Medical Device Regulation:
A necessary step towards more patient and user safety

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Abstract
The new Medical Device Regulation (MDR) has recently been approved, and after a transition period of 5 years, all medical devices will be approved and marketed according to these new regulations. This article compares the main changes of the MDR to the still-valid Active Implantable Medical Device Directive (AIMD) and Medical Device Directive (MDD). Some changes will have a great impact on the way that devices are marketed, but many others are unpredictable and may disrupt the medical device market. Until manufacturers and authorities adapt to the changes, the transition years will pose difficulties for all stakeholders.

Introduction
The objective of this article is to provide the reader with an overview of the most important changes and additions in the Medical Device Regulation (MDR) that will replace the Medical Device Directive (MDD) and Active Implantable Medical Device Directive (AIMD), which are still valid. This article is NOT intended to guide the reader on how to work with the Medical Device Regulation (MDR) once it has been approved. The MDR is too complex to make a complete and in-depth analysis of its content within the context of this article.

First, let's take a look at a few simple numbers:

- The MDD has 23 articles, 12 annexes, and 60 pages. The AIMD has 17 articles, 9 Annexes, and 35 pages.
- Together that's 40 articles, 21 annexes, and 95 pages.
- The proposed MDR has 10 chapters, 97 articles, 16 annexes, and 352 pages.

I know that this is not particularly frightening for regulatory managers coming from the pharmaceutical industry, but it is quite scary for regulatory managers and medical writers that, like me, are used to working with the MDD. The

question if the MDD really needed such a thorough revision surely has many answers depending on whom we ask. The victims of the PIP scandal would most probably support the changes (for details please see the feature on page 39). The physicians willing to test and use the latest technological advances and gimmicks might not like all of the changes. The manufacturers that will be forced to generate, update, and manage a lot more documentation will be unhappy. The notified bodies in charge of evaluating this information might struggle with the new workload, but the competent authorities might welcome the new control mechanisms that protect patients and prevent future scandals.

There are many gaps and fuzzy terms in the MDD, and anybody with a bit of common sense would agree that they should be closed or redefined. The new MDR addresses these issues and reacts to developments in the medical device market, such as the increased use of software applications (apps), devices that include medicinal products or nanoparticles, and remote patient monitoring systems that work via the internet.

The following is a by-chapter analysis of the most relevant changes in the MDR:

Chapter I: Scope and definitions (articles 1-3)

The MDR adds some extra comments and conditions to the existing list of devices to which the MDD does not apply and clearly lists the corresponding regulations. Some new products – not currently covered by the AIMD/MDD – are now covered by the MDR, and other older products – currently on the market in some member states – are now excluded. Whether this regulation is self-consistent and complete has still to be seen in practice.

Altogether, the MDR provides 50 definitions (compared with the MDD's 14). Many of the new definitions are related to the concept of medical devices eg: "procedure pack" (devices to be used in a procedure), and "aggregate" (related with nanomaterials). Fortunately, the definitions are classified by concept of medical device, introduction in the market, economic operators and users, clinical evaluation, etc. Definitions will be aligned with the Global Harmonization Task Force (GHTF) guidance documents for medical devices.[1]

Chapter II – Making available and putting into service of devices, obligations of economic operators, reprocessing, CE marking, free movement (articles 4-22, Annexes I, II, and III)

This section has been expanded considerably and adds many new concepts and requirements. For instance:

1. A "qualified person" should be responsible for regulatory compliance within the manufacturer's organisation. This is similar to medicinal products and in the national laws of some member states.
2. The reprocessing of single use devices is regulated.
3. The "Essential Requirements" have become "General Safety and Performance Requirements" (Annex I) and include a list of up to 200 items to be checked.
4. Patient implant cards for implantable devices are required.
5. The concept of "State of the Art" is introduced.
6. Combination devices with software or substances to diffuse in the body are addressed.
7. Which stand-alone software are considered devices is defined.

The minimum contents of the technical documentation for the EU declaration of conformity are addressed in Annexes II and III.

Chapter III: Identification and traceability of devices, registration of devices and of economic operators, summary of safety and clinical performance, European databank on medical devices (articles 23-27)

This chapter addresses one of the main issues related with the medical device market: the difficulty to trace medical devices. In a complex market with more than 28[1] member states and many different local regulations, the Unique Device Identification (UDI) number[2] should improve traceability of medical devices. The UDI is a numeric or alphanumeric code for each medical device consisting of two parts: the device identifier and the production identifier. Proper labelling should contribute to market transparency, help during recalls, and discourage counterfeiting.

Manufacturers of class III and implantable medical devices will have to up-load summaries of safety and clinical performance to the central EUDAMED databases. EUDAMED will be accessible to manufacturers, notified bodies, competent authorities, and the EU Commission. All of these entities will have to input their "chunk" of required information, thus requiring a coordinated effort to implement it. These databases should organise data on devices being placed on the market, manufacturers, certificates, clinical investigations, UDIs, vigilance cases and post-market surveillance, information on the notified bodies, and device nomenclature.

Nobody really expects EUDAMED to be running when the MDR is approved. Unfortunately, many believe that it will take a long time before the EUMAMED is fully functional and can reduce administrative work and "regulatory compliance" costs.[3]

Chapter IV: Notified bodies (articles 28-40)

As notified bodies assess the clinical evaluation provided by the manufacturer, they play a key role in the approval and marketing process of medical devices. The MDR stresses the importance of their proper functioning and a coherent process to "designate" and monitor them throughout Europe. This should reduce discrepancies in the member states. The member states still "designate" and assess the notified bodies, but multinational teams will oversee these assessments. Notified bodies will be regularly controlled to ensure quality and ethical standards.

The workload for the notified bodies will increase substantially, since under the MDR the notified bodies will carry out unannounced factory inspections and conduct physical or laboratory tests on devices. The experts assessing medical devices are expected to rotate at regular intervals to ensure a neutral relationship with manufacturers. This is good news for regulatory experts, as experts with the background and experience described in Annex VI (see box with list of annexes) will be in high demand.

Chapter V: Classification and conformity assessment (articles 41-48, Annex VII, VIII to X)

Classification of medical devices has not changed very much. The MDD included 18 rules; the

MDR draft to which I had access includes 23 rules.[4] The new rules are:

1. Nano-materials and substances absorbed or dispersed in the body are classified according to their internal exposure potential.
2. Non-viable tissue of human or animal origin are class III.
3. Software devices can be of different risk classes.
4. Active therapeutic devices with integrated diagnostic functions that automatically influence the therapy delivered by the device are class III (typical example are external defibrillators, which sense the correct or incorrect functioning of the heart and react to this).

For conformity assessment of class III and class IIb devices that administer a medicinal product, the notified bodies will not be completely independent. They will have to send their clinical evaluation assessment of the device to an expert panel via the EU Commission (Annex VIII, Chapter II, Section 6.0). The notified bodies will only be able to certify the device once the expert panel has either issued comments or has not issued an opinion within 60 days, a procedure similar to the current regulation of medical devices that include animal tissues (Commission Directive 2003/32/EC).

Chapter VI: Clinical evaluation and clinical investigations (articles 49-59, Annexes XIII and XIV)

The clinical evaluation and clinical investigations in the MDR have a more stringent set of conditions and rules based on the MEDDEV 2.7/1 rev. 4 and parts of ISO 14155. This is particularly good news for freelance medical writers like me that have an engineering background and specialise in medical devices. But manufacturers will have to write more clinical investigation plans, reports, systematic reviews, and vigilance documents, meaning that the cost of regulatory management could increase so much that they might think twice before expanding their product portfolio.

Chapter VII: Post-market surveillance, vigilance and market surveillance (articles 60-75, Annex X)

The MDR addresses the need for a vigilance system for medical devices, particularly for implantable medical devices: "the Commission shall, in collaboration with the Member States, set up and manage an electronic system to collate and process" vigilance information. Manufacturers will have to report serious incidents and the corrective actions implemented. This information will be shared with the national authorities of other member states and similar incidents will be compared.

The MDR also defines vigilance documentation that includes the reporting of adverse events during clinical studies, the summaries of safety and clinical performance, and the market and surveillance reports.

At defined intervals, the manufacturer will have to issue a Safety Update Report for devices placed in the market that evaluates the risk/benefit of the device, provides PMCF data, sales volumes, and number of devices in use. The reports of class III and implantable devices will be reviewed by the notified bodies and then made available to the competent authorities.

Timelines are provided to report incidents (Article 61). Field Safety Notices and Field Safety Corrective Actions will likely be made public.

Chapter VIII: Cooperation between member states, medical device coordination group, expert laboratories, expert panels, and device registers (articles 76-83)

A Medical Device Coordination Group (MDCG) will be established with representatives of the competent authorities the member states. The MDCG will contribute to:

- The assessment of notified bodies.
- The effective and harmonised implementation of new regulations.
- The continuous monitoring of the technical progress and assessment of whether the general safety and performance requirements are adequate.
- The development of medical devices standards.
- The coordination of competent authorities and member state activities.

List of Annexes

I	General safety and performance requirements
II	Technical documentation and Technical documentation on post-market surveillance
III	EU Declaration of conformity
IV	CE marking of conformity
V	Information to be submitted with the registration of devices and economic operators in accordance with Article 25a and core data elements to be provided to the UDI data base together with the device identifier in accordance with Article 24a and the European Unique Device Identification System
VI	Requirements to be met by Notified Bodies
VII	Classification criteria
VIII	Conformity assessment based on a quality management system and assessment of the technical documentation
IX	Conformity assessment based on type examination
X	Conformity assessment based on product conformity verification
XI	Procedure for custom-made devices
XII	Certificates issued by a notified body
XIII	Clinical evaluation and post-market clinical follow-up
XIV	Clinical Investigations
XV	List of groups of products without an intended medical purpose referred to in Article 1(1a)
XVI	Correlation table

The MDCG will also provide advice for problems that arise in the implementation of these regulations and harmonise medical device administrative practice across the member states.

Chapter IX: Confidentiality, data protection, funding, and penalties (articles 84-87)

Personal data, commercially confidential information, trade secrets, and intellectual property rights are protected unless disclosure is in the public interest. Does this mean that the press will have access to sensitive information, concerning results of audits and inspections? This is not clear yet, and it depends on how public interest is defined or interpreted!

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Member states may levy fees for the activities set out in the MDR. These should be set in a transparent manner and on the basis of cost recovery principles. Whether these fees will impose a considerable burden on small and medium local medical device manufacturers is not yet known. Eventually, this could lead to "fee's dumping" by the different member states to attract medical devices manufacturers or to a concentration of the business in the hands of a few big international corporations that can manage the regulatory costs.

Chapter X: Final provisions (articles 88-97)

This chapter lists amendments, defines transitional provisions, and sets date of application. The MDR will become applicable 3 years after its approval so that the member states, notified bodies, and manufacturers can adapt to the new legislation.

And the future?

So, that was it! Do I dare predict whether the MDR will make the use of medical devices safer? In general, I believe that it will. Will it have negative consequences, such as marketing approval delays due to lack of qualified personnel and increased health care costs? Most probably, yes. I use "in general" and "probably" because what will really happen depends on the interpretation of the different rules, new definitions, and changed words by the notified bodies and competent authorities.

For sure, the first year will be a struggle and a bit of a hazardous game with an open end, but as with all new legislations, the manufacturers and the authorities will adapt to the changes and finally settle into a reasonable cooperative scheme.

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Claudia Frumento holds a PhD in medical technology. She has more than 17 years' experience in international medical device corporations and has been a freelance medical writer since 2006. She leads the EMWA workshops on medical writing for medical devices.