UNDERSTANDING EUROPE'S NEW MEDICAL DEVICES REGULATION (MDR 2017/745)

New requirements, key changes, and transition strategies for device companies

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Disclaimer: *This White Paper reflects the information available to Emergo in May 2018. This information is subject to changes and readers should not base their regulatory policies on this document alone.*

Executive Summary: The Consequences of the MDR

The Medical Devices Regulation is a complex piece of legislation and detailed interpretation is required. The following points are the essential takeaways:

1. Time is of the essence. The transition started in May 2017 and will take until May 2020. Some changes may be delayed, but your organization and your staff need to understand the technical documentation of most of your devices, the MDR, and be ready by that date.

2. Emergo estimates that placing a device on the European market and keeping it there will require 2-4 times more working hours by your staff. You will need additional budgets for staff, outsourcing, and training. You should also start looking for software tools that enable your staff to do their work more efficiently.

3. Consider the availability of the suppliers you currently use for outsourcing regulatory, clinical, or certification activities. All resources (including Notified Bodies and consultants), Competent Authorities, and the European Commission will be stretched beyond their limits. Add 50% additional time to any plan you make.

4. The compliance of all devices will have to be assessed again, this time against the current requirements (and the current standards). Some devices rely on past data that has not been sufficiently updated, and may no longer be compliant or fully available. Missing data, especially clinical data, can prevent a device from being certified. Therefore, you should have the availability and quality of all data for your devices reviewed as soon as possible.

5. Users can claim compensation for damage caused by defective devices. Manufacturers must have measures in place to compensate for that. In case of non-European manufacturers, the Authorized Representative will be held liable jointly with the manufacturer. Expect the Authorized Representative, if they are not part of your organization, to review their agreements considerably and to exercise more due diligence on who they accept as clients.

6. These additional requirements and challenges will also be faced by your competitor. Companies that anticipate adequately will create a better position for themselves. So, start acting now.

7. Last but not least, consider the turnover depending on CE marked devices. Not only the European Union – the largest single market, with a wealthy, aging population – uses the CE marking. The CE marking can also be leveraged to other markets. This probably helps set priorities when considering budgets for the MDR transition.

The Medical Devices Regulation (EU) 2017/745

The European Single Market comprises 28 Member States of the European Union (including the United Kingdom[1]), the European Economic Area (Iceland, Liechtenstein, and Norway) and, through bilateral treaties, Switzerland and Turkey. It is the largest single market with a wealthy, aging population of over 500 million consumers.

Free movement of goods is one of the cornerstones of the European Single Market. To enable this free movement concept, a product allowed on the market in one member state will also be allowed on the markets of other member states. The 2016 version of the Blue Guide on the implementation of EU products lists three conditions that must be met for goods to move freely:

1. Essential requirements for the products involved must be defined.
2. Methods must be established to describe how product compliance with the requirements is addressed.
3. Mechanisms to supervise and control the actions of all Economic Operators and others involved in the manufacturing and distribution of the products must be created.

The predecessors of the Medical Devices Regulation (MDR) (EU) 2017/745 – the Active Implantable Medical Devices Directive (AIMDD) 90/385/EEC, and the Medical Devices Directive (MDD) 93/42/EEC - do just that. These directives defined Essential Requirements and introduced harmonized standards, helping to demonstrate conformity to the Essential Requirements. The directives also defined conformity assessment procedures and organized market surveillance functions by Competent Authorities (CAs) and Notified Bodies (NBs). These directives, introduced in early 1992, have worked well and helped create the single market for medical devices in Europe.

However, the directives had some inherent weaknesses and the changes in technology and medical science demanded changes in legislation. These shortcomings challenged national member states and the interpretation of the directives was not consistent across all national governments. Directive 2007/47/EC modified the MDD and AIMDD in an attempt to address these concerns but this amendment did not achieve all goals. The scandal involving defective breast implants manufactured by Poly Implant Prosthesis (PIP) in France demonstrated additional structural weaknesses in the system.

The regulations were formally published in the *Official Journal of the European Union* (OJEU) in May 2017, ushering in the official transitional period to implementation in May 2020.

[1] *Brexit is briefly discussed on page 18.*

Main Themes of the Regulation

Compared to the MDD, the MDR promotes a shift from the pre-approval stage (i.e., the path to CE Marking) to a life-cycle approach. This approach is similar to the life-cycle view advocated by the US Food and Drug Administration (FDA) and advanced by many international standards.

The life-cycle approach is illustrated by the incorporation of European guidance (MEDDEVs) into the regulation. Guidance on authorized representation, clinical evaluation, vigilance, and post-market clinical follow-up have been integrated into the MDR. As the MEDDEVs are not legally binding, this change reduces the flexibility in interpretation by industry as well as the authorities and NBs. The current MEDDEVs do not apply to the MDR, although many elements from the MEDDEVs have been incorporated in the Regulations. The Regulations do not rule out the use of guidance documents by the authorities. It is likely, although not formally confirmed, that the European Commission would support guidance documents being published through the vehicle of MDCG Working Groups.

The compliance of all devices with Essential Requirements has to be reassessed, with reference made to current standards and state of the art. This means there will be no grandfathering. However, devices with valid certificates issued under the current directives can still be placed on the market until May 2024, provided no significant change in design or intended purpose is made.

According to the current document, NBs would be placed under a strict regimen of supervision, although it remains unclear whether intended sanctions against an NB that violates MDR requirements could be implemented against the will of a member state. The qualification requirements for auditing and reviewing NB staff have steeply increased.

Much greater emphasis will be placed on clinical data and clinical evaluations. Equivalence, currently commonly used to justify references to studies done with other devices, will be more rigorously interpreted. This will be a far more challenging way to demonstrate clinical safety or performance for medical devices.

For implantable Class III devices, clinical investigations will be expected since NBs will effectively no longer accept the equivalence approach (Article 61(5)), although some exceptions can be made. Clinical investigation requirements will not always be applicable for devices lawfully placed on the European market in accordance with the AIMDD and MDD. These devices demonstrate conformance based on sufficient clinical data and applicable Common Specifications (CS) or are of a specific family per Article 61(6). (CS will be developed by the European Commission after consulting the MDCG and stakeholders. CS will be published as implementing act by 26 May 2020 and will become effective six months later or six months after their date of publication, whichever comes last. NBs will require a high level of quality with regard to investigations and clinical evidence in general.)

The MDR attempts to make the time frames for review by various parties for different activities more transparent. In general, the regulations provide greater details and codify information from guidance and standards. Finally, the MDR concentrates the harmonization efforts between European member states by means of a new regulatory body called the Medical Device Coordination Group (MDCG). The objective of the MDCG is to foster cooperation between the member states while increasing the Commission's power to act as needed in acute cases. The MDCG is in the process of establishing sub-groups consisting of various stakeholders. This will closely resemble the current Medical Device Experts Group (MDEG) structure.

The main concepts introduced in the MDR described in more detail are:

1. The complete overhaul of Eudamed. Introducing UDI and international nomenclature on medical devices as well as on incidents (Chapter 3 and Annex VI).
2. The inclusion into the scope of products without a medical purpose (Annex XVI).
3. Supply chain regulation that obliges each entity in the supply chain to check compliance of the previous supplier. See Chapter II.
4. The introduction of a special procedure for NBs for certain high-risk devices. See Article 54.
5. The introduction of manufacturers' liability specific to medical devices and in line with the Liability Directive 85/374/EEC. Authorized Representatives will be jointly and severally liable for the devices they represent. See Articles 10(16) and 11(5) respectively.
6. Substances that are carcinogenic or that have other potential high-risk effects on the human body can only be used together with a strictly defined justification (Annex I, Section 10.4).
7. The introduction of strict rules for clinical investigations and alignment to the Clinical Trials Regulation. See Chapter VI, Articles 62-82.
8. The introduction of detailed rules for the execution and the results of Post-Market Surveillance and Post-Market Clinical Follow-up.
9. Reprocessing of single-use devices is only allowed under specific conditions – permission by the member state is one of them. See Article 17.
10. Rules for devices produced in hospitals to be used exclusively for its own patients have been added. See Article 5(5).
11. The rules for designation of NBs have tightened. These are provided in Chapter IV, Annex VII and Annexes IX to XII. Procedures for vigilance and post-market surveillance are described in more detail, and the fact that they have to be used for ongoing conformity assessment of the device are given in detail. See Chapter VII.

Organization of the Regulation

The MDR combines legislation for medical devices and active implantable medical devices into one document. The regulation commences with an explanatory memorandum and with recitals that are explanatory in nature and not legally binding. One recital of particular interest, Recital 4, acknowledges the guidance of the Global Harmonization Task Force (GHTF) and its successor organization, the International Medical Device Regulators Forum (IMDRF). The recital emphasizes the importance of global convergence of regulations and Unique Device Identification (UDI) as well as other areas that would benefit from global regulatory harmonization.

The official version of the regulation consists of 92 pages plus 83 pages of annexes. The highest article number is 123, with Recital 101 being the last. The regulation is further organized into ten chapters that address important concepts and identify weaknesses. The articles reference an additional 17 annexes.

Definitions and Scope of the Legislation

Article 1, regarding the scope of the MDR, brings products without an intended medical purpose that are listed in Annex XVI within its scope. The article also states that medical devices, their accessories, and the products listed in Annex XVI will be referred to as devices. In the definition of accessories, no exception is made for products without a medical purpose that will be considered medical devices and therefore their accessories will also fall within the scope of the MDR.

Another significant extension of the MDR, compared to the MDD, can be found in the definition of a medical device. Devices for cleaning, disinfection, or the sterilization of devices will themselves be considered medical devices. Previously, these products were considered accessories to medical devices. This placed them within the scope of the Directive. However, accessories to these accessories were not considered devices. Under the MDR accessories to this new group of medical devices will also be within its scope.

Products that fall within the scope of the MDR, together with other directives or regulations, are brought within the MDR. In addition, depending on their function and mode of action, they are placed within the other legislation while the relevant safety and performance requirements for the device remain applicable. This means that a product that is implanted to control fertility by slow release of hormones will be considered a medicinal product, but the implant itself must meet requirements applicable for medical devices, including the requirements for risk management, biocompatibility, and user information. This requirement may be new to some pharmaceutical companies.

Article 2 contains a total of 71 definitions. This section is significantly expanded as the MDD only contained 14 definitions.

As stated above, the definition of medical devices is extended to include products for cleaning, disinfection, and/or sterilization. The article also covers In Vitro Diagnostics (IVD) in order to align the MDR and the In Vitro Diagnostic Device Regulation (IVDR).

The definition of accessory is expanded to assist and enable a device to be used for its intended clinical use. The understanding of products that could be classified as accessories to medical devices is broadened. The term *label* is defined by Article 2(13) as the physical label on the device or package. *Risk* is now defined as in the EN ISO 14971:2012 standard. The consequence is that risk can be limited by controlling the occurrence or severity of a harm. The term Common Technical Specifications (CTS) was introduced in the EU Commission draft. The EU Council draft deleted the word Technical and simply refers to CS. This term is borrowed from the In Vitro Diagnostic Devices Directive (IVDD) 98/79/EC and prescribes technical specifications as a way to augment standards. Many definitions currently found in the MEDDEVs have been added to the regulation, such as those concerning clinical evaluation and vigilance.

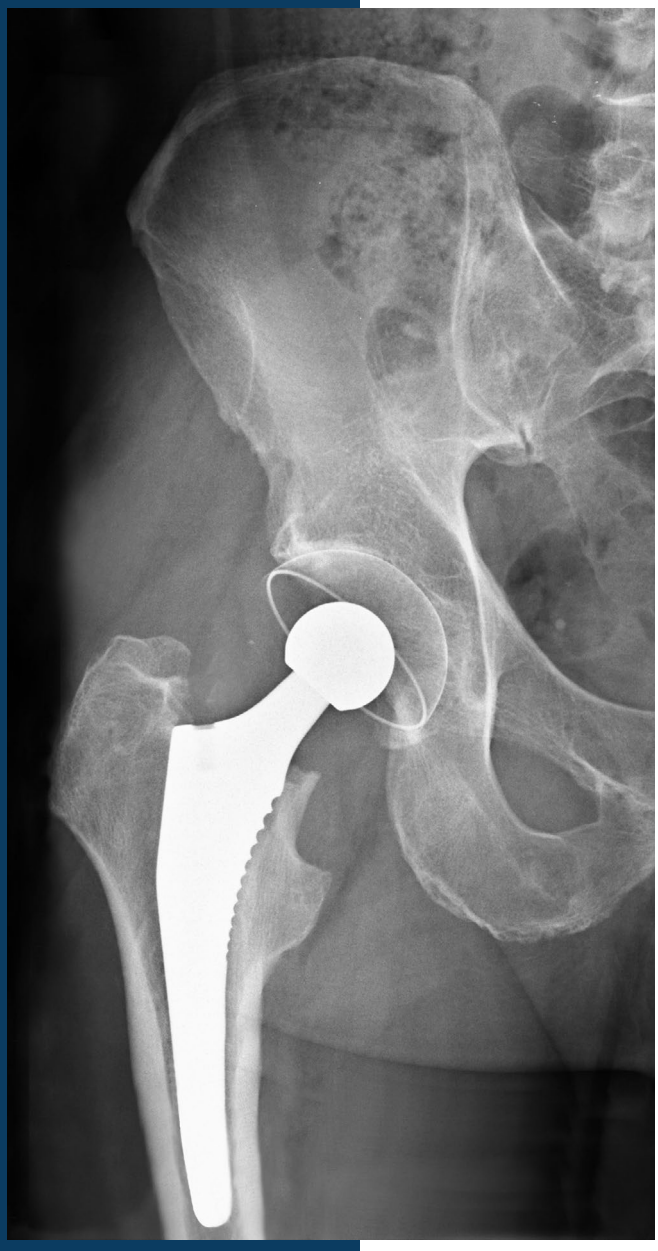
There is no mention of stand-alone software as a separate regulatory concept. Software, whether embedded or not, may have a medical purpose, in which case it falls within the scope of the MDR. Annex VIII, Classification Rules now refers to “software that drives a device or influences the use of a device” versus software that is “independent of any other device.”

Chapter I provides substantial definitions and responsibilities of the respective economic operators (EOs). This chapter delineates a demarcation between the responsibilities of the Authorized Representative (AR), the distributor, and the importer. The current MEDDEV on ARs is essentially incorporated into the Regulation, which highlights the complementary but incompatible roles of the AR and the two other EOs (distributor and importer). There is an article that describes the process to change an AR. “Distance sales” are regulated in such a way that devices sold to European citizens through the internet must also comply with the Regulations. It is not clear how this will be controlled.

Chapter II also introduces the person responsible for regulatory compliance. This role should be filled by a highly educated and experienced person and is intended to safeguard regulatory compliance within the manufacturer or AR where he/she works. Measures to ensure an injured patient can claim damage for defective products have also been introduced.

Article 10(8) of Chapter II requires the manufacturer to supply CAs with all information necessary to demonstrate conformity, as well as to share that information with patients or their representatives claiming compensation. These requirements will obviously have an impact on manufacturers’ technical documentation.

The AR is made jointly and severally liable for defective devices with the manufacturer. The importer also shares liability according to Product Liability Directive 85/374/EEC. Liability requirements may put further pressure on the willingness of manufacturers, ARs, and importers to share information with CAs. The responsibilities of the importer and distributor are laid out, but there are no indications regarding who would be liable in cases of non-compliance. It can be foreseen that the AR in such cases may not agree to be held fully liable.



Article 17 of Chapter II addresses the reprocessing of single-use devices. Reprocessing may only take place where permitted by national law and under strict conditions. Full product liability is placed on the re-processor while the original manufacturer will no longer be mentioned on the label even though they will continue to be on the IFU.

Note: *The requirements for conformity assessment and the technical documentation that needs to be available will effectively eliminate the position of the Own Brand Label manufacturer. This will have a significant impact on companies.*

The MDR retains Article 3 of the MDD as Article 5(2) where medical devices must be compliant to relevant Annex I, General Safety and Performance requirements. Similarly, Article 5(1) of the MDD exists as Article 8(1) to comply with EN harmonized standards published in the *Official Journal of the European Union* (OJEU) with presumed compliance to Annex I. Furthermore, Article 18 requires that patients with implantable medical devices be provided implant cards. Distance sales and internet services are addressed in Article 6, which states that a device not placed on the market, but used for a diagnostic or therapeutic service to a person established in Europe, must also comply with the MDR. This also means that manufacturers of such devices not based in Europe must appoint ARs.

Companies that sterilize procedure packs or systems must either comply with the requirements in Annex IX (Quality System) or Annex XI (Product Verification) and allow NB involvement regarding sterility (Article 22(3)).

General Safety and Performance Requirements (Annex I)

Annex 1 resembles the Essential Requirements of the current MDD. This annex is now called General Safety and Performance Requirements (GSPR). Chapter 1, Section 1 remains identical except for the important insertion of “taking into account the generally acknowledged state of the art.” Of course, the use of current standards and published literature facilitates addressing this requirement.

For non-medical products that are treated as medical devices and products for which there are no sufficient standards, the CS will be applied. Reduction of risk as far as possible is explained as reducing risk “without adversely affecting the risk benefit ratio.” Also, the manufacturer must use a risk management system per Section 1a. The number of Essential Requirements and the level of detail have increased. An initial count indicates that the new GSPR Checklist would have more than 220 items to review. Manufacturers using certificates issued under the current MDD should be aware that they must demonstrate state of the art under the new MDR. They should monitor competitors whose products, including devices, suddenly outdate their medical devices by introducing new technologies.

Chapter 2 retains many of the Essential Requirements from the MDD, Requirements regarding design and manufacture, and adds the following sections:

- Devices incorporating a medicinal product and devices composed of substances or combinations of substances intended to be absorbed or locally dispersed in the human body
- Devices incorporating materials of biological origin
- Construction of devices and interactions with their environment
- Software in devices and software that are devices in and of themselves
- Particular requirements for active implantable devices
- Risks concerning medical devices for lay persons

Devices that contain more than 0.1% in weight of a carcinogenic, mutagenic, toxic substance, or substances having endocrine disrupting properties need to have a justification for their presence. Unauthorized access to active devices must be avoided.

Chapter 3, Requirements regarding the information supplied with the device, covers labeling and instructions for use. Another addition by the Council, Section 23.2 (q), states that there should be an indication on the label that the product is a medical device, similar to the current identification of an IVD. This may lead to the introduction of a new 'MD' symbol.

The challenge of how to keep track of devices placed on Europe's borderless yet fiercely sovereign markets is addressed by a combination of mandatory inputs by NBs, EOs, and member states into EUDAMED. Eudamed consists of seven databases (see below) that are working together. Part of Eudamed will be publicly accessible. The European Commission is responsible for Eudamed, but users will all be responsible for their own content. There will be an extensive amount of information collected and transmitted electronically as well as a mandate to use UDI.

Class III and implantable medical device manufacturers must generate a summary of safety and clinical performance (SSCP) in language that can be understood by the intended patient in Article 32. The SSCP will be assessed by the NB who uploads it into EUDAMED. There, it will be publicly accessible. It must be clear in EUDAMED who the EOs are, where they are based, and their relationship with each other in terms of who supplied what to whom. Distributors and importers must work together with the manufacturer or AR regarding traceability of devices. This will limit, if not eradicate, parallel imports into the EU and all these details will be registered.

Note: *Mandatory Unique Device Identification (UDI) is introduced with the intention to facilitate the traceability of devices. Devices will be allocated a device identifier (DI) and production series or batches will be identified with a production identifier (PI). The Basic UDI-DI must also be referenced in the Declaration of Conformity (DoC). Various databases for clinical investigations, product registration, and vigilance are introduced under the aegis of the EU Commission. Member States will have to issue a Single Registration Number to each EUDAMED user. As this is the gateway into EUDAMED, this is expected to be a complex and demanding process, which may take more time than anticipated.*

The regulation attempts to professionalize the implementation of compliance by mandating a Person Responsible for Regulatory Compliance similar to the requirement placed on manufacturers under the Medicinal Products Directive.

Note: *EUDAMED will be part of a system of several databases, closely interacting with each other:*

1. *Economic operators*
2. *Devices*
3. *UDI*
4. *Certificates (issued, suspended, withdrawn etc.)*
5. *Clinical Investigations*
6. *Vigilance (incident reports and Field Safety Corrective Actions, but also Periodic Safety Update Reports)*
7. *Market Surveillance*

Closely linked to Eudamed are the databases with nomenclature for medical devices and for incident reporting. Lastly, the database with Notified Body information, NANDO, will be related to Eudamed although it will remain independent and controlled by the European Commission.

Apart from the general public, EUDAMED will be accessible for EOs, NBs, CAs, and Commission. These stakeholders will also upload their information directly into EUDAMED. They will each have different levels of access to information. For EUDAMED to properly function, access to international medical devices nomenclature will be provided free of charge. It is expected that around the end of December 2018 the nomenclature for devices in Eudamed will be announced. The nomenclature for incidents will be based on the terms proposed by IMDRF.

By far the greatest change brought by the MDR is the metamorphosis of the role of NBs from an industry partner into a police-like extension of the CAs' market surveillance apparatus.

On legal grounds, the formal designation and assessment of NBs is left to member states in practice. However, the power to notify, manage the scope and notification, and prescribe corrective measures is transferred from the CAs to peer-reviews by multi-national Joint Assessment Teams. NBs are monitored to ensure they are competent and ethical.

For Class III implantable devices, as well as Class IIb devices intended to administer and/or remove a medicinal product, the NB will be obliged to send its clinical evaluation assessment report to the relevant expert panel through the EU Commission per Annex IX, Chapter II, Section 5.1. The expert panel may decide to issue an opinion on the application, in which case the panel will do so within 60 days. After that, or after the expert panel has declined providing an opinion, the NB can certify the device. These expert panels (Article 106) will be appointed by the Commission as considered necessary in relevant fields of expertise or specific risks.

Costs related to these expert panels may be covered by fees paid to the Commission by the manufacturer. The size of the manufacturer will be considered when setting the fee.

Under the proposed conditions, a major challenge for most NBs will be to gain and retain highly qualified staff with the education and experience mandated in Annex VII. Both Chapter IV and Annex VII describe the demise of NBs and how to monitor the competence of the remaining ones.

NBs are required to take out liability insurance to cover cases where they may be obliged to withdraw, restrict, or suspend certificates as stated in Annex VII, section 1.4. NBs will also have to make public a list of standard fees for their conformity assessment activities.

NBs will be accredited by the authority responsible for Notified Bodies (which may be the national CA) in the member state where they are based. This authority will do a review of such a request and pass their conclusions on to the Commission, which then transmits the decision to the MDCG. The MDCG will assign joint assessment teams consisting of at least three experts, who will review the application documentation. This joint assessment team, together with the national authority responsible for Notified Bodies, will perform an on-site assessment, including sites in other member states or outside the Union. The process entails strict timelines, but there are no consequences for the authority responsible for Notified Bodies or the MDCG if they do not meet these timelines.

***Note:** As Notified Bodies are required to have similarly competent staff for Technical File/Design Dossier reviews and audits, it is easy to foresee a shortage in the availability of qualified personnel. This may lead to significant delays and higher costs for manufacturers.*

Classification remains essentially the same under the MDR, but it is recommended to do a thorough assessment of all devices and not to rely on current classification schemes. The definitions and basic principles have some minor changes.

There are 22 classification rules in Annex VIII, some of which are new and some have changed. Rule 3 now places substances in contact with cells, tissues or organs before administering in the body into Class III. Rule 4 also applies to invasive devices that come into contact with injured mucous membranes. Rule 6 keeps the reusable surgical instruments in Class I, but at the same time these devices get a similar status as sterile or measuring devices, and NB involvement is required. A new classification, Class Ir, applies to these devices as well.

Additional classification changes under the MDR include the following:

- The MDR considers surgical meshes Class III
- Rule 11 – A new rule for classification of software. Software can fall under any risk class, with Class I now being the exception
- Rule 18 states that non-viable tissue of human or animal cells will be considered Class III
- Rule 19 classifies nano-materials depending on their potential for internal exposure
- Rule 20 places devices intended for inhalation of medicinal substances in risk Classes IIa or IIb
- Rule 21 places devices composed of substances absorbed or dispersed in different classes based on their level of internal exposure
- Rule 22 places active therapeutic devices with an integrated diagnostic function, which provides data on patient management in Class III (e.g., closed loop systems or automated external defibrillators)

The MDCG is expected to provide expeditious judgments of difficult classification cases (Article 51). The choice of conformity assessment route has been simplified by conformity assessment Annexes IX through XI, with many instances for mandatory Quality Management Systems. There is better correlation between risk and data requirements.

The technical documentation elements specified in Annex II are largely based upon the GHTF STED guidance. (The STED document can be found on the IMDRF website.) Annex III describes the technical documentation on post-market surveillance. This consists of the post-market surveillance plan, the post-market performance follow-up plan, and the periodic safety report. Annex IV describes the Declaration of Conformity (DoC).

Class I self-certified medical devices must set up a quality system “in the most effective manner and in a manner that is proportionate to the risk class,” according to Article 10(9). They must then compile the technical documentation according to Annexes II and III and sign the DoC.

Annex IX, Conformity Full Quality Assurance and Assessment of Technical Documentation

This is the equivalent of MDD, Annex II, Section 3.3 Audits, and Section 4, Examination of the design of the product.

Section 3.3 states that NB audits and assessments of quality management systems and post-market surveillance processes should occur at least yearly. Section 3.4 adds that the NB is to perform unannounced inspections of the manufacturer and of the manufacturer's suppliers or subcontractors at least once every five years. The NB will be mandated to test samples from the production or manufacturing process. NBs are also encouraged to analyze samples from the market. Nevertheless, it is unclear who will pay for testing of these samples.

As expected, the roles of clinical evaluation and clinical investigation become far more prominent under the MDR. Inclusion of MEDDEV 2.7/1 and parts of ISO 14155 into the MDR is to be applauded. Informed consent and the protection of incapacitated subjects get special attention.

Note: *New and tighter criteria are introduced for demonstrating equivalence. As a result, more clinical data must be obtained from clinical investigations of the device. Implantable and Class III devices generally require clinical investigations, unless a rationale can be provided for why this should not be the case. Manufacturers of implantable and Class III devices may consult an expert panel on a voluntary basis prior to the clinical evaluation. A manufacturer may rely on clinical data of another device if the new device is a modification of the old device, if the NB has confirmed this is only a modification, and if the manufacturer has full access to the technical documentation of the other device.*

To avoid having to perform clinical investigations on devices that are currently considered compliant and that have been used for years without major incidents, an exception is made for implantable and Class III devices currently placed on the market. These devices must comply with the current requirements for clinical data and with possible future CS. Data concerning clinical investigations needs to be entered into EUDAMED, as well. The electronic system must also be used for PMCF studies. The design, execution, and requirements for documentation of a PMCF study have to meet many requirements applicable to clinical investigations.

Article 83

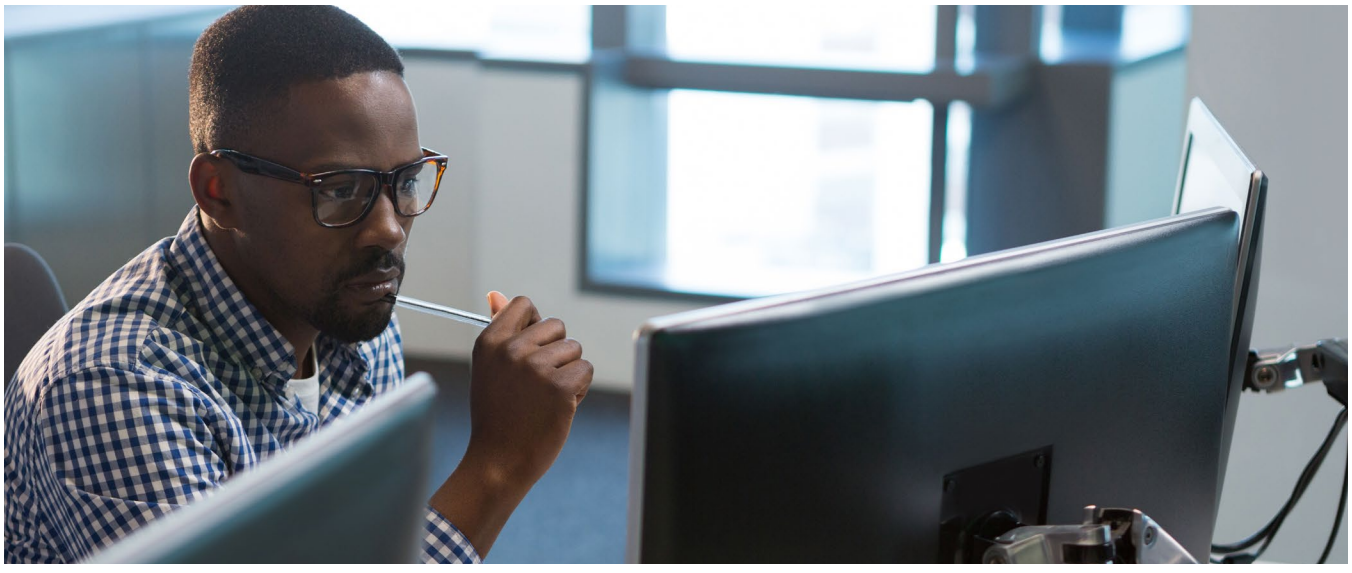
PMS is explicitly intended for gathering and analyzing information with the aim of deciding about preventive and corrective actions. This implies that information must be collected and analyzed about incidents and adverse events, trend reporting, relevant literature, information from users and publicly available information about similar devices.

Also, the manufacturer's Periodic Safety Update Report (PSUR) and Field Safety Corrective Actions (FSCA) are sources of information. The PMS system may result in preventive or corrective actions, changes in the Clinical Evaluation Report (CER), changes in the Periodic Safety Update Report, reports for the NB and/or the CA and alterations in EUDAMED. The Summary of Safety and Clinical Performance, required for implantable and Class III devices and written in language for lay users, may also have to be updated as a result of PMS. PSURs of Class III and implantable devices must be uploaded to EUDAMED for review by the NB and then be available to the CAs together with the comments made by the NB.

Manufacturers are required to report a serious incident or Field Safety Corrective Action (FSCA), to the relevant CAs by using EUDAMED within 15 days. In case of death or unanticipated serious health deterioration, the maximum time allowed is 10 days. In case of a serious public health threat, this timeframe is limited to two days per Article 87.

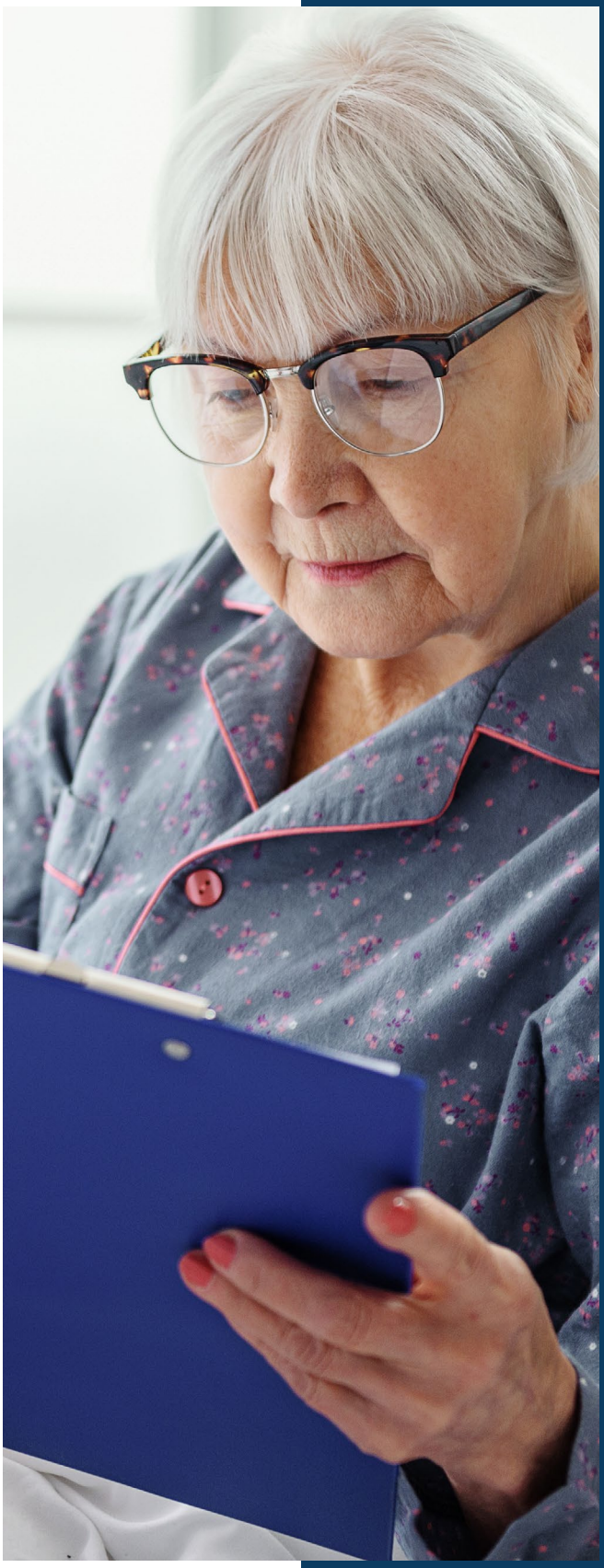
Based on Article 92, the EU database will be used to share these vigilance reports to the following member state where the incident occurred, member state(s) where the FSCA is undertaken, the Member State where the manufacturer or their AR is based, and for all vigilance reports to the NB. It is expected that FSCAs and Field Safety Notices (FSNs) will be made publicly available and this may also apply to reports on serious incidents. It is anticipated that other authorities or international organizations will also have access to this database.

The draft FSN needs to be submitted for review "except in case of urgency (Article 89(8))." In practice, our experience has been that currently all manufacturers treat the release of the FSN as urgent and have not shared the draft for review.



Confidentiality

Article 109 ensures confidentiality of certain information, but patients seeking compensation will likely get access to detailed information about the device through Article 10(14). For non-European manufacturers, their ARs will have to supply this information. Also, Article 1(16) ensures freedom of information for the press as dealt within any individual member state. It is currently not clear how this potential conflict of interest and possible misuse may be resolved. Confidentiality of information provided to any database as part of this regulation is respected as far as this concerns personal data or commercially confidential information, unless disclosure is in the public interest. This disclaimer appears to be in slight conflict with the intention to safeguard confidentiality in order to promote effective implementation of this Regulation, as the results of inspections, investigations, and/or audits may be considered to be of public interest.



Article 103-106

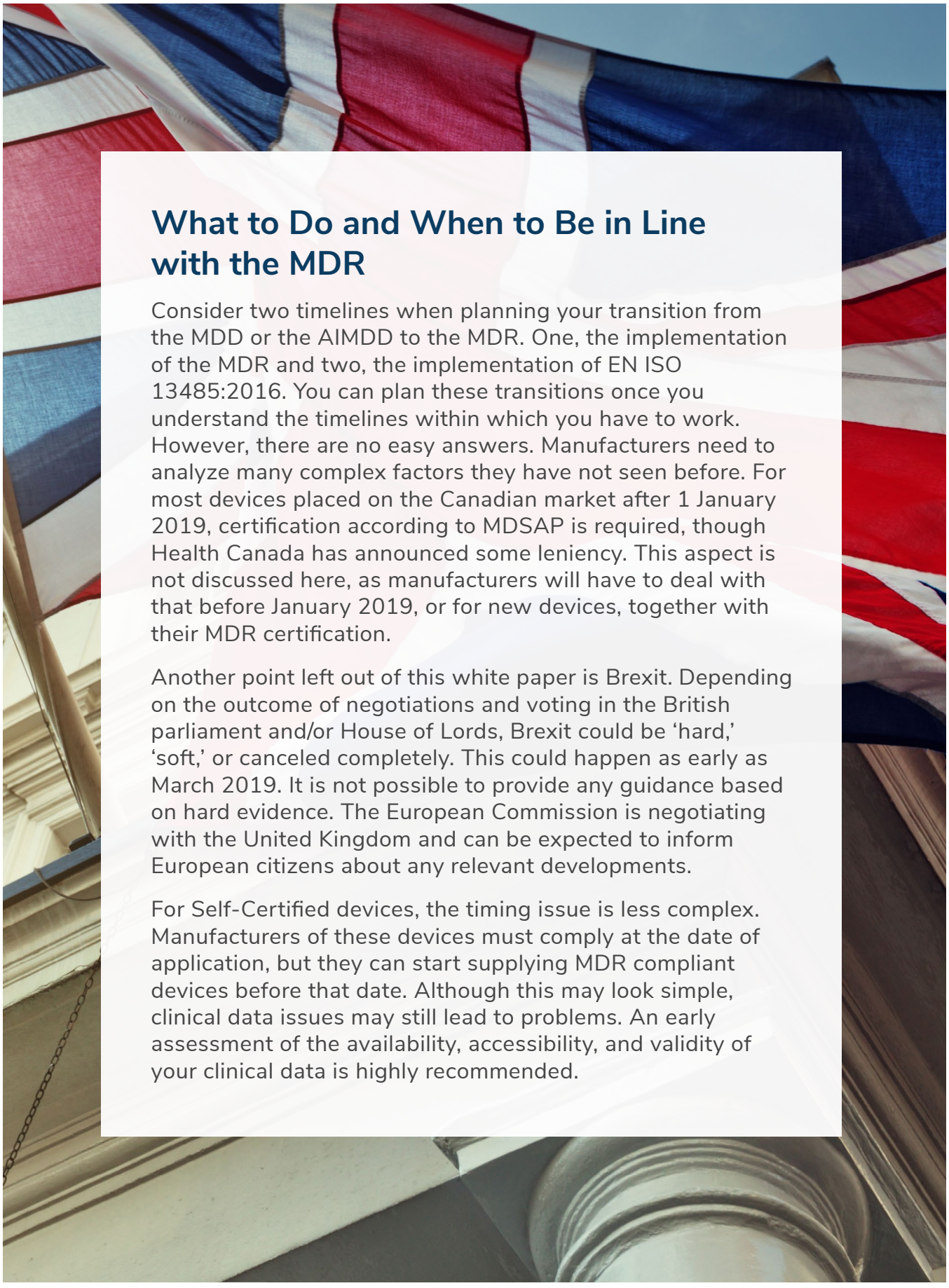
The MDCG seems intended to replace the proliferating member state-only bodies (CMC, COEN, MSOG) and the structures that are trying to coordinate the CAs. Apart from the fact that it has proven impossible to find even a 75% consensus in all but a few MDEG meetings, the difficulty to find truly independent experts - as witnessed by the FDA in its expert panels and the lack of sanctions for exceeding the review periods - does not bode well. In any case, an appeal procedure is sorely missing. The MDCG may be assisted by expert panels and expert laboratories. These experts have to be independent from NBs or manufacturers when providing their scientific opinion. Expert panels must take into account relevant information from stakeholders. The CAMD will provide guidance and harmonization between Member States.

Standards

The role of standards seems to be maintained. Articles 8(1) and 9(2) state that if there are standards and CS, and the manufacturer complies with them, the manufacturer is presumed to be compliant to the relevant aspects of the Regulation. The MDCG will play an important role in developing CS and scientific guidelines. However, it should be noted that this will introduce a system where the MDCG is empowered with significant responsibilities, without the necessary accountability for their actions to anyone. However, Member States do not currently agree on the scope of the harmonization mandate in relation to the MDR. Some Member States only want to see a few horizontal standards, where others would like to see many vertical, device group-related standards.

Penalties

Article 113 defines the need for penalties but not against whom, nor does it define the penalty for member states if they transgress their powers or violate their obligations. This would be a good addition because several steps in placing devices on the market depend on actions done by CAs. If they do not have the resources to perform these processes, the manufacturer may suffer damage. Or worse, patients may not receive the treatment they need.



What to Do and When to Be in Line with the MDR

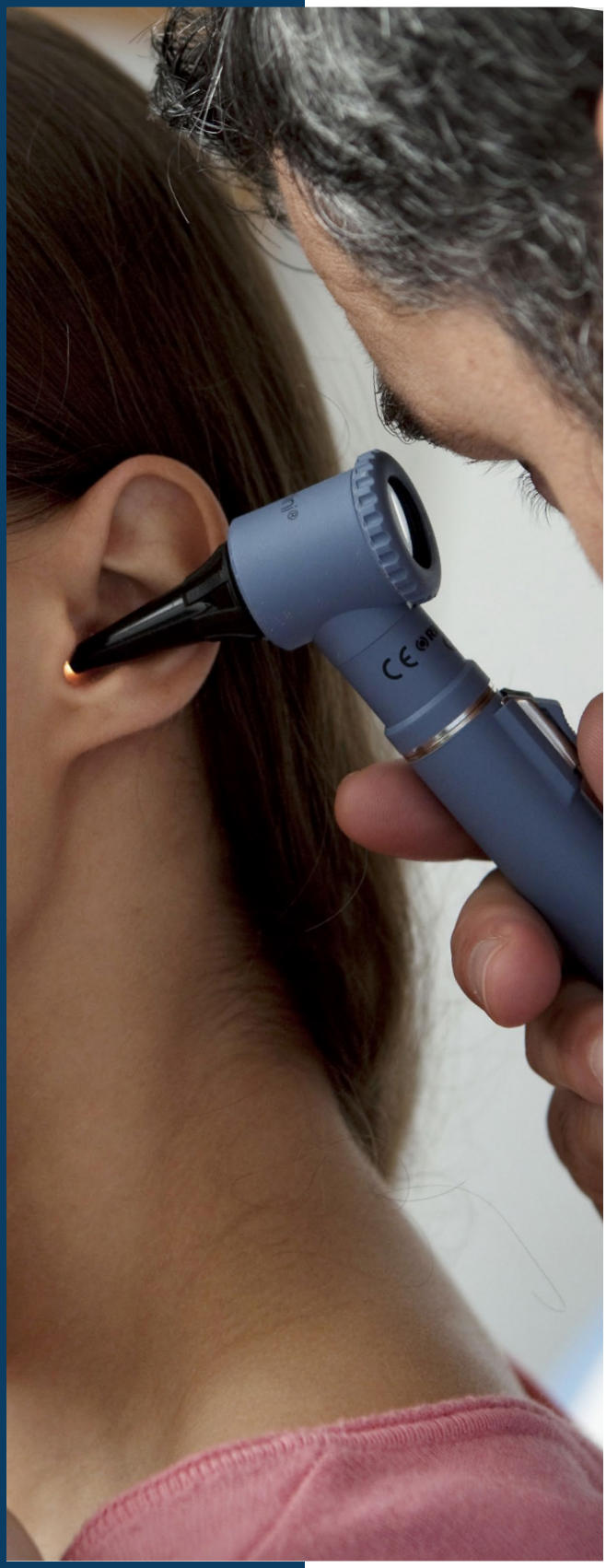
Consider two timelines when planning your transition from the MDD or the AIMDD to the MDR. One, the implementation of the MDR and two, the implementation of EN ISO 13485:2016. You can plan these transitions once you understand the timelines within which you have to work. However, there are no easy answers. Manufacturers need to analyze many complex factors they have not seen before. For most devices placed on the Canadian market after 1 January 2019, certification according to MDSAP is required, though Health Canada has announced some leniency. This aspect is not discussed here, as manufacturers will have to deal with that before January 2019, or for new devices, together with their MDR certification.

Another point left out of this white paper is Brexit. Depending on the outcome of negotiations and voting in the British parliament and/or House of Lords, Brexit could be 'hard,' 'soft,' or canceled completely. This could happen as early as March 2019. It is not possible to provide any guidance based on hard evidence. The European Commission is negotiating with the United Kingdom and can be expected to inform European citizens about any relevant developments.

For Self-Certified devices, the timing issue is less complex. Manufacturers of these devices must comply at the date of application, but they can start supplying MDR compliant devices before that date. Although this may look simple, clinical data issues may still lead to problems. An early assessment of the availability, accessibility, and validity of your clinical data is highly recommended.

Important Dates	
May 2017	• MDR published, the 3 year transition period begins
November 2017	• Notified Bodies can apply for designation • MDCG installed
April 2018	• First Joint Assessment Audits for Notified Body designation performed
January 2019	• MDSAP certification of the QMS for manufacturers of Class II, III, and IV medical devices required for Canada[2]
March 2019	• Transition deadline for ISO 13485:2016 in Europe • The United Kingdom (possibly) leaves the European Union, a transitional period may start (Brexit)
March 2020	• Eudamed goes live (however, there are provisions for delay)
May 2020	• MDR becomes applicable and enforceable : o All Class I, self-certified devices and custom-made devices (excluding Class III implantable) must be compliant to the MDR o Class I reusable surgical instruments, Class III implantable custom-made devices, devices new to MDR scope (including Annex XVI), and devices up-classified from Class I self-certified must be certified by a Notified Body according to the MDR o Combination products of a pharmaceutical and a medical device that are considered medicinal products must comply with the General Safety and Performance Requirements, with notified body involvement if applicable o Clinical investigations must comply with the MDR o UDI must be added to technical documentation o All PMS and PMCF requirements of the MDR apply, unless exempted by article 123
May 2021	• UDI must be placed on the label of Class III devices that are MDR certified
May 2022	• Certificates issued in accordance with Annex 4 of AIMDD and Annex IV of MDD that have not yet expired will become void
May 2023	• UDI must be placed on the label of Class IIa and Class IIb devices that are MDR certified
May 2024	• Other certificates issued under current Directives that have not yet expired will become void
May 2025	• Devices that were CE marked under the MDD or AIMDD may no longer be marketed or put into service in Europe • UDI must be placed on the label of Class I devices

[2] *Health Canada has announced (18-104451-938, April 2018) some accepted delays for MDSAP.*



ISO 13485:2016 - Transition by March 2019

All ISO standards typically have a three-year transition period. This would normally allow manufacturers to update their quality systems as part of the normal maintenance of their certificates and would imply that all manufacturers who elect to demonstrate compliance with the standard must switch to ISO 13485:2016 by 1 March 2019.

However, this transition is slightly different for CE marking. Sections 1 and 2 of the General Safety and Performance Requirements, currently known as the Essential Requirements, require conformity with the generally acknowledged state-of-the-art technology, which would include any harmonized standard used. In November of 2017 the 2016 version of ISO 13485 was published in the *Official Journal of the European Union* (OJEU). This means it is now the harmonized standard and has become the new state of the art. If a manufacturer chooses to certify their QMS to this standard, they must comply with the new version by the March 2019 date. In practice, manufacturers are given some time by NBs. However, certificate renewal will now require updating to the 2016 version.

There is a very small gap in the timeline to have the EN ISO 13485:2016 certification synchronized with the MDR transition in only one step; however, based on the timing for Notified Body designation to the MDR, it is probably best to synchronize the EN ISO 13485:2016 certification with recertification under the MDD/AIMDD.

Clinical Data

If you expect to have sufficient clinical data for the transition, you can consider going for early certification. If it looks like you first need to conduct extensive clinical investigations/post market studies, your transition will take longer. Under the Directives, you can conduct Post-Market Clinical Follow-up (PMCF) studies that could provide you with this vital clinical evidence. In order to decide on your transition strategy, you must analyze your current clinical evidence and how to close any gaps. It is recommended to ask your NB for feedback to your proposal.

General Safety and Performance Requirements

There is a major obstacle for companies aiming for an early switch to the MDR. Annex I of the MDR contains the General Safety and Performance Requirements, which are similar to the Essential Requirements of Annex I of the MDD. Currently there are no harmonized standards or Common Specifications available and there are no timelines as to when they will be published. This makes it difficult to verify compliance with the Requirements. Whatever the manufacturer is planning to do, switching to the MDR has to wait until the harmonized standards and/or Common Specifications are published. Until then the manufacturer can only presume current standards published in the OJEU to the MDD/AIMDD reflect the state of the art.

Notified Body Designation

European medical device market observers anticipate that there will be about 40 NBs that will remain active once the MDR is in place. A few of these entities will operate as large and possibly more expensive broad scope organizations while the rest will have a more specialized focus. TEAM-NB has published a list of members and their intentions. Other NBs may also plan to be designated under the MDR, but that information is currently not available. The scopes for which they applied are also not publicized. In order to plan your transition, you must also make sure you are using an NB that can assess your types of devices. Emergo expects most NBs will remain close to their current scope, although they may have to drop some scope codes due to staff shortages. So, until reliable data is available, a manufacturer should analyze the current scope of the NB, but it may behoove you to explicitly ask for the NB's transition plan.

Designation audits have started in April 2018 and the first NB may be designated in Q1 of 2019. However, it is not certain all NBs will be designated by May 2020. Article 33(11) of the MDR allows NBs to perform their activities only after they have been designated. However, they may decide to perform gap analysis audits and assessments in anticipation of their designation and perform the formal verification once they are designated. Even then, you have to wait for your NB to be designated before your MDR certificates are issued, which may take until close to the end of the transition period.

Notified Bodies may also present an arrangement to use current audit results for extending or renewing current certificates to perform a gap analysis regarding the MDR. Notified bodies designated for the new MDR can keep issuing current MDD certificates until May 2020 when the new MDR applies. However, it is expected that it will be increasingly difficult to have new MDD certificates issued after May 2019 due to NBs being occupied by MDR certification activities. For renewals of certificates, something similar will apply.

Certificate Expiration Date

Devices that are CE Marked under MDD or AIMDD certificates can be placed on the market as long as the certificates are valid, but not after 26 May 2024. Stock in distributors' warehouses or at health institutions can be made available or put into service until five years after the date of application. This allows for these old stocks to be sold. By creating extra stock in the warehouses of independent distributors, it is possible to bridge a situation where no certificate is available. There are two situations where a manufacturer may decide to use this option:

1. The manufacturer plans to introduce a new device but expects a gap between the expiration date of the old certificate and the introduction of the new device
2. When tracking the process of getting certified under the MDR, the firm becomes aware of serious delays that may lead to an interruption in the continuity of care

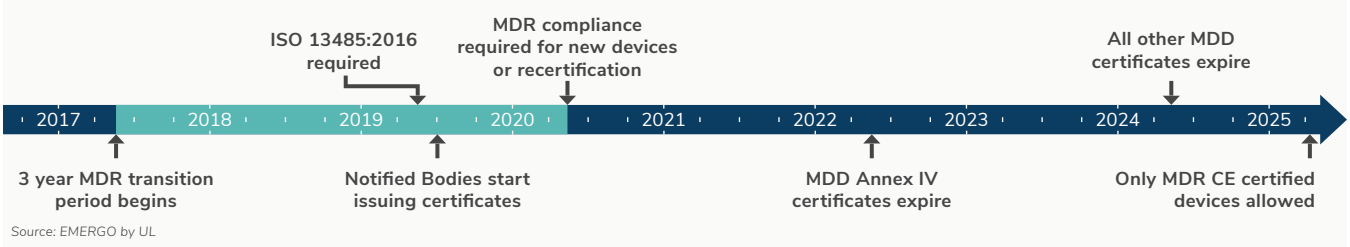
Both options are used to keep current users supplied. The first option is driven by commercial motives while the second pertains to a public health interest. Based on experience with manufacturers that have been confronted with their certificates suddenly become invalid, Emergo expects that as long as there are no public health risks associated with this strategy, CAs appear to accept this bridging solution.

Timing Strategies

Medical device manufacturers can utilize four basic strategies for the transition:

1. Certify under the MDR as soon as possible
2. Remain certified under the MDD or AIMDD as long as possible, possibly until 2024
3. Plan this switch around the date of application
4. Go for a mixed approach with some devices certified early, others very late and the rest somewhere in between

Option 1 – Get MDR Certified as Soon as Possible



A special group of products are current Class I, Self-Certified reusable surgical instruments that require NB intervention under the MDR, and devices that are up-classified from Class I, Self-Certified. MDR certification will be required from the date of application. Their manufacturer will be in the first wave of certificates issued under the MDR. It can be expected that the first real-life experience with MDR certification will therefore be gained in a population of companies with on average less experience with NBs. Any evaluation done on the quality of documentation and quality systems should consider these confounding factors.

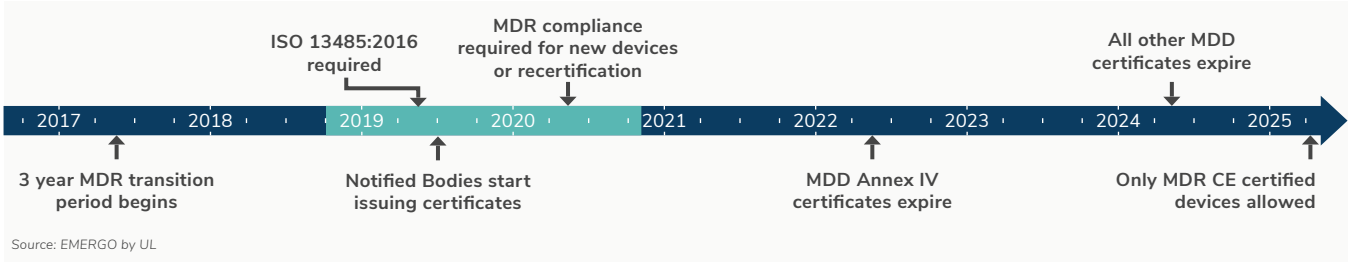
If your NB is able to facilitate either the gap analysis option or a real certification, and you have sufficient clinical evidence, you can go for the as-soon-as-possible option. This option is especially recommended if your device design will soon change significantly or you want to place a new generation of the device on the market. You will know about the continuity of your business early in the transition and, if there is a waiting list at your NB, you will be at the front of the line.

There is still one uncertainty to address: can you stay with your current NB, or do you have to change? You can only know this after your NB has committed itself and you only have certainty once they obtain designation or formally announce they will no longer be active in this field. Most NBs have expressed their interest in being designated in November 2017 or shortly after. None of them disclosed the scope they are aiming for.

Option 1 is required and/or recommended if you:

- Know your device is currently Class I self-certified, but will be NB-certified under the MDR
- Know your product is currently not considered a medical device, but will be an NB-certified device under the MDR
- Have sufficient clinical evidence for your device
- Have CE marking now and expect to make design changes in the next few years
- Are introducing a new device

Option 2 – Get Certified in the 'Second Wave'



Source: EMERGO by UL

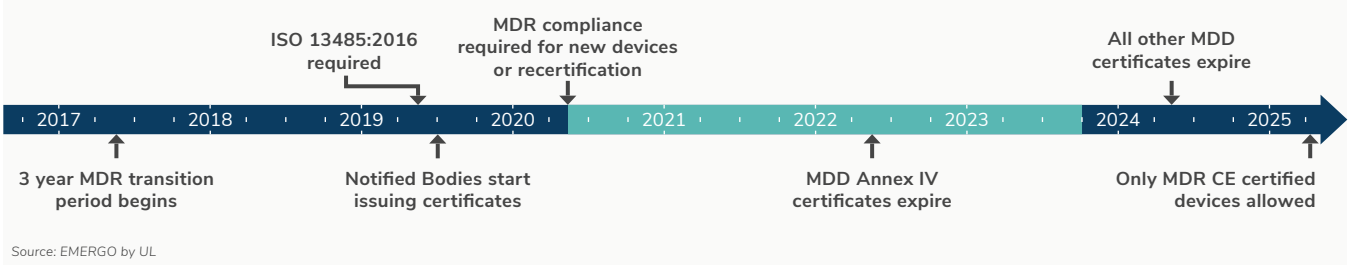
If you plan to introduce new devices between 2020 and 2022 and you expect to have sufficient clinical data, you may want to certify under the MDR around the date of application. This path also applies if it is not possible to extend your certificates for more than two years after the date of application. This option mixes some of the advantages of the previous options with their disadvantages:

1. You will probably know in time which NB is designated for what scope, so you can plan your transition with fewer unknowns. Manufacturers will be recertified for the MDR by a Notified Body that was designated. You will have only one certification procedure to go through, which cuts costs. This will have to happen during a period when NBs are dealing with huge workloads.
2. You may make good use of this time to update your clinical data by performing PMCF studies under the current legislation, but that will only help for identical, or practically identical, devices.
3. You will probably have sufficient time to make the switch, yet you will not join at the end of the line. This option provides a relatively smooth transition and may pose limited risks only to the continuity of your business.

Option 2 is recommended if you:

- Plan to introduce new devices between 2020 and 2022
- Have sufficient clinical evidence
- Follow Annex IV of the MDD or AIMDD
- Expect your Notified Body will remain active in medical devices

Option 3 – Get MDR Certified as Late as Possible



If you do not expect any major design or production changes for your device, it is not necessary to fully update your certificate. In this case you may choose to keep your device under the MDD as long as possible. Your switch to the new requirements will come when Notified Bodies, Competent Authorities, the MDCG, and all other parties have more experience with the new regulations. It will give you a lot of time to generate clinical data for your current devices, although this may not be useful for a new device.

Because you will need certificates that carry your device as far as possible beyond the date of application, you need to plan your next recertification carefully. There are ***five risks*** you should bear in mind:

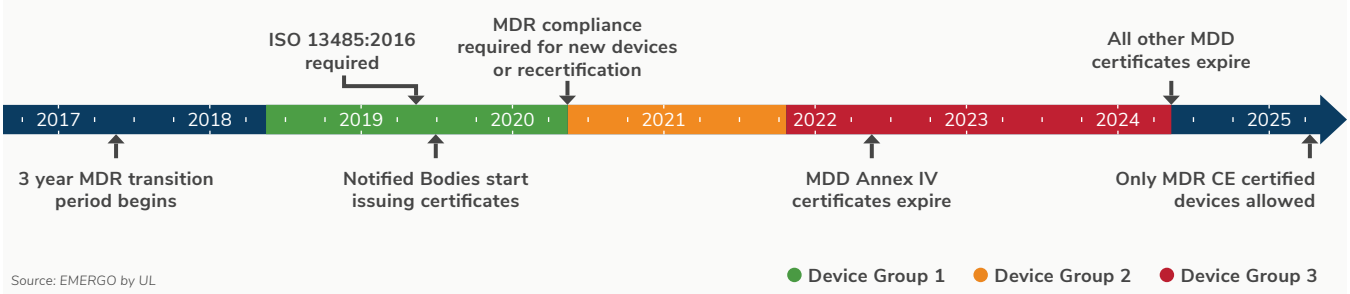
1. Your recertification will have to take place shortly before the date of application, which will be a high workload period for your Notified Body.
2. You will be at the back of the line, and NBs may be flooded with work. You may get stuck with outdated certificates before your new certification.
3. You will know which NBs will be in business, but your current NB may stop its activities around the date of application. In that case your MDD/AIMDD certificates may no longer be supported and therefore become void.
4. This option does not allow for significant changes in the design of the device. This design freeze can become a problem if a competitor introduces an innovation that implies a change in state of the art of medical technology, or worse, if an incident requires a significant preventive or corrective action.

Option 3 is recommended if you:

- Have CE marking now but do NOT expect to make design changes in the next few years
- Need more time to gather clinical data needed for existing CE marked devices
- Don't expect the classification of your device will change
- Are unsure whether you will be changing Notified Bodies

Note: *UDI will have to be added to the technical documentation of all devices from 26 May 2020. However, for MDD/AIMDD certified devices it is not necessary to add the UDI on the label, even where this would be required for MDR certified devices. This label change can therefore be synchronized with the transition to the MDR.*

Option 4 – Take a Mixed Approach

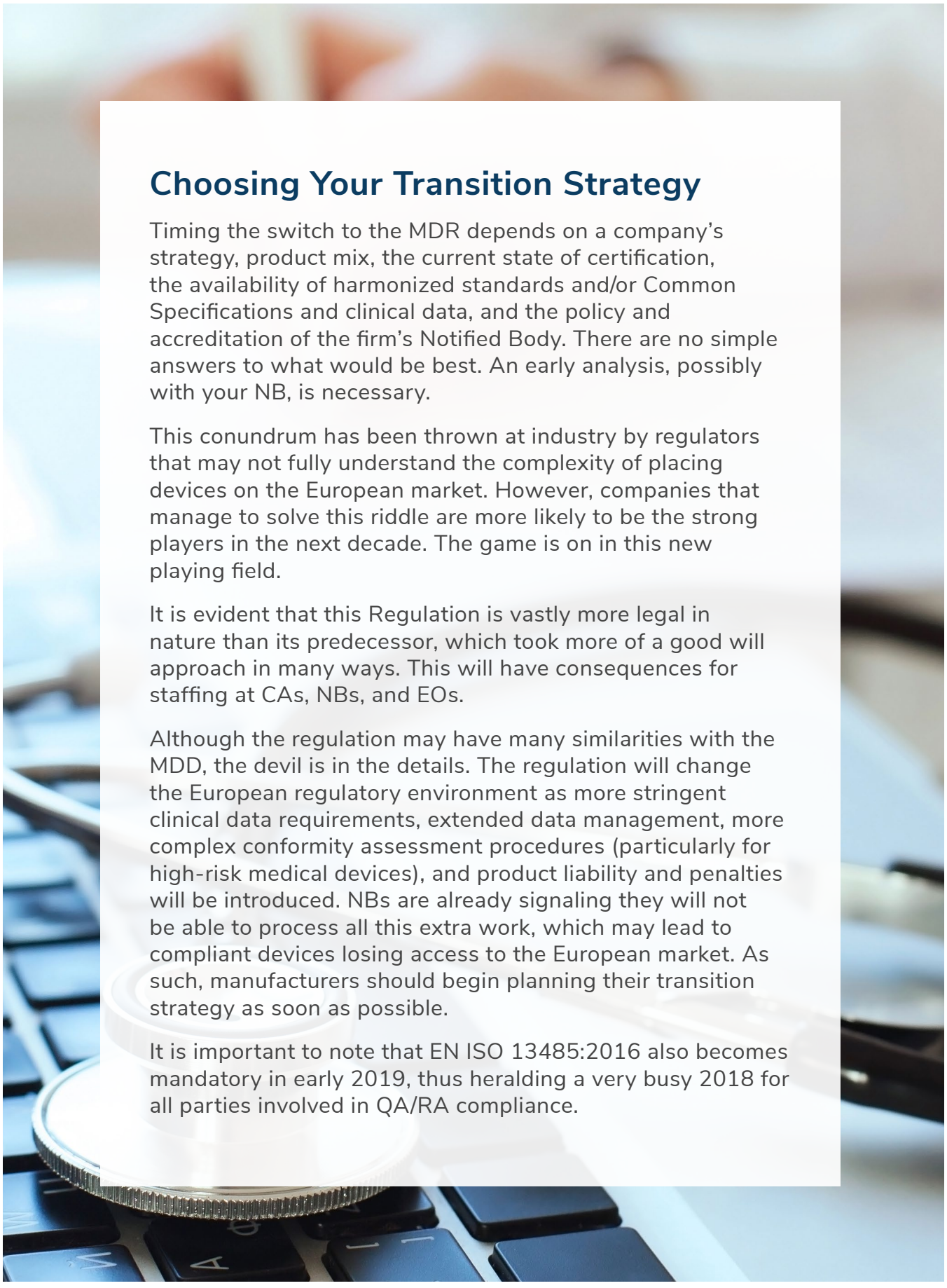


Expect manufacturers with a wide range of devices to take a mixed approach to the MDR transition. They can time the switch for each device or device family separately to account for the current expiration of their certificates, expectations regarding the development of new devices, and the risk they want to take regarding the continuity of their business.

Option 4 is recommended if you:

- Need to transition a wide variety of devices and do not have internal bandwidth to tackle them all at once
- Have a mix of devices, some with excellent clinical evidence, others that need more data
- Are introducing new products in the next few years and working on recertification of existing legacy devices

***Note:** A mixed transition strategy is likely to see MDD Annex II certified devices manufactured in parallel with MDR Annex IX certified devices within the same company. Emergo expects NBs will accept the use of two quality management systems in parallel, one for the MDD, the other for the MDR compliant devices.*



Choosing Your Transition Strategy

Timing the switch to the MDR depends on a company's strategy, product mix, the current state of certification, the availability of harmonized standards and/or Common Specifications and clinical data, and the policy and accreditation of the firm's Notified Body. There are no simple answers to what would be best. An early analysis, possibly with your NB, is necessary.

This conundrum has been thrown at industry by regulators that may not fully understand the complexity of placing devices on the European market. However, companies that manage to solve this riddle are more likely to be the strong players in the next decade. The game is on in this new playing field.

It is evident that this Regulation is vastly more legal in nature than its predecessor, which took more of a good will approach in many ways. This will have consequences for staffing at CAs, NBs, and EOs.

Although the regulation may have many similarities with the MDD, the devil is in the details. The regulation will change the European regulatory environment as more stringent clinical data requirements, extended data management, more complex conformity assessment procedures (particularly for high-risk medical devices), and product liability and penalties will be introduced. NBs are already signaling they will not be able to process all this extra work, which may lead to compliant devices losing access to the European market. As such, manufacturers should begin planning their transition strategy as soon as possible.

It is important to note that EN ISO 13485:2016 also becomes mandatory in early 2019, thus heralding a very busy 2018 for all parties involved in QA/RA compliance.

Learn More

Need help transitioning to the EU MDR? Emergo helps medical device companies with regulatory compliance and market access in Europe and other markets worldwide. Here's how we can help:

- Technical File and CER compilation and review
- European Authorized Representation
- MDR gap audits and transition consulting
- ISO 13485:2016 certification and audits

Learn more about how we can help you with European medical device compliance at EMERGObyUL.com.

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