Keywords: High-risk medical device • Clinical investigation • Medical device directive (MDD) • European commission • New regulations • CE mark

Introduction

On May 5, 2017, the Official Journal of the European Union issued two new legislations: Regulation (EU) 2017/745 on Medical Devices (MDR) and Regulation (EU) 2017/746 on *In Vitro* Diagnostic Medical Devices (IVDR). It is applicable in all European Union (EU) member states unless having to be transcribed into federal legislation because they are Regulations rather than Directives. They will have a significant impact on the investigation, approval, and monitoring of high-risk medical devices. The new MDR regulations must be understood by all healthcare practitioners in Europe, as they will impact their everyday clinical operation. This article gives an overview of the correct as well as an accurate summary of the important plan of the rules that are pertinent to the reforms. It emphasises the novel task of healthcare practitioners and clinics in implementing the modifications, and it summarises how physicians with a curiosity in medical appliances can add almost to higher clinical evidence criteria for novel high-risk apparatus and upgrade performance monitoring. The CE mark is necessary to demonstrate the device's safety and also perform as the manufacturer designed [1]. In recent years, medical device technology has advanced dramatically, increasing both the figure of medical instruments (calculated to be around 500000 in Europe) and the invasiveness and the vital role such devices serve. Almost everyone will be disclosed to a medical apparatus at some point in their lives, and a lot more individuals are being inculcated with long-lasting apparatus that are frequently not removable. Among the objectives of the EU, public health schemes are steps to establish high quality and safety standards for medical equipment, as well as a variety of other areas of cooperation [2]. New medical device regulations improved safety and efficacy with clinical assessment for high-risk medical instruments and implantable has become essential. This will almost certainly enlarge the number of clinical trials, including MDs, with cardiologists playing a larger role in these studies. Finally, with the new MDR, the evidence of similarity between medical appliances will replace considerably. Three terms must be met to demonstrate such equivalence:

1. The clinical assessment for the previously CE-mark devices had to be a plan in accordance with the new medical device regulations standards.
2. The medical device maker of the new device should supply unambiguous proof of such assessment to the Notified Body.
3. A agreement should be made between the two medical device producers, providing the new MD's manufacturer complete access to the previously approved MD's technical documentation [1].

In this article, we will discuss core principles of medical device regulations in Europe, as well as changes in regulations and an update on regulatory progress.

Background of the study

The European medical device regulation was reviewed in 2012 after years of debate, and the new regulation went into effect in May 2017. The new restrictions will take effect 3 years after medical instruments are published and 5 years after *in vitro* diagnostic (IVD) medical devices are published. Industry representatives, on the other hand, have voiced their opposition to the review, claiming that more severe regulation will result in delayed access to new

***Address for Correspondence:** Natarajan Jawahar, Department of Pharmaceutics, JSS College of Pharmacy, JSS Academy of Higher Education & Research, Ooty, Nilgiris, Tamil Nadu, India, Tel: +919791439545, E-mail: jawahar.n@jssuni.edu.in*

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technologies and a "human cost" [3]. The novel regulatory plan supersedes two commands (the 90/385 on active implanted medical devices and the 93/42 on medical devices, referred to together as MDD). Medical-device manufacturers who obtained a " (CE) marking" - this document specify that a product conforms with European Union safety, health, and environmental safeguard demands, as well as a rule established by the International Organization for Standardization (ISO) - were granted EU-large market approach for their products under these directives. The MDD streamlined the regulatory operation over the European Union, but its application necessitated its incorporation into member states' national regulations [4]. The MDD divides medical devices into four categories: class I, class IIa, class IIb, and class III. Using the classification standards provided in Annex IX of the medical device directive, the manufacturer must assess whether their product falls into one of these four groups during the CE marking procedure. The category defines the conformity standards, with higher-risk devices (class III being the most stringent) requiring more testing. The MDR does not change the medical device classification premise, but it does change the classification rules and conformance standards. It's worth noting that the MDR reclassifies some device types as class III. Changing from a lower-risk class to a higher-risk class significantly influences the CE marking process since the conformity assessment approach may vary. A producer should determine that the instrument meets the MDD's necessary criterion during the CE marking process. The medical device regulations won't change the foundation of notified bodies in any way, except class III and implantable devices, more stringent procedures have been introduced, which necessitate a clinical evaluation process [1] (Table 1) (Figure 1).

Materials and Methods

New contents of medical device regulations

A qualified individual with professional know-how in the field of medical instruments must be appointed by the manufacturer qualified

1. The activities of the notified bodies, as well as their review certification, will be standardized across Europe (MDR certificate).
2. The conformity evaluation technique will be modified. There is no longer a method analogous to Annex VI of the MDD.
3. Classifications will change: A few implantable items that are currently classified as class IIb will link up the conditions for classification as class III products, and software will hardly be classified as a class I.
4. Increased demand for the recycling of biodegradable products.
5. MDD's technical documentation retention time was increased from five to ten years for the MDR.

The new regulations include several significant enhancements that will help to improve the present system. The new legislation aims to solve some fundamental flaws in previous instructions, as well as the accelerated advancement of science and technology in the area of medical appliances. It accomplishes this by introducing a number of significant enhancements, including

1. Stronger advanced command for a highly-risk gadget by the latest pre-market examination procedure, including an EU-wide pool of experts.
2. Support of designation norm and control operations for notified bodies.
3. Following international guidance recommendations, in-vitro diagnostics medical devices and a new risk classification method have been devised.
4. Unique Device Identification (UDI) has enhanced transparency.
5. Patients will be given an "implant card" with information on medical equipment that has been implanted.
6. Reinforcement of clinical evidence rules, including a coordinated EU-wide approach for authorizing multicentre clinical trials.
7. Manufacturers' post-market surveillance obligations will be strengthened.
8. Strengthened in the vigilance and surveillance of the market.

New timelines of medical device regulations

- April 5, 2017: The European Union's Medical Device Regulation has been followed.
- May 5, 2017: Regulation was published in the European Union's Official Journal.
- May 26, 2017: The Regulation went into effect and will run concurrently with the present medical device's directive, MDD 93/42/EEC, for a three-year transition period.
- December 2017: Under the new regulation, the process of redesignating Europe's Notified Bodies commences. The initial titles are scheduled to be completed within twelve to eighteen months of the law's release.
- May 25, 2020: The Medical Devices Regulation takes effect after the transition has ended (Figure 2).

New features of regulatory system

Medical Device Regulations (MDR) and *In Vitro* Diagnostic Medical Devices (IVDR) (Figure 3).

Table 1. Classification of the new medical devices [10].

Classes	General Description	Examples	Time Period
Class I	• Generally observed as low risk • General safety standards • Manufacturers can declare compliance with the essential requirements. The Class I MDs are approved by regulatory authorities, and the manufacturers themselves can issue the Comformité European mark (CE mark).	Bedpans, Sterile dressings, Gloves, Hospital beds	There is no need for approval.
Class II a	• Generally observed as medium-risk • General standards, quality systems, special controls. • Manufacturers must submit a dossier containing all essential supporting documentation, both clinical and non-clinical.	Surgical blades, Ultrasonic diagnostic equipment, suction equipment, powered wheelchairs, hearing aids	1 to 3 months
Class II b	• Generally observed as a medium to high risk • General standards, quality systems, special controls. • The maker must file a Manufacturer's Declaration stating that the product conforms to the medical device regulations and other important requirements.	Infusion pumps, ventilators, some implants, surgical lasers, radiotherapy equipment	3 to 6 months
Class III	• Generally regarded as high-risk. • Although clinical trials are advised, the majority of them are nonrandomized and single-arm. • Require pre-market review, including bench testing, clinical trials, and animal studies, providing proof of safety and effectiveness.	Many implants: replacement heart valves, breast implants, Drug-eluting cardiac stents, pacemakers, implantable defibrillators	6 to 9 months

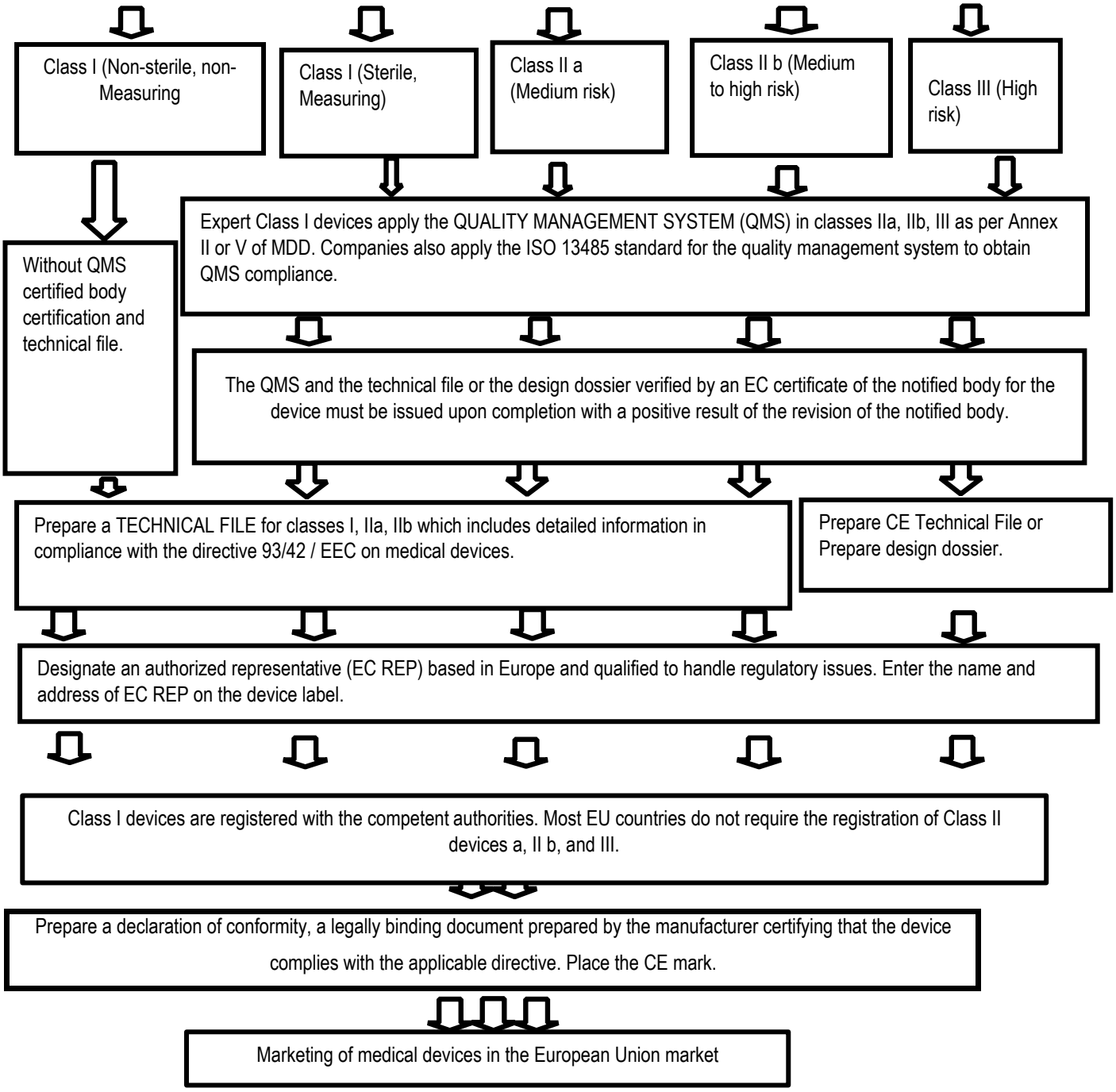

Figure 1. Medical devices approval process in E.U (European Union) [4].

New major changes in medical device regulations

The following are the most significant changes brought forth by the MDR:

1. Registered notified bodies (NB), manufacturers, and importers (MDR certificate) will be required.
2. A new inspection procedure will be implemented for Notified Bodies (Class IIb and III devices).
3. Technical documentation (Annex II) must be kept up to date at all times.
4. The amount of information that must be labelled has been greatly expanded.
5. More than 20 articles regulate clinical investigations and assessments.
6. It will be necessary to have a Unique Device Identification (UDI).
7. The EUDAMED electronic information service will be expanded in the future:
   - Obtaining information from relevant authorities, producers, Notified Bodies, and the general public.
   - Certificates, vigilance reports, clinical investigations, and PMCFs are displayed.
8. Evaluation of high-risk devices in a unified manner [5].

Key changes:

The three primary modifications in the improved rule will assure equal market access for medical appliances producers:

1. High quality, safety, and appropriateness of medical appliances.
2. Superior clarity for consumers.
3. Strengthened in the vigilance and surveillance of the market.

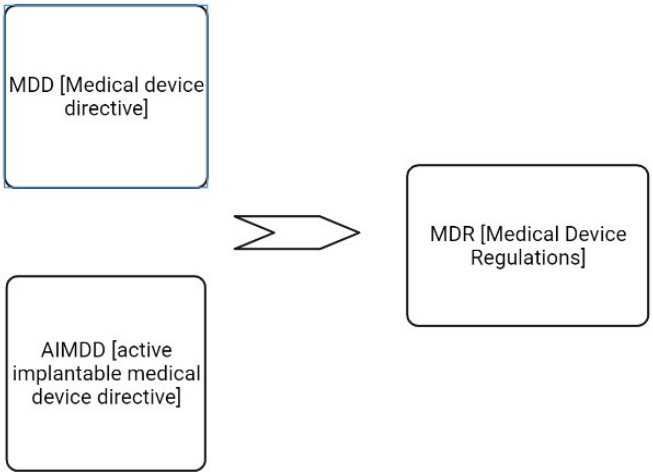

Figure 2. Changes in EU regulations [4].

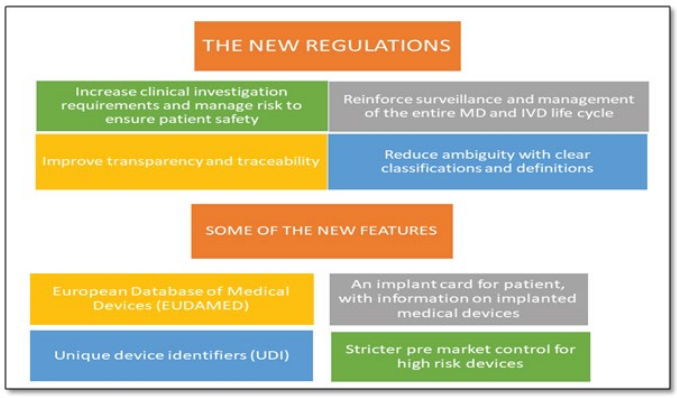

Figure 3. Key aspects of new medical device and in-vitro diagnostics rules. Reproduced with permission of the European Commission [10].

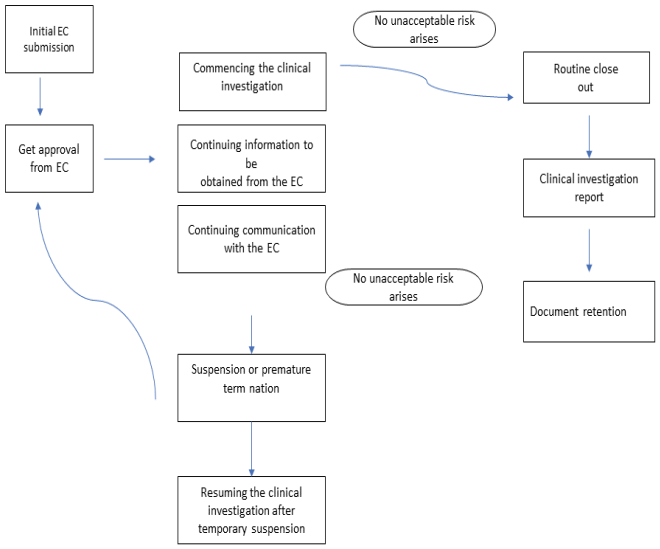

Figure 4. Procedure to conduct a clinical investigation of medical device [9].

Several transitional provisions have been established and outlined to ensure a smooth transition. The following are the major changes in the MDR:

- Annex I, which defines new conditions that must be met for CE-approved products under MDD, identifies general safety and performance requirements. Existing items must be recertified in accordance with current rules.
- Most companies comply with new rules by updating clinical data, labelling, and technical documentation.
- The definition of medical devices has been expanded to encompass non-medical and cosmetic gadgets that were previously unregulated.
- When manufacturers must disclose all accidents, injuries, and deaths to the EU portal, patients will possess their way to safety-associated knowledge. The time limit for describing occurrences that did not result in loss of life or major health worsening has been shortened from 15 to 30 days.
- Active implanted devices, nanomaterials, and compounds delivered into the body are all subject to classification requirements.
- In comparison to Annex VI of the MDD, the conformity evaluation methods have altered.
- The term "essential requirements" in MDD has been renamed "essential safety and performance requirements," which is a much more detailed term.
- Manufacturers must give each device a unique identifier that includes the production number and a device identifier. UDI is more than just a modification in labelling regulations.
- Post-market data and unique device-identifying data must be reported to the EU database (EUDAMED).
- In MDD, the clinical evaluation will be included on one page; however, post-market clinical follow-up will not be covered. Several articles and annexes of the MDR detail the various requirements.
- Post-marketing surveillance is not addressed in MDD, but it is now handled and regulated in MDR.
- The EU commission has the authority to adopt "common specifications" due to a lack of or insufficient harmonised standards. So far, no harmonised standards or common specifications have been produced [6].

New medical devices regulation standards

Device makers correlate their devices' working and clinical data and notify bodies to assess it against guidance from the International Organization for Standardization and the International Electrotechnical Commission, as well as their European equivalent, the European Committee for Standardization, and the European Committee for Electrotechnical Standardization. In November 2017, the EU's Official Journal formally acknowledged almost 300 of their standards. The MDR empowers the European Commission (EC) to publish uniform technical specifications [7].

New clinical evaluation regulations for medical devices

The new EU rule dramatically raises the standards for proving safety and efficacy by clinical review. This verification of a medical instrument's clinical efficacy and safety of the patient is often undertaken under the MDR by a clinical assessor using a professional clinical evaluation of medical apparatus. Clinical trials are more likely to be the omission than the law. Clinical assessment will be done without clinical study in a huge proportion of cases in the coming time. In their assessment, notified entities may also take into account additional manufacturer claims, which may then be clinically confirmed [8].

Results and Discussion

Opportunities for clinical investigation design

Numerous terms for projects involving computer modelling, convenience approaches, actual data clarifying, and new medical devices have been published by the European Commission. Some will come in handy in the future. Progress in illness management using computer modelling and simulation is a European power, and many commitments Support Systems have been advanced for several medical fields. The European Commission

hopes to use the capability of bulky data and high-performance computers to develop new individualised preventative measures and treatments through its novel efforts on digital health and care as part of the Digital Single Market agenda. Existing European activities on the subject will cover the economic aspects (e.g., TBMED, MedTechHTA, Impact-HTA projects) [9].

European Union clinical investigation guide

- MEDDEV 2.7/1 Clinical Data: Producers and Notified Bodies' Guidance.
- The 2.7/1 Clinical Data Evaluation: Appendix 1 Clinical Evaluation of Coronary Stents: A Guide for Makers and Notified Bodies.
- MEDDEV 2.7/2 Competent Authorities Guidelines to Follow When Validating or Evaluating Clinical Investigation Applications in accordance with Directives 90/385/EEC and 93/42/EC.
- MEDDEV 2.7/3 Clinical investigations: serious adverse events reported in accordance with Directives 90/385/EEC and 93/42/EC-SAE reporting form.
- MEDDEV 2.7/4 Clinical investigation guidelines: a guide for producers and notifying bodies [9].

New method to conduct clinical investigation of medical devices

The clinical investigation plan defines the foundations, aim, idea, and planned study, observance, procedure, performance, and record of clinical investigation in ISO 14155: 2011. It's also a proper document that serves as a contract, with the scrutiny group related to the clinical investigation plan as well as the acceptable clinical study time and cost. Therefore, during a clinical study, the finance and principal investigator should keep each other updated on any information obtained from the regulatory body and the European Commission (Figure 4).

Clinical Investigation Plan (CIP)

Sponsors, investigators, and monitors use the clinical investigation plan on a regular basis. This document contains all of the information necessary to complete the clinical investigation. In general, the following information must be provided:

- Administrative data in general
- Instructions for using the medical gadget under investigation
- The goal of the analysis
- The study's layout
- Inclusion and Exclusion Criteria
- Statistical justification and methods of data analysis
- Management of adverse events
- The analysis came to an unexpected conclusion
- Ethical Consideration
- Quality Control (QC) and Quality Assurance (QA)
- Financial and insurance arrangements
- Publication guidelines [10,11].

Conclusion

The new laws aim to boost the safety and effectiveness of medical appliances on the EU market, as well as address inadequacies in the implementation of Medical Device Directives that have been highlighted by various medical device makers. Regulatory agencies may benefit from developing regulatory equipment for assessing medical appliances prior to permitting authorization to place them on the market. CE marking/certification is required for any device sold in the European Union. Medical instruments are controlled by National Authorities and Notified Bodies in a new way. All clinical trial participants, including investigators, device manufacturers, and government regulators, must work together to approach the main objective of superior performance and safety assessment of novel, inventive apparatus for the cure of diverse diseases. While waiting for a revised Medical Device Directive (MDD), patients have to be protected by limiting the market distribution of new high-risk devices with insufficient clinical evidence to medical practitioners with the compulsory guidance and competence. Under current European regulations, premarket clinical efficacy and safety should be proved via a randomized controlled study, if possible, as well as clarity in clinical evaluation, ideally centralized. Unique research approaches for evaluating innovative devices may be necessary for the current environment.

Expert Opinion

The adjustment in legislation is aimed at achieving global harmonisation. Regulatory authorities may find it advantageous to establish a regulatory framework for assessing medical devices before allowing them to be placed in the market. There are several opportunities for medical writers as Europe's transparency policies become more stringent. The new MDR rules will also boost post-market surveillance systems by requiring manufacturers to gather data on product performance once devices are on the market; at the same time, EU Member States will be expected to improve vigilance and market surveillance coordination structures. In order to comply with the new MDR, manufacturers, authorized representatives, importers, and distributors will all be adversely impacted. Some specific concerns have been expressed about the new MDR's implementation and its potential influence on the availability of new medical devices. There is a lack of quality in existing research, as well as a lack of methodological understanding, and as a result, there are high standards for help from individuals involved in clinical study protocol creation. European medical device businesses might benefit immensely from a clarification of new MDR standards due to a lack of understanding and training in clinical trial abilities.

The following risks\benefits arise as a result of new European regulations:

- The contemporary observation on the lack of high-quality clinical trials,
- The high safety of expectations on the part of patients and healthcare professionals,
- The loss of enhancement of Europe for performing clinical studies,
- The goal for a "smooth transition" from directives to MDR without having the necessary resources,
- The awarding of a CE mark by a variety of private entities,
- The lack of a centralized procedure and the multiplicity of approaches taken by different notified bodies.

Acknowledgements

Declared none.

Conflict Of Interest

The authors declare no conflict of interest, financial or otherwise.

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