SQUIRE PATTON BOGGS

EU Medical Device Regulation Overview
Part 2

This publication is the second in a series of three that examines the new European Union (EU) regulations governing Medical Devices and *in vitro* Diagnostic Medical Devices. Focusing on the Medical Devices Regulation (MDR), this publication will examine the MDR and focus on the medical device-specific provisions therein regarding classification, clinical evaluations and data, and conformity assessments. Specifically, this publication will cover:

- Medical device classification, including a general explanation of the classification rules
- Clinical investigation and clinical evaluation requirements for medical devices
- Medical device-specific conformity assessments and an explanation of each route

Classification of Medical Devices

Compared to the Medical Devices Directive, the classification regime for medical devices did not undergo a significant change; most medical devices are not proposed to change classes between the Medical Devices Directive and the MDR, with several notable exceptions:

- Some devices, such as spinal disc replacement implants and other devices that come into contact with the spinal column are up-classified into Class III[1]
- Devices that penetrate the body through mucus membranes are newly included in the definition of "surgically invasive devices"[2]
- Manufacturers of software medical devices, such as medical mobile apps, should pay special attention to Rule 10a, as it has the potential to change a software medical device's classification

It should be noted that the EU does not follow the US Food and Drug Administration's Medical Device Data Systems guidance, so manufacturers with these data systems especially should analyze the device against the new classification rules. Products that seem like medical devices but for a non-medical purpose, such as decorative contact lenses and cosmetic implants, are included in the scope of the MDR and classified according to their mode of action and intended use.[3]

Medical devices will remain classified in four risk-based classes: Class I, Class IIa, Class IIb and Class III. The MDR uses 23 rules to classify devices, taking into account the device's mode of action, inherent risks and the manufacturer's intended use.[4] These rules are divided into four broad device categories:

- Non-Invasive Devices, which are generally in Class I unless one of the rules specify otherwise
- Invasive Devices, including devices that are invasive via a body orifice and those that are surgically invasive
- Active Devices, including Rule 10a specifically for software
- Special Rules for innovative devices and devices that incorporate additional substances[5]

Because a given device's classification drives many of the manufacturer's requirements for clinical evidence and conformity assessments, the initial determination of the device's class remains critical. Manufacturers should analyze current future devices with the new classification rules to determine how their device is affected.

Clinical Evaluations and Investigations

One of the hallmarks of the MDR is the increased emphasis on clinical data and clinical evaluation in the conformity assessment for devices. Manufacturers may already feel pressure from notified bodies to supply more, and more robust, clinical data to support the device's conformity. While a clinical evaluation has always been a requirement, the MDR makes it clear that the clinical evaluation is a "systematic and planned process to continuously generate, collect, analyze and assess the clinical data pertaining to a device in order to verify the safety and performance, including clinical benefits, of the device when used as intended by the manufacturer."[6] In recent years, this has been a major point of contention between competent authorities and notified bodies, with competent authorities challenging notified bodies on the certificates issued based on out-of-date clinical evidence. Clinical evaluations are a part of the technical documentation, and should be updated throughout the life cycle of the device with the clinical data the manufacturer gathers through its post-market clinical follow-up studies and post-market surveillance.[7]

One of the inputs to a clinical evaluation is data gathered from clinical investigations, which the MDR makes mandatory for class III and implantable devices in some circumstances.[8] For example, Article 50 states that a clinical investigation shall be carried out for the purpose of establishing and verifying:

- That the device is designed, manufactured and packaged in a way that it conforms to the definition of a "medical device"
- The clinical benefits of a device are what its manufacturer specifies
- The clinical safety of the device, as well as any side effects, and whether these side effects constitute acceptable risks when weighed against the benefits of the device[9]

[1] MDR Annex VII(4.4).

[2] MDR Annex VII(2.2).

[3] MDR Annex XV.

[4] MDR Article 41(1).

[5] MDR Annex VII.

[6] MDR Article 2(32).

[7] MDR Article 49(4).

[8] MDR Article 49(2a).

[9] MDR Article 50.1.

Article 50 also includes conditions that must be met before a clinical trial may begin. Article 50aa includes informed consent principles that must be followed.

The MDR does give some respite to legacy and high-risk device manufacturers, however. If the device is equivalent to one the manufacturer put on the market prior to the MDR taking effect and the device's clinical evaluation "is sufficient to demonstrate conformity of the modified device with the relevant safety and performance requirements," then an additional clinical investigation is not required.[10] In these cases, notified bodies are instructed to ensure the manufacturer's post-market clinical follow-up plan is "appropriate and includes post market studies to demonstrate the safety and performance of the device."[11] Also, a clinical investigation is not required for a new device that is equivalent to another that was previously placed on the market by another manufacturer, provided that (1) the two manufacturers have an agreement in place that allows the second manufacturer "full access to the technical documentation on an ongoing basis," and (2) the original device's clinical evaluation was performed according to the new regulatory requirements.[12] A manufacturer determines equivalency by examining three characteristics between the two devices:

- Technical characteristics: the design, conditions of use, specifications, properties and similar principles of operation
- Biological characteristics: the same materials or substances are in contact with the same human tissues or bodily fluids for a similar kind and duration
- Clinical characteristics: the devices are used for the same clinical conditions or purposes, have the same kind of user and are used in the same site of the body in the same population, etc.[13]

Changes made to devices already on the market may need to be assessed by a notified body. Notified bodies must have documented procedures for checking the significance of any changes a manufacturer makes to a medical device, and procedures for assessing such change to ensure the device continues to comply with the regulatory requirements.[14]

Conformity Assessments

Another major difference between the MDR and the current Medical Devices Directive is the number of conformity assessments from which the manufacturer may choose. There are only three annexes containing conformity assessments, whereas the Medical Devices Directive included five. Under the MDR, as in the Directives, a notified body assesses the conformity of the medical device and the manufacturer's quality management system (QMS) using the conformity assessment the manufacturer chooses. Notified bodies generally assess the manufacturer's QMS and the device's technical documentation for conformity to the regulatory requirements. The manufacturer's QMS is examined, generally, to ensure that it will lead to the manufacture of conforming product. The technical documentation is how the manufacturer proves the device conforms to the Essential Requirements in Annex 1 of the MDR. The manufacturer's QMS is what must produce the conforming device, and how the device conforms is shown through the technical documentation, so the conformity assessment includes both a review of the QMS and the technical documentation. A notified body should find documents like the clinical evaluation, labeling, and the draft Summary of Safety and Clinical Performance in the technical documentation.

Manufacturers may generally choose between the conformity assessments depending on the structure of the QMS and the company. The main difference between the conformity assessments is the scope of the QMS assessed. It is important that the manufacturer weigh the choice of conformity assessment carefully to determine which is its most efficient option.

Annex VIII: Assessment Based on a Quality Management System and on Assessment of the Technical Documentation

In this assessment, the notified body assesses the manufacturer's QMS and the device's technical documentation during audits as described in sections 3.3 and 4 of Annex VIII. The notified body also assesses the technical documentation of implantable and Class III devices through this conformity assessment. The anticipated "scrutiny" procedures apply to Class III implantable devices and Class IIb active devices intended to administer and/or remove a medicinal product. The additional scrutiny it applied to the manufacturer's clinical evaluation and the notified body's clinical evaluation assessment report, which concludes on various aspects of the clinical evaluation. Notified bodies submit these documents to the European Commission, which then involves an expert panel to weigh in on the evidence. This expert panel has 60 days to render an opinion, or not, which the notified body will take into account when making its certification decision.

The entire QMS is assessed in this conformity assessment, including design and development. This conformity assessment also includes a review and assessment of the technical documentation for the device. Consultation procedures necessary for special medical devices, such as those that contain medicinal substances, are included in Section 6 of Annex 8 as well.

Annexes IX and X: Type Examination and Production Conformity Verification

The second conformity assessment choice is Annexes IX and X together, meaning the notified body uses the procedures in both Annexes IX and X to assess the conformity of the manufacturer's QMS (Annex X) and technical documentation (Annex IX). Annex IX, the type examination, is generally a review of the technical documentation for the device type. Operationally, these reviews function in a similar way to design dossier reviews for Class III devices. Additionally, Annex IX includes references to the specific consultation procedures outlined in Annex VIII(6) and VIII(5.3) for Class III, implantable devices and other special devices.

In terms of the QMS assessment, Annex X has an additional two options for manufacturers: Part A, Production Quality Assurance, and Part B, Product Verification. Annex X Part A is similar to Annex V of the Medical Devices Directive, in that it is a review of the manufacturer's QMS for manufacturing and final inspection of the devices. Annex X Part B is similar to Annex IV in the Medical Devices Directive, in that it requires the manufacturer examine each manufactured device to confirm its conformity with the technical documentation. While a complete QMS is not needed for Annex X Part B, the manufacturer must have a post-market surveillance system in place.

[10] *Id. at 49.2a.*

[11] *Id. at 49.2a.*

[12] *Id. at 49.2aa.*

[13] MDR Annex XIII, Part A(4a).

[14] MDR Annex V, Part 4(4.10).

Our lawyers have significant expertise advising clients on EU medical device regulatory issues. For more information about these regulations, or for help, contact your principal lawyer or any of the lawyers listed in this alert.

Contacts

Aline Doussin
T +44 207 655 1146
E aline.doussin@squirepb.com

Maren Ebner
T +49 69 1739 2448
E maren.ebner@squirepb.com

Joachim Heine
T +49 69 1739 2430
E joachim.heine@squirepb.com

Colleen Hermann
T +1 214 758 3402
E colleen.hermann@squirepb.com

Adrian Spooner
T +44 207 655 1067
E adrian.spooner@squirepb.com

Sarah Stec
T +1 202 457 6304
E sarah.stec@squirepb.com

John Wyand
T +1 202 626 6676
E john.wyand@squirepb.com