AFDO - 2017
2017/745 - Medical Device Regulation (MDR)

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Overview of the MDR

Changes in Classification

Changes in QMS

Changes in Clinical Requirements

Changes in Reporting
What is happening in Europe?

- Medical Device Regulation
- In-Vitro Device Regulation
- MEDDEV 2.7/1 Rev. 4
- ISO 13485:2016
- Joint Assessments
- Notified bodies preparation
Contents

1 Legislative acts

REGULATIONS


What is included?

90/385 AIMD Directive

93/42 MD Directive

98/79 IVD Directive

17/745 MD Regulation

17/746 IVD Regulation

May 2017
Important Changes and Improvements

- **Stricter pre-market control** of high-risk devices with the involvement of a pool of experts at EU level
- **Reinforcement of** the criteria for designation and processes for **oversight of notified bodies**
- **Inclusion of certain aesthetic products** which present the same characteristics and risk profile as analogous medical devices
- **Introduction of a** new risk classification **system** for diagnostic medical devices based on international guidance

- **EUDAMED - EU database** on medical devices and a device traceability system
- **EU-wide requirement for an 'implant card'** to be provided to patients
- **Reinforcement of the rules on clinical data**, including an EU-wide coordinated procedure for the authorisation
- **Reinforced requirement for manufacturers to collect data** about the real-life use of their devices
MDR – Transition – Article 120

Grace period – “place on the market”
No change! / Follow PMCF of MDR

2017 May 26
Entry Into Force (EIF)
(2017 May 5 + 20)

2020 May 26
Date of Application (DOA)

2022 May 27
2 years after DOA
AIMD / Class III

2024 May 27
4 years after DOA

MDR

MDD

AIMD

NB

MDSAP
## Overview of Structure: Chapters

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## Overview of Structure: Chapters

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Overview

1. Overview of the MDR
2. Changes in Classification
3. Changes in QMS
4. Changes in Clinical Requirements
5. Changes in Reporting
### Classification

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- More rules, some existing rules reworded
- Changes in the classification rules of medical devices might lead to change in classification for particular medical devices.
- Manufacturers shall check if the applied classification rule is still right
## Classification

### MDR Classification
- **Class I**
  - sterile
  - w/ measuring function
  - **reusable surgical instruments**
- **Class IIa**
- **Class IIb**
- **Class III**

### Additional / Specific requirements
- implantable **class IIb**
- Medicinal substance
- Medicinal substance derived from human blood/plasma
- Introduced thru body orifice
- Absorbed thru skin
- Tissues or cells:
  - Animal origin
  - Derivates of human origin

### Scrutiny procedure after certification
- implantable **class III**
- active devices delivering medicinal products
Classification

‘Reusable surgical instrument’ means an instrument intended for surgical use in cutting, drilling, sawing, scratching, scraping, clamping, retracting, clipping or similar procedures, without a connection to an active device and which is intended by the manufacturer to be reused after appropriate procedures such as cleaning, disinfection and sterilization have been carried out.

Article 7
Reusable surgical instruments, involvement of the notified body is limited:
“... to the aspects relating to the reuse of the device, in particular cleaning, disinfection, sterilization, maintenance and functional testing and the related instructions for use.”
Rule 8 – Implantable devices
- Total and partial joint replacements are class III
  with the exception of ancillary components such as screws, wedges, plates and instruments. (IIb implantable new category)

- Spinal disc replacement implants and implantable devices that come into contact with the spinal column are class III
  with the exception of components such as screws, wedges, plates and instruments. (IIb implantable new category)
Rule 11 - Software with diagnostic or therapeutic purpose

Class Ila
Except if such a decision may cause
Death or an irreversible deterioration of health

Class III
Serious deterioration of health or surgical intervention

Class Iib
for monitoring physiological processes

Class Ila
Unless immediate danger to the patient

Class Iib
Rule 19 – Nanomaterials

All devices incorporating or consisting of nanomaterial are:

– Class III if they present a high or medium potential for internal exposure.

– Class IIb if they present a low potential for internal exposure.

– Class IIa if they present a negligible potential for internal exposure.
Rule 20 – Inhalation devices

Devices for inhalation of medicinal products:
- are Class IIa;
- are Class IIb in case impact on the efficacy and safety of the administered medicinal product / intended for treating life-threatening condition;

Rule 21 – Absorbable substances

Substances introduced into the human body or applied to the skin;
- are class III if introduced through body orifice;
- are class III if absorbed in the stomach or lower gastrointestinal;
- are class IIa if applied to the skin / nasal or oral cavity;
- are class IIb in all other cases;
Rule 22 – “Closed loop” systems

Therapeutic devices with an integrated or incorporated diagnostic function which significantly determines the patient management by the device, such as closed loop systems or automated external defibrillators, class III
## Overview

1. Overview of the MDR
2. Changes in Classification
3. Changes in QMS
4. Changes in Clinical Requirements
5. Changes in Reporting
Changes in QMS - Obligations

Article 10 – General obligations of manufacturers

Follow EN ISO 13485:2016 (13485:2016)

Article 13 / 14 General obligations of importers / distributors

Verification of product registration
Keeping register of complaints
Copy of Declaration of Conformity
Changes in QMS - Obligations

**Article 15 - Person responsible for regulatory compliance**

**Responsibilities**
- Conformity of the device is appropriately checked
- TD / DoC up-to-date
- post-market surveillance
- vigilance reporting

**Qualification**
- Minimum university degree
- Four years of experience
- Special rule for micro and small companies

**Article 61 – Clinical evaluation**
Shall be updated throughout the life cycle of the device concerned with clinical data obtained from the implementation of the manufacturer's PMCF plan
Changes in QMS – Technical Documentation

OEM – PLM (Recommendation 2013/473/EU)
Notified bodies should note that manufacturers:

a) have to fulfil their obligations themselves regardless of any partial or total outsourcing of the production via subcontractors or suppliers;

b) do not fulfil their obligation to have at their disposal the full technical documentation and/or of a quality system by referring to the technical documentation of a subcontractor or supplier and/or to their quality system;
Changes in QMS – New processes

Article 27 – UDI – Unique Device Identification
Annex VI

**UDI-DI** – device identifier, specific to a manufacturer and a device
**UDI-PI** – specific to the unit produced

![Barcode Image]
Changes in QMS – New processes

Article 33 - EUDAMED

Article 29(4) for registration of devices;
Article 28 for the UDI-database;
Article 30 on registration of economic operators;
Article 57 on notified bodies and on certificates;
Article 73 on clinical investigations;
Article 92 on vigilance and post-market surveillance;
Article 100 on market surveillance;
Conformance Assessment Procedures

Class III, IIb implantable

Annex I General Safety and Performance Requirements
Annex II TECHNICAL DOCUMENTATION
Annex III Technical Documentation on Post Market Surveillance

Annex IX Part I: Production Quality Assurance

Annex IX Section 4: Assessment of TD (every)

Annex X
... TYPE EXAMINATION

Annex XI Part A: Product Quality Assurance

Annex XI Part B: Product Verification

EU EXPERT PANEL

Declaration of Conformity → CE0123
Conformity Assessment Procedures

Annex IX, Chapter II, Section 5.1 (Scrutiny)
Class III implantable
Class IIb active devices intended to add or remove a medicinal substance

Notified Body Review

21 days

Notified Body Review

39 days

Notified Body Review

• Manufacturer’s Clinical Evaluation
• NB Clinical Evaluation Assessment Report
• PMCF Plan
• IFU
• Summary of Safety and Performance

EU Commission Expert Panel

• Benefit: Risk Determination
• Consistency with indications
• PMCF Plan

No ‘scientific opinion’

• Restrict indications
• Limit duration of certificate
• Undertake specific PMCF studies
• Adapt IFU or Summary of Safety and Clinical Performance
• Impose other restrictions
• Duly justify if advice not followed

Complete Conformity Assessment

Notified Body Certificate

Notified Body Certificate

Notified Body Certificate

Annex IX, Chapter II, Section 5.1 (Scrutiny)
Class III implantable
Class IIb active devices intended to add or remove a medicinal substance
Conformity Assessment Procedures

MDR Article 52

Class IIb

Annex I General Safety and Performance Requirements
Annex II TECHNICAL DOCUMENTATION
Annex III Technical Documentation on Post Market Surveillance

Annex IX  PART Chapter I: Production Quality Assurance

Annex IX  Section 4: Assessment of TD (sampling)

Annex XI  PART A: Product Quality Assurance

Annex XI  PART B: Product Verification

Certificate

Certificate

Certificate

Declaration of Conformity → CE0123

CERTIFICATION

Annex X ... TYPE EXAMINATION

Sampling

Generic device group

TÜV SÜD
Conformity Assessment Procedures

MDR Article 52

Class IIa

Annex I General Safety and Performance Requirements
Annex II TECHNICAL DOCUMENTATION
Annex III Technical Documentation on Post Market Surveillance

Annex IX PART Chapter I: Production Quality Assurance

Annex IX PART Chapter II: Production Quality Assurance

Annex IX Section 4: Assessment of TD (sampling)

Annex XI PART A: Product Quality Assurance

Annex XI PART B: Product Verification

Annex XI Section 10: Assessment of TD (sampling)

Annex XI Section 18: Assessment of TD (sampling)

Declaration of Conformity → CE0123

Certificate

Certificate

Certificate

sampling
device category
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Clinical requirements

June 29, 2016 – Publication of the new Revision MEDDEV 2.7.1 Rev. 4

May 5, 2017 – Publication of the official MDR

June 2017 – Publication of the new Revision MEDDEV 2.7.1 Rev. 5 ???
Clinical requirements – MED DEV 2.7.1 rev4

Using Your Notified Body to Accelerate Speed to Market

September 22, 2015

Documentation requirements including plans/protocols for appraisal, methods, clinical investigation, PMCF studies, registries and for related reports.

Examples:
- Detailed information for sources of literature (MEDLINE, EMBASE, CENTRAL, ICTRP and clinicaltrials.gov)
- Literature research on device in question/equivalent device and on State of the art
- Detailed principals of clinical evaluation
- Reference to relevant Directives in more details and better structure
- GAP analysis on compliance of clinical data generated outside of EU
- Points for sufficient clinical evidence intended purpose, clinical performance and benefits, risk mitigation/avoidance, usability, target population
- Requirements for updating CER
- Need and concept of PMCF studies
- Risk/benefit profile
- Scope of clinical evaluation before and after CE marking
- State of the Art Current knowledge concept
- Scientific validity
- Relevance of data
- Weighting criteria for data
- Analysis to demonstrate the compliance to Essential Requirements
- Release criteria for a CER
- Structure and content of CER
- Equivalence (clinical, technical, biological)
- Considerations for a clinical investigation and state of the art, compare to alternative methods
- Role of NB
Clinical, technical and biological characteristics shall be taken into consideration for the demonstration of equivalence.

For assuming equivalence:

- only be based on a single device
- all three characteristics (clinical, technical, biological)
- no clinically significant difference in the performance and safety of the device
- the differences between the device under evaluation and the device presumed to be equivalent need to be identified, fully disclosed, and evaluated
- manufactured via a special treatment (e.g. a surface modification, a process that modifies material characteristics)
- if measurements are possible, clinically relevant specifications and properties should be measured both in the device under evaluation and the device presumed to be equivalent
Clinical requirements – MED DEV 2.7.1 rev4

Clinical

- same clinical condition
- same intended purpose
- same site in the body
- in a similar population
- have no clinically significant difference
Clinical requirements – MED DEV 2.7.1 rev4

- Be of similar design
- Used under the same conditions of use
- Have similar specifications and properties
- Use similar deployment methods (if relevant)
- Have similar principles of operation and critical performance requirements
Biological

Use the same materials or substances in contact with the same human tissues or body fluids.

Exceptions can be foreseen for devices in contact with intact skin and minor components of devices.

In these cases risk analysis results may allow the use of similar materials taking into account the role and nature of the similar material.
The notified body should challenge the ability of the manufacturer to access information that are relevant to the demonstration of equivalence. Demonstration of equivalence might be difficult or impossible in case of limited access to the technical documentation of the devices.
Typically the clinical evaluation is updated:

- when the manufacturer receives new information from post-market surveillance that has the potential to change the current evaluation;
- if no such information is received, at least
  - annually if the device carries significant risks and/or is not yet well established;
  - every 2 to 5 years if the device is not expected to carry significant risks and is well established;
- Justification
To ensure a high level of safety and performance, demonstration of compliance with the general safety and performance requirements should be based on clinical data that, for class III medical devices and implantable medical devices should, as a general rule, be sourced from clinical investigations to be carried out under the responsibility of a sponsor who can be the manufacturer or another legal or natural person taking responsibility for the clinical investigation requirements.
Clinical requirements - MDR

Article 61 / 4

In the case of implantable devices and devices falling within class III, clinical investigations shall be performed, except if:

• the device has been designed by modifications of a device already marketed by the same manufacturer
• the modified device has been demonstrated by the manufacturer to be equivalent to the marketed device
• the clinical evaluation of the marketed device is sufficient to demonstrate conformity of the modified device with the relevant safety and performance requirements.
Article 61 / 5 - a manufacturer of a device demonstrated to be equivalent to an already marketed device not manufactured by him, may also rely on paragraph 4 in order not to perform a clinical investigation provided that the following conditions are fulfilled in addition to what is required in that paragraph:

- the two manufacturers have a contract in place that explicitly allows the manufacturer of the second device full access to the technical documentation on an ongoing basis
- the original clinical evaluation has been performed in compliance with the requirements of this Regulation,
- the manufacturer of the second device provides clear evidence thereof to the notified body.
Article 61 / 6
The requirement to perform clinical investigations pursuant to paragraph 4 shall not apply to implantable devices and devices falling into class III:

- which have been lawfully placed on the market or put into service in accordance with Directive 90/385/EEC or Directive 93/42/EEC and for which the clinical evaluation
- is based on sufficient clinical data
- is in compliance with the relevant product-specific common specification for the clinical evaluation of that kind of device, where such a common specification is available
Article 61 / 6 - The requirement to perform clinical investigations pursuant to paragraph 2a shall not apply to implantable devices and devices falling into class III:

- that are sutures, staples, dental fillings, dental braces, tooth crowns, screws, wedges, plates, wires, pins, clips or connectors for which the clinical evaluation is based on sufficient clinical data and is in compliance with the relevant product-specific common specification, where such a common specification is available.
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Summary of Safety and Clinical Performance (SSCP) is for the USER and shall be:

- **Written by the manufacturer for class III and implantable devices** other than custom-made or investigational devices.
- **Written in a way that is clear to the intended user** and, if relevant, **to the patient**.
- **Updated annually with data from PMCFR** (if indicated) see Art. 83.3.
- **Part of the documentation to be submitted to the notified body involved in the conformity assessment**.
- **Validated by NB and final version of SSCP uploaded to EUDAMED**.
- **Information where the SSCP can be found** must be provided on the label of a device.
Periodic Safety Update Report

Per device and where relevant per category or group of devices, the manufacturer shall prepare a **PSUR** summarizing the results and conclusions of PMCRF together with a rationale and description of any preventive and corrective actions taken.

Throughout the lifetime of the device this report shall set out:

- The conclusion on the **benefit risk determination**;
- The main findings of the **Post Market Clinical Follow-up Report (PMCFR)**;
- The volume of sales of devices estimate of the **population** that use the device and, where practicable, the usage frequency.

**Updated**
- Class III and IIb - Annually;
- Class IIa - Every 2 year;

**Reviewed by NB**
- Class III and Implantable - annually off site
- Other devices – sampled during on site audit
Reporting

CER: Clinical Evaluation Report
PMS: Post Market Surveillance Plan
PSUR: Periodic Safety Update Report
SSCP: Summary of Safety and Clinical Performance
PMCFR: Post-Market Clinical Follow-Up Evaluation

- CER: Prepare by considering the post-market experience
- PSUR: Start after approval
- SSCP: Summarise the technical documentation

PMCFR • Annual for Class III and Implants

- t= 0Y (The conclusion on the risk benefit determination)
- t= 1Y (The summary of the clinical evaluation)
- NOW START AGAIN

All
All
Class IIa, IIb and III
Class III and Impl
Everybody is impacted by this!

No Grandfathering!
Take away

"BY FAILING TO PREPARE, YOU ARE PREPARING TO FAIL."

- Benjamin Franklin

If you start the preparation today
IT IS ALREADY LATE!

Consider pre-certification services by your NB!

Clinical audit
Mock evaluation of TD / DD
Mock MDR audit
Questions, Comments?

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Global website: www.tuv-sud-america.com/medical
Stay informed and updated with our Healthcare & Medical Device newsletter: www.tuv-sud.com/essentials