Medical Device Regulation:
Overview and Implementation

EDQM
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Paul Piscoi
European Commission, DG SANTE, Unit B6

Revision of the EU Medical Devices Legislation

Directive 90/385/EEC on active implantable medical devices
Directive 93/42/EEC on medical devices

Regulation on medical devices – Regulation (EU) 2017/745

Directive 98/79/EC on *in vitro* diagnostic medical devices

Regulation on *in vitro* diagnostic medical devices – Regulation (EU) 2017/746

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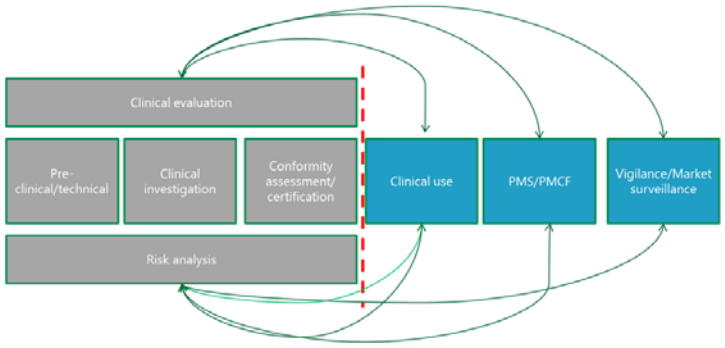
Life cycle approach



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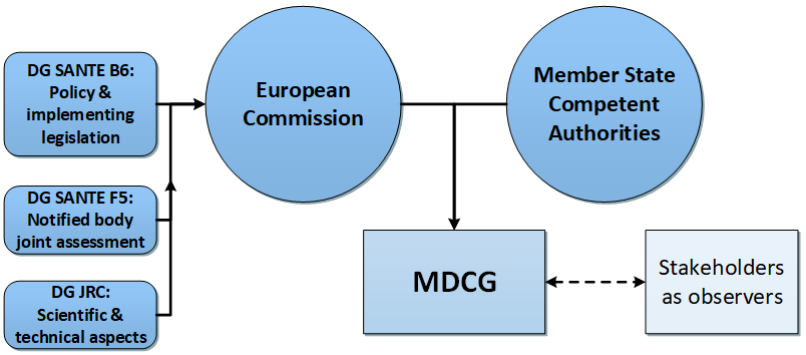
The European governance map for medical devices



MDCG = Medical Device Coordination Group

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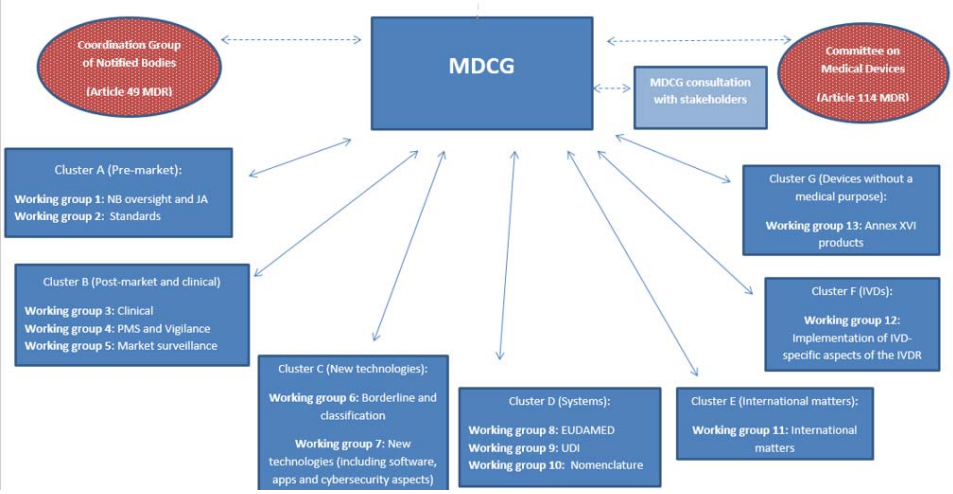
MDCG Working Groups



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CLASSIFICATION OF BLOOD BAGS

Classification rules - MDD

- The current Directive 93/42/EEC classification rules state under Rule 18 that:

"By derogation from other rules, blood bags are in Class IIb."

- Rule 13 MDD states:

*All devices incorporating, as an integral part, a substance which, if used separately, can be considered to be a medicinal product, as defined in Article 1 of Directive 2001/83/EC, **and which is liable to act on the human body** with action ancillary to that of the devices, are in Class III.*

Classification guidance - MDD

- The current MEDDEV guidance on classification under MDD states under Rule 18:

"Blood bags (including those containing or coated with an anticoagulant).

Where blood bags have a function greater than for storing purposes and include systems for preservation other than anti-coagulants then other rules (e.g. rule 13) may apply."

Classification rules - MDR

- Under the MDR, blood bags are listed under Rule 2, which states:

"[…] blood bags are classified as class IIb.

[…]

- Rule 14 states:

All devices incorporating, as an integral part, a substance which, if used separately, can be considered to be a medicinal product, as defined in point 2 of Article 1 of Directive 2001/83/EC, including a medicinal product derived from human blood or human plasma, as defined in point 10 of Article 1 of that Directive, and that has an action ancillary to that of the devices, are classified as class III.

Classification rules - MDR

- Under the MDR, the wording 'liable to act on the human body' has been removed from the text of Rule 14 (equivalent Rule 13 under MDD).
- Therefore medical devices which contain an ancillary medicinal substance will fall under rule 14.
- As a consequence there is no longer a requirement for the manufacturer to determine whether the ancillary medicinal substance is liable to act on the body.

CLINICAL EVALUATION

Clinical evaluation – Art 61

Confirmation of conformity with relevant general safety and performance requirements[…] shall be based on clinical data providing sufficient clinical evidence […].

The manufacturer shall specify and justify the **level of clinical evidence** […]. That level of clinical evidence shall be appropriate in view of the characteristics of the device and its intended purpose.

Clinical evaluation – Art 61

4. In the case of implantable devices and class III devices, 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[…], and

— the clinical evaluation of the marketed device is sufficient to demonstrate conformity of the modified device with the relevant safety and performance requirements.

In this case, the notified body shall check that the PMCF (Post Market Clinical Follow-up) plan is appropriate and includes post market studies to demonstrate the safety and performance of the device.

Clinical evaluation – Art 61

6. The requirement to perform clinical investigations pursuant to paragraph 4 shall not apply to implantable devices and class III devices:

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**, and

— is in compliance with the relevant product-specific CS for the clinical evaluation of that kind of device, where such a CS is available;

Clinical evaluation – definitions

(48) 'clinical data' means information concerning safety or performance that is generated from the use of a device and is sourced from the following:

— clinical investigation(s) of the device concerned,

— clinical investigation(s) or other studies reported in scientific literature, of a device for which equivalence to the device in question can be demonstrated,

— reports published in peer reviewed scientific literature on other clinical experience of either the device in question or a device for which equivalence to the device in question can be demonstrated,

— clinically relevant information coming from post-market surveillance, in particular the post-market clinical follow-up;

Relevant guidance - equivalence

MDCG 2020-5 Clinical Evaluation - Equivalence

https://ec.europa.eu/health/sites/health/files/md_sector/docs/md_mdcg_2020_5_guidance_clinical_evaluation_equivalence_en.pdf

Relevant guidance – sufficient clinical evidence

MDCG 2020-6 Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC
https://ec.europa.eu/health/sites/health/files/md_sector/docs/md_mdcg_2020_6_guidance_sufficient_clinical_evidence_en.pdf

'**well-established technology**': […] The common features of the devices which are well-established technologies are that they all have:

- relatively simple, common and stable designs with little evolution;
- their generic device group has well-known safety and has not been associated with safety issues in the past;
- well-known clinical performance characteristics and their generic device group are standard of care devices where there is little evolution in indications and the state of the art;
- a long history on the market.

Relevant guidance – sufficient clinical evidence

Appendix III - "Those devices which are well-established technologies may be able to confirm conformity with the relevant GSPRs via an evaluation of cumulative evidence from additional sources as listed below. Reliance solely on complaints and vigilance is not sufficient."

- equivalence data (reliable / quantifiable);
- evaluation of state of the art, including evaluation of clinical data from similar device;
- complaints and vigilance data (curated data);
- active PMS data, such as that derived from surveys;
- individual case reports on the subject device;
- compliance to non-clinical elements of common specifications considered relevant to device safety and performance;
- simulated use / animal / cadaveric testing involving healthcare professionals or other end users;
- pre-clinical and bench testing / compliance to standards.

Consultation of authorities for medicinal products

Consultation procedure - MDD

The current Directive 93/42/EEC Annex I 7.4 requires that:

"Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product as defined in Article 1 of Directive 2001/83/EC and **which is liable to act upon the body** with action ancillary to that of the device, the quality, safety and usefulness of the substance must be verified by analogy with the methods specified in Annex I to Directive 2001/83/EC.

For the substances referred to in the first paragraph, the notified body shall […] seek a scientific opinion from one of the competent authorities designated by the Member States or the European Medicines Agency(EMEA) […]"

Consultation procedure - MDR

Annex IX to the MDR (also referenced by X)

"(a) Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product within the meaning of point 2 of Article 1 of Directive 2001/83/EC, including a medicinal product derived from human blood or human plasma and that has an action ancillary to that of the device, the quality, safety and usefulness of the substance shall be verified by analogy with the methods specified in Annex I to Directive 2001/83/EC.

(b) Before issuing an EU technical documentation assessment certificate, the notified body shall, […], seek a scientific opinion from one of the competent authorities designated by the Member States in accordance with Directive 2001/83/EC or from the EMA […]"

Relevant guidance - consultation

MDCG 2020-12 Guidance on transitional provisions for consultations of authorities on devices incorporating a substance which may be considered a medicinal product and which has action ancillary to that of the device, as well as on devices manufactured using TSE susceptible animal tissues

https://ec.europa.eu/health/sites/health/files/md_sector/docs/md_mdcg_2020-12_guidance_transitional_provisions_en.pdf

CMR and ED substances in medical devices

Hazardous substances in medical devices

Annex I General Safety and Performance Requirements

Article 5 Placing on the market and putting into service

"2. A device shall meet the general safety and performance requirements set out in Annex I which apply to it, taking into account its intended purpose."

Annex I General Safety and Performance Requirements

"1. Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose. They shall be **safe and effective** and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that **any risks** which may be associated with their use constitute **acceptable risks when weighed against the benefits** to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged **state of the art**." [*emphasis added*]

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Hazardous substances in medical devices
Annex I General Safety and Performance Requirements

10.4.1. Design and manufacture of devices

"Devices shall be designed and manufactured in such a way as to reduce **as far as possible** the risks posed by substances […]

Devices, or those parts thereof or those materials used therein that:

— are invasive and come into direct contact with the human body,
— (re)administer medicines, body liquids or other substances, including gases, to/from the body, or
— transport or store such medicines, body fluids or substances, including gases, to be (re)administered to the body,

shall only contain the following substances in a concentration that is above 0,1 % weight by weight (w/w) where **justified** pursuant to Section 10.4.2:

(a) substances which are carcinogenic, mutagenic or toxic to reproduction ('CMR'), of category 1A or 1B […]
(b) substances having endocrine-disrupting properties for which there is scientific evidence of probable serious effects to human health […]"

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Hazardous substances in medical devices
Annex I General Safety and Performance Requirements

10.4.2. Justification regarding the presence of CMR and/or endocrine-disrupting substances

The justification for the presence of such substances shall be based upon:
(a) an analysis and estimation of potential patient or user **exposure** […];
(b) an analysis of possible **alternative** substances, materials or designs, including[…];

(c) argumentation as to why possible substance and/or material substitutes, if available, or design changes, if feasible, are **inappropriate** in relation to maintaining the functionality, performance and the benefit-risk ratios of the product; including taking into account if the intended use of such devices includes treatment of children or treatment of pregnant or breastfeeding women or treatment of other patient groups considered particularly **vulnerable** to such substances and/or materials; and

(d) where applicable and available, the latest **relevant scientific committee guidelines** in accordance with Sections 10.4.3. and 10.4.4.

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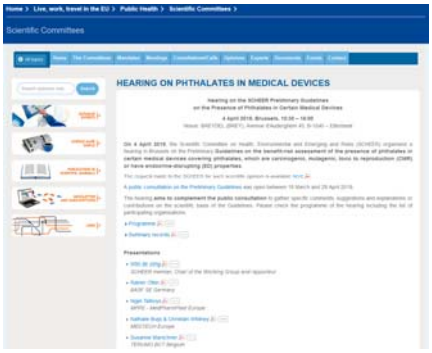
Hazardous substances in medical devices

Annex I General Safety and Performance Requirements

Guidelines on phthalates

10.4.3. Guidelines on phthalates

10.4.4. Guidelines on other CMR and endocrine-disrupting substances



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Guidelines on phthalates in medical devices

Guidelines on the benefit-risk assessment of the presence of phthalates in certain medical devices covering phthalates which are carcinogenic, mutagenic, toxic to reproduction (CMR) or have endocrine-disrupting (ED) properties

https://ec.europa.eu/health/scientific_committees/consultations/public_consultations/scheer_consultation_08_en

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Time to adapt – 8 + 1 years for MD

25 May 2017	26 May 2021	26 May 2022
Entry into force of the Regulations	Full application of MDR	Full application of IVDR

– 26 May 2025: Maximum period of validity of certificates issued under current Directives

– 26 May 2026: Making available of devices placed on the market pursuant to current Directives

IVDR Implementation priorities

Establishment of EU Reference Laboratories

- Implementing Acts on tasks, criteria and fees under preparation
- Legally may be designated no earlier than 25 November 2020 (IVDR Art 113d). They are currently foreseen to be available in 2021.
- COM will work to map the demand for EURL services

Common Specifications

- CTS under IVDD in the process of transposition to IVDR (will be adopted as an Implementing Act)
- New Common Specifications will be added (e.g. Kidd and Duffy blood grouping devices)
- One single Act

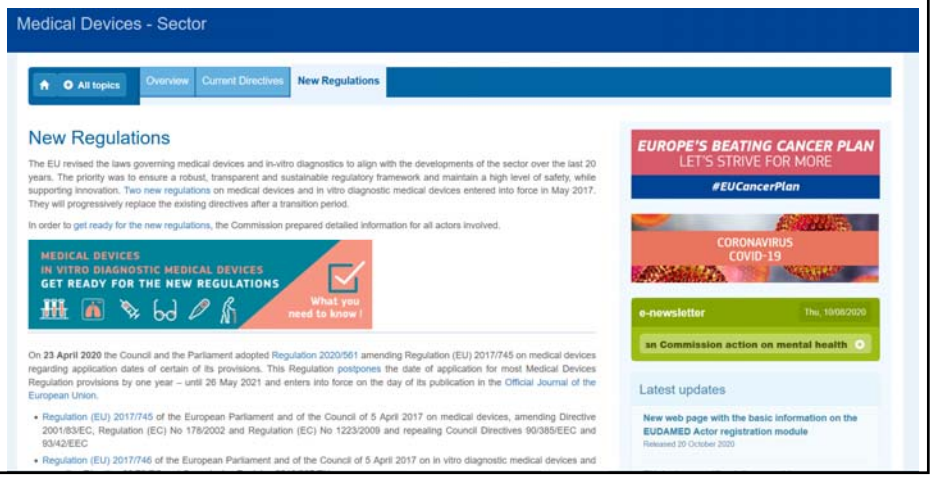
Guidance

- Classification guidance agreed by the IVD WG and transmitted to MDCG for endorsement
- Performance Evaluation guidance with regulators, imminent stakeholders consultations
- Guidance on Batch testing for notified bodies in preparation
- Explanatory note on IVDR codes under preparation
- Guidance on in-house devices under consideration

Our webpage

Old and new legislation, MDCG consensus documents

https://ec.europa.eu/health/md_sector/overview_en



Thank you for your attention!

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