

# PLANNING FOR THE NEW EUROPEAN REGULATORY ENVIRONMENT

## *Medical devices and in vitro diagnostics*

### ARE YOU READY?

The new EU Medical Device Regulations are finally here and manufacturers now face increased challenges to ensure compliance before 2020 for medical devices and 2022 for in vitro diagnostic devices. IQVIA Medtech Regulatory group can be your partner to advise and support in all aspects of device regulatory and quality compliance.

#### AT A GLANCE

After 5 years of drafting, the new Medical Devices (MD) Regulation 2017/745<sup>1</sup> and the In Vitro Diagnostic Devices (IVD) Regulation 2017/746<sup>2</sup> were both adopted on 5 April 2017 and came into force on 25 May 2017. These regulations will impact all medical devices, including active implantables, "general" medical devices, in vitro diagnostics, drug delivery devices and companion diagnostics, plus a new group of "devices without a medical purpose" (such as cosmetic fillers).

#### NEED TO ACT NOW

With publication of the texts, the extent of the changes that all manufacturers will be required to make in order to affix the CE Mark to their devices under the regulations are now known.

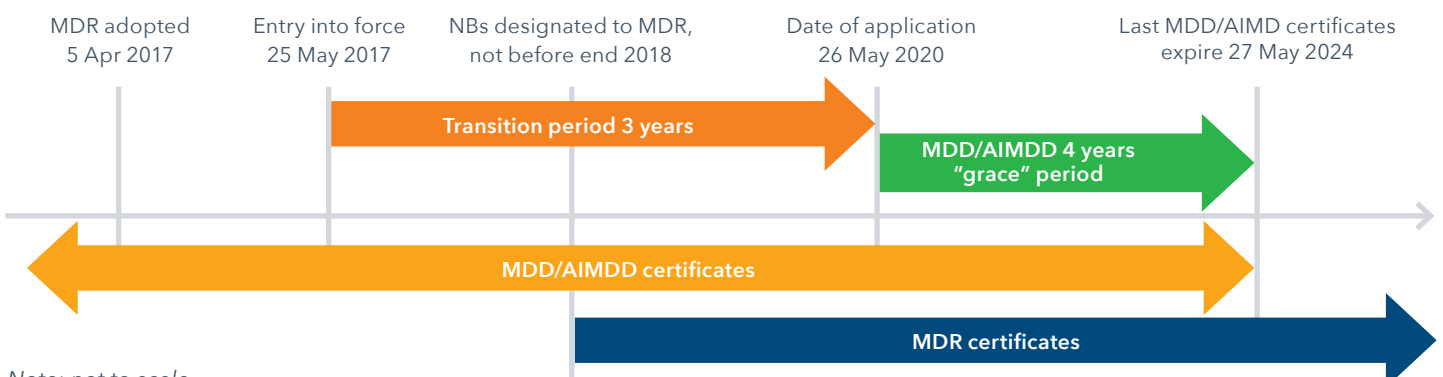
There is no "grandfathering" of products from the current Directives to the new Regulations, so the new regulations will impact every device manufacturer wanting to provide devices to the EU market.

The respective three- and five-year transition periods for medical devices and IVDs will soon pass. Although some of the elements of the new system are not yet in place, manufacturers should already now be taking some key initial steps in preparation.

The timeline (Figure 1) shows the various factors in the transition timeline for the Medical Devices Regulation. A similar transition timeline applies to the IVDR with an extra 2 years to the end of transition. For any device requiring Notified Body (NB) intervention (all devices with the exception of MD Class I and IVD Class A) the

**Figure 1: Transition Timeline to Medical Devices Regulation 2017/745**

MDR Article 120 (transitional provisions)



re-designation process for NBs to grant certification under the regulations will consume 18-24 months of the transition periods. On the other hand, some certificates to the directives granted during the transition period will be valid for 4 years following the date of application of the regulation (May 2020 for MDR and May 2022 for IVDR with some important restrictions).

## SO WHAT'S NEW?

Whilst many of the fundamental principles of the European regulatory system remain in place (CE Marking; classification rules based on risk (newly introduced to the IVDR); conformity assessment for most devices using third-party Notified Bodies; manufacturer self-certification for the lowest classes (Class I MDR and Class A IVDR), the Regulations build on the past 20 years' experience of the directives to create a more robust system to safeguard patient health and safety. See Figure 2 for some of the key new elements of both the MD and IVD Regulation.

**Figure 2: Key elements new to both the MD and IVD Regulations**

### A LARGE AMOUNT OF NEW TEXT

Both Regulations have more than doubled in length.

### PERSON RESPONSIBLE FOR REGULATORY COMPLIANCE

Both the manufacturer and the Authorized Representative have to appoint this person each for their own entity; having formal qualification with 2 years' experience, or no formal qualification with 5 years' experience in a QA/RA role. Responsibilities include batch release, maintaining Technical Documentation and vigilance overview.

### VIGILANCE

Most of the current MEDDEV guidance on vigilance is moved into the Regulation texts, thus becoming compulsory. Current 30-day reporting is reduced to 15 days; central portal for reporting; increased focus on trend reporting.

### UNIQUE DEVICE IDENTIFICATION

EU system intends to align with the U.S., although there will be a separate EU UDI database.

### EUDAMED DATABASE

Several processes will rely on the European database for medical devices e.g. device UDI; manufacturers; ARs; importers; NB certificates; clinical investigations; vigilance; market surveillance. Some elements will be open to the public.

## SOME KEY NEW ADDITIONS TO THE MEDICAL DEVICES REGULATION

The MDR introduces an additional pre-market scrutiny stage for Class III and implantable devices, whereby the Notified Body must consult a new Commission Expert Panel in the conformity assessment process.

For all devices, a renewed focus on clinical evaluation and clinical data will require manufacturers to focus on this area early on to ensure they have sufficient data available. New restrictions on equivalence will mean that, for higher risk devices, reliance on clinical data from an equivalent device will be possible only if there is full access to technical documentation of the equivalent device. Equally manufacturers will need to ensure they have robust post-market clinical follow-up plans in place. For Class III and implantable devices, manufacturers are now required to produce a summary of safety and clinical performance, to be validated by the NB before being uploaded to the Eudamed database, allowing additional transparency.

### IMPLEMENTING AND DELEGATED ACTS

The Regulations are not the full story: additional detail will be written, mainly by the Commission. These Acts will follow soon after entry into force of the Regulations - 14 are expected very soon. There could be 30+ other acts.

### NOTIFIED BODIES

Notified Bodies have to re-apply to be NBs under the Regulations, some may not apply, some may cut down their scope, some may not be successful. We are expecting a continued reduction in Notified Body capacity in both MD and IVD.

### ECONOMIC OPERATORS

Economic operators are defined, including importer, distributor, AR. The importer and distributor must ensure that devices are CE marked, the DoC is in place and that device labelling is compliant. Both must keep a register of complaints and have a role in ensuring that only safe products are on the market. The importer is identified by name/address on the device label, and must ensure that products are entered into the central database. A key new element in the MDR is that, where the manufacturer does not meet his general obligations, the Authorized Representative is legally liable for defective devices on the same basis as the manufacturer.

### NEW PRESCRIBED FORMAT OF TECHNICAL DOCUMENTATION

New prescribed format of technical documentation with additional detail on content to ensure presentation in a clear, organized, readily searchable and unequivocal way. And with the essential requirements being replaced with "safety and performance requirements" all technical files will have to be re-written to reflect this.

## IN VITRO DIAGNOSTICS AND COMPANION DIAGNOSTICS

IVD manufacturers face a particular challenge with the new IVD Regulation, the impact of which is huge. It is estimated that 80-90% of all IVDs will need some level of NB intervention, compared to only around 10-20% under the directive. And for companion diagnostics a large number of assays that were self-declared under the IVD directive are moved to Class C under the IVD Regulation, requiring NB assessment for the first time. The IVD industry will be competing for the same resources as the MD industry. And new clinical evidence requirements for IVDs will demand time, resource and investment to ensure an acceptable level of evidence is available.

The longer five-year transition should not allow IVD manufacturers to be complacent. The comparatively higher hurdles for IVD manufacturers mean much more work, so the process needs to begin now.

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### SUPPLIER SYNC-UP

There is another group that needs to pay special attention to the regulations to avoid being caught out. Virtual manufacturers using contract manufacturers and biopharma companies that rely on partner companies for drug delivery devices and companion diagnostics need to ask the right questions to ensure that these suppliers are also preparing for the MDR and IVDR. The plans for both the product brand owner and the supplier have to be synchronized to ensure product availability is maintained. In cases where different NBs are used at the legal manufacturer and supplier, there may be delays if the NB designation and transition timings to the MDR and IVDR differ.

### IMPACT BEYOND EU AND REGULATORY

We cannot forget the ripple effect of changes to CE Marking documentation on other registrations outside the EU, which may rely on CE Marking. Action needs to

be taken to assess which country registrations may be affected in order to ensure a smooth transition for non-EU registrations also.

The EU regulatory changes are happening in parallel to some key quality changes. Manufacturers have until February 2019 to transition their quality systems (GMP) to the 2016 version of ISO 13485. And the Medical Device Single Audit Program (MDSAP) is going to be the only way to the Canadian market from 1 January 2019.

The cumulative effect of all these regulatory and quality changes on device manufacturers coming together at the same time requires planning and investment in resources.

In order to navigate the complexities of the transition, manufacturers should look to engage with a partner with deep understanding of EU device regulatory. Through extensive experience, IQVIA experts can provide support in areas such as strategic planning, technical documentation updates, clinical evaluation report preparation and provision of interim in-house staff, to help ensure a smooth transition over the next few years.

### HELPING CLIENTS TO COMPLY

Since 1989 the IQVIA MedTech Regulatory team of industry professionals and former FDA officials has helped many clients across all classes and types of device to develop effective regulatory strategies. Our experts can provide your company with a balanced perspective and "business-optimized" solutions gained through experience with:

- Medical device and diagnostic companies, from small start-ups to large global corporations
- Pharmaceutical companies and their contract manufacturers of drug delivery devices and companion diagnostics
- All classes of devices, from patient-use (blood glucose monitors, contact lenses) to high-risk devices for professional use (stents, orthopedic implants, HIV test kits)
- Organizations requiring flexible, experienced interim assignments for on-site support

We are now ready to advise clients on understanding the financial and business impact of the new Regulations, managing the transition from the existing Directives and establishing necessary budgets. Here are some key steps where we can help support; to:

- **Assess the regulation and its impact on your devices**, being aware that there will be more detailed regulations coming along to support key aspects, such as vigilance, devices without a medical purpose, reprocessing, UDI
- **Advise on the transition strategy to move over to the regulation**, given your current status in the audits and certification cycle under the directive
- **Liaise with and interview Notified Bodies to understand their timetable for re-designation under the regulation**. Lack of NB capacity is a major concern to all stakeholders. If you are considering switching NBs you need to make sure of a place in the queue for the new NB.
- **Consider the product portfolio** and work to identify products which can be retired to save on transition costs
- **Identify required clinical evidence** for all products and work on a plan to supplement with new data
- **Author Clinical Evaluation Reports**, following MEDDEV 2.7.1 rev. 4 guidance
- **Revise the format and content** of all technical files
- **Design labelling strategies**, for compliance with the MDR/IVDR, language, translation and UDI requirements
- **Start revising vigilance and post-market surveillance procedures**, especially to take account of the new 15-day vigilance reporting time for most incidents

## THE IQVIA REGULATORY, QUALITY AND COMPLIANCE TEAM

With offices and staff across the U.S. and Europe, and a corporate presence throughout the world, IQVIA offers a major advantage to clients. Our multi-lingual, multidisciplinary group is made up of well-known experts who have come to us from the FDA and other government agencies, as well as some of today's most technologically advanced companies. With a demonstrated track record of successfully delivering regulatory and quality projects, our consultants have helped clients, from small start-ups to multinational companies, develop efficient and effective regulatory and market strategies. During this time, we have conducted hundreds of projects focused on review, development and implementation of regulatory and quality documentation, plus training. Our team members are available to supplement your team's resources with interim in-house regulatory, quality and compliance assignments to your specification.

Our experienced and well-respected staff including former FDA Investigators and Center officials possess an average of over 20 years of experience, providing a unique knowledge and understanding of the Agency's expectations. This is a key differentiator that enables us to help companies prioritize their compliance activities and zero in on areas that will provide the highest benefit at the lowest risk.

Utilizing established and defined methodologies for conducting audits and helping companies to implement appropriate corrective actions, our methodologies have been successfully used for hundreds of audits and quality system improvement projects. We can support manufacturers with Mock Notified Body, ISO 13485:2016 and Medical Device Single Audit Program (MDSAP) audits; and quality systems support including design controls, supplier audits and remediation.

1. <http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32017R0745>

2. <http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32017R0746>

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### CONTACT US

One IMS Drive | Plymouth Meeting, PA 19462 | USA  
regulatory\_quality\_compliance@iqvia.com

[iqvia.com/contactus](http://iqvia.com/contactus)