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30 YEARS OF EXPERTISE

Changing medical device regulatory environment in the EU

05-09-2017

What is changing in legislation?
– Background information

New medical device regulations

- Two new regulations on medical devices approved in April 2017 and entered into force in May 2017
  - Regulation (EU) 2017/745 on medical devices
  - Regulation (EU) 2017/746 on in vitro diagnostic medical devices

- Regulations will replace the three old directives
  - Directive 93/42/EEC concerning medical devices
  - Directive 98/79/EC on in vitro diagnostic medical devices
  - Directive 90/385/EEC relating to active implantable medical devices

Main targets of new regulations

- Same rules for all parties in Europe
  - Interpretations of the directives and practices among the member states vary too much
  - Regulations are binding as such without national implementation meaning that at least the written laws are identical in all member states

- To restore public confidence in reliable product assessment and supervision process
  - Credibility of the current system has suffered due to scandals (e.g. PIP implants)
  - Tighter requirements for all product classes but especially for high risk products
  - Tighter Notified Body control
  - Bring some transparency to the system

- Up-to-date rules which take into account technological progress and new innovations
  - Directives don't reflect the technological progress made -> hard to modify
  - EU commission empowered to adopt delegated acts / implementing acts

New medical device regulations

- The "spirit" of New Approach Directives remains in the regulations
- New Approach is EU originated regulatory technique that
  - Sets only general essential requirements for the concerned product groups
  - Reduces the control of public authorities prior to a product being placed on the market
  - Integrates quality assurance techniques as part of the conformity assessment procedure

  ⇨ The basic principles remain unchanged but there are more & tighter requirements

- Products must have a CE marking before they can be placed on the European market
- Main goal: CE marking allows free movement of goods in EU

Transitional periods

MD & IVD regulations entered into force on 26 May 2017

- For class I medical devices can be applied immediately (not possible in practice)
- For other classes not possible as NBs must first be designated according to the regulation

First NBs designated

MD regulation 2017/745 applies from 26 May 2020

- All new devices released on the market after that must comply with the MDR
- NBs can only issue certificates in accordance of the MDR

IVD regulation 2017/746 applies from 26 May 2022

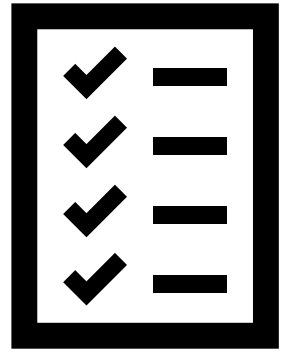
- All new devices released on the market after that must comply with the IVDR
- NBs can only issue certificates in accordance of the IVDR

MDD / IVDD certificates are no longer valid

Only devices complying with the regulation can be placed on the market

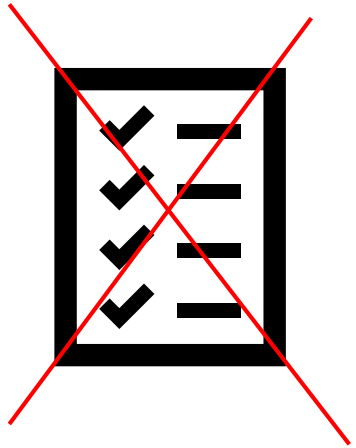
Transitional challenges

- Notified Bodies can apply for designation as per the MDR / IVDR earlies six months after the regulation has entered into force (11/2017)
- Competent authorities and the Commission have 18 months to review the submissions, to carry out the joint audits and to make their designating decisions
- First designations expected sometimes during 2019
- Open questions concerning NB designation
  - How the NB application will be prioritized, i.e. in which order the application will be assessed?
  - All applications can't be assessed at the same time – what will be the actual handling time?



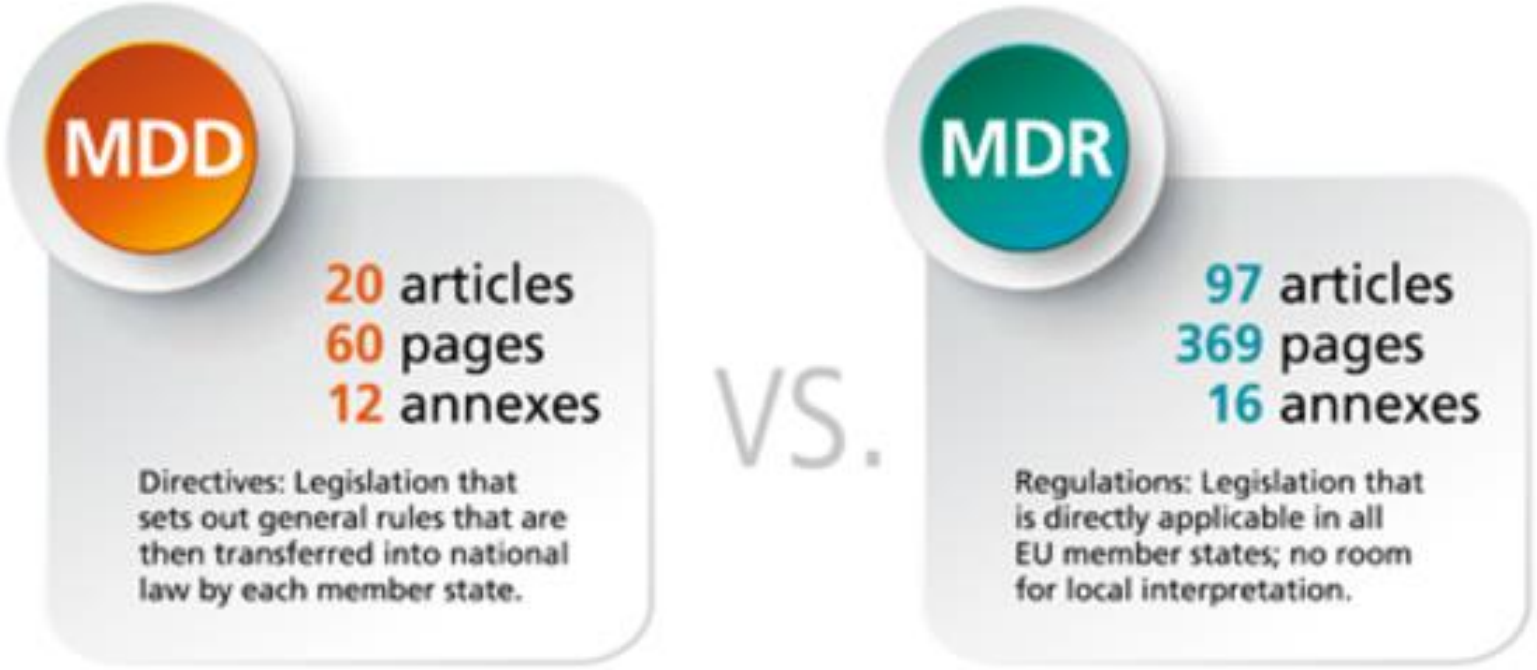
Transitional challenges

- Problems that NB designation process causes to manufacturers
  - You don't know if your NB receives re-designation
  - You don't know when your NB receives re-designation
  - The scope of the re-designation can be different that the current scope
- All current NBs don't apply for the re-designation
- It might be difficult to find NB that takes new clients as they will have hands full of work with their current customers
- It's essential to create detailed regulatory strategies especially for
  - Old products whose classification will change from class I to higher risk class
  - Products in R&D pipeline and intended to be released in the market during the transitional period
- Contact your NB early enough and discuss & agree how to proceed!



What is changing in practice?
– A few examples of remarkable changes

A lot is changing…



Medical device definition

Medical device means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:

- diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury or disability
- investigation, replacement or modification of the anatomy or of a physiological or pathological process or state
- providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations,

and which does not achieve its principal intended action by pharmacological, immunological or metabolic means in or on the human body, but which may be assisted in its function by such means.

The following products shall also be deemed to be medical devices:

- Devices for the control or support of conception
- Products specifically intended for the cleaning, disinfection or sterilization of devices

In vitro diagnostic medical device

In vitro diagnostic medical device means any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, piece of equipment, software or system, whether used alone or in combination, intended by the manufacturer to be used *in vitro* for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information on one or more of the following:

(a) concerning a physiological or pathological process or state;
(b) concerning congenital physical or mental impairments;
(c) concerning the predisposition to a medical condition or a disease;
(d) to determine the safety and compatibility with potential recipients;
(e) to predict treatment response or reactions;
(f) to define or monitoring therapeutic measures.

Specimen receptacles shall also be deemed to be *in vitro* diagnostic medical devices;

Scope: Aesthetic products included

- This regulation shall also apply to the groups of products without an intended medical purpose that are listed in Annex XVI:
  - Contact lenses with aesthetic purpose
  - Implants meant for aesthetic purposes
  - Injectable fillers for facial or other dermal or mucous membrane filling
  - Equipment for liposuction, lipolysis or lipoplasty
  - High intensity electromagnetic radiation emitting equipment intended for use on the human body for skin resurfacing, tattoo or hair removal or other skin treatment
  - Equipment intended for brain stimulation

Scope: Viable organisms excluded

- This regulation does not apply to:
  - products that contain or consist of viable biological material or viable organisms, including living micro-organisms, bacteria, fungi or viruses in order to achieve or support the intended purpose of the product;
  - e.g. vaginal products including living lactobacillus bacteria which produce lactic acid

IVD classification

- Old "list based" classification system is replaced with a risk based system
- Devices are divided into classes A, B, C and D taking into account the intended purpose of the devices and their inherent risks
- Notified body involved in the conformity assessment of class B, C and D devices
  - Currently only one in five in vitro diagnostic medical devices is checked by a Notified Body before they are placed on the market
  - In the future four out of five in vitro diagnostic medical devices are checked by a Notified Body before they are placed on the market

Clinical evaluation

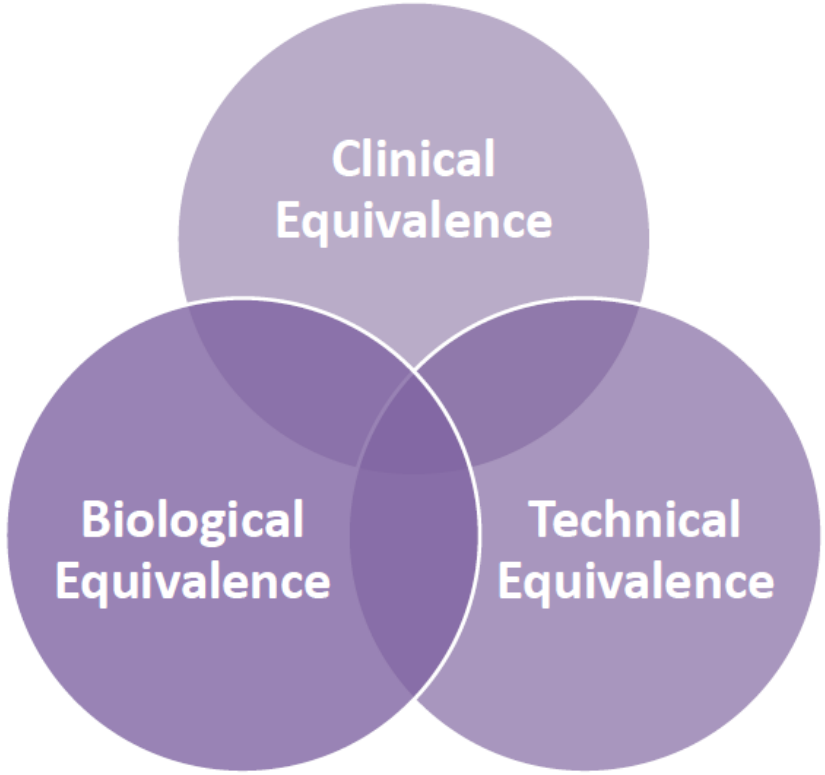
- The bar is clearly rising on clinical data

- Purpose of clinical evaluation:
  - Confirm the conformity with relevant general safety and performance requirements
  - Evaluate the undesirable side-effects and the acceptability of the benefit-risk-ratio

- Clinical evaluation can be based on:
  - Critical evaluation of the relevant scientific literature currently available when the following conditions are satisfied
    - Equivalence of the devices must be demonstrated
    - Data demonstrates compliance with the relevant safety and performance requirements
  - Critical evaluation of the results of the clinical investigations ; and
  - Consideration of currently available alternative treatment options for that purpose, if any.

Clinical evaluation

- What does "equivalent" mean?
- Very detailed definition for equivalence in MDR
- Three aspects
  - Technical
  - Biological
  - Clinical

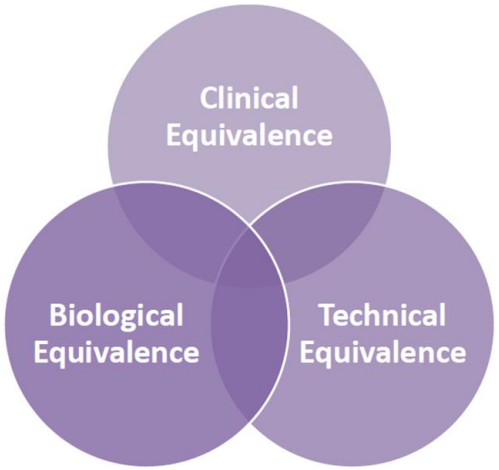


Clinical evaluation

- **Technical:** the device is of similar design; is used under similar conditions of use; has similar specifications and properties including physicochemical properties such as intensity of energy, tensile strength, viscosity, surface characteristics, wavelength and software algorithms; uses similar deployment methods, where relevant; has similar principles of operation and critical performance requirements;

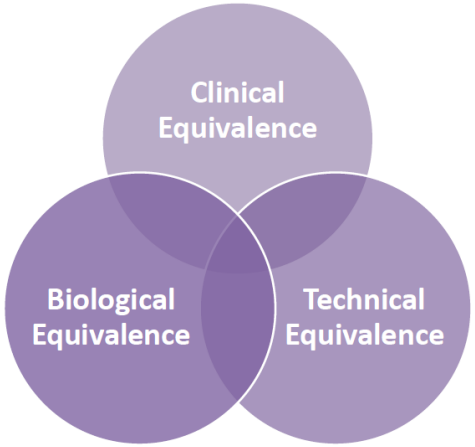
- **Biological:** the device uses the same materials or substances in contact with the same human tissues or body fluids for a similar kind and duration of contact and similar release characteristics of substances, including degradation products and leachables;

- **Clinical:** the device is used for the same clinical condition or purpose, including similar severity and stage of disease, at the same site in the body, in a similar population, including as regards age, anatomy and physiology; has the same kind of user; has similar relevant critical performance in view of the expected clinical effect for a specific intended purpose.



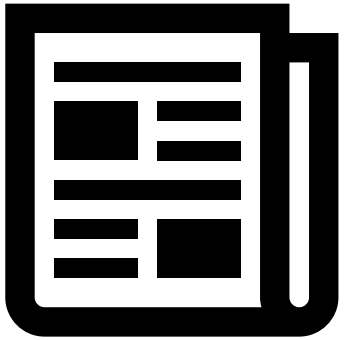
Clinical evaluation

- Clinical AND technical AND biological equivalence must be met for each device considered equivalent
- Differences must be fully disclosed and evaluated
- Same therapeutic results achieved by different means ≠ equivalent
- Equivalent devices must be CE marked (exceptions considered)
- Public data may not contain sufficient information for demonstration of equivalence
- **Tight equivalence requirements strongly limit the possibility to rely on available literature of other devices in clinical evaluations**
- Same requirements for all devices regardless of product history
  - Clinical investigations may be require for products being on the market for decades



Post-market requirements

- Very detailed post-market requirements
  - Article 83: Post-market surveillance system of the manufacturer
  - Article 84: Post-market surveillance plan
  - Article 85: Post-market surveillance report
  - Article 86: Periodic safety update report
  - Annex III: Technical documentation on post-market surveillance
  - Article 61: Clinical evaluation / Post-market clinical follow-up
  - Annex XIV Part B: Post-market clinical follow-up
  - Articles 87-89: Vigilance



Transparency - Eudamed database

- Set up of European database on medical devices ('Eudamed') for the following purposes:
  - to enable the public to be adequately informed about devices placed on the market, the corresponding certificates issued by notified bodies and about the relevant economic operators;
  - to enable unique identification of devices within the internal market and to facilitate their traceability;
  - to enable the public to be adequately informed about clinical investigations;
  - to enable the competent authorities of the Member States and the Commission to carry out their tasks relating to this Regulation on a well-informed basis and to enhance the cooperation between them.

Transparency - Eudamed database

- Eudamed shall include a system on vigilance and post-market surveillance to collate the following information:
  - the reports on serious incidents and field safety corrective actions;
  - the periodic summary reports of incidents;
  - the trend reports of incidents;
  - the PSURs;
  - the field safety notices;

- The Commission shall ensure that healthcare professionals and the public have appropriate levels of access to the electronic system.

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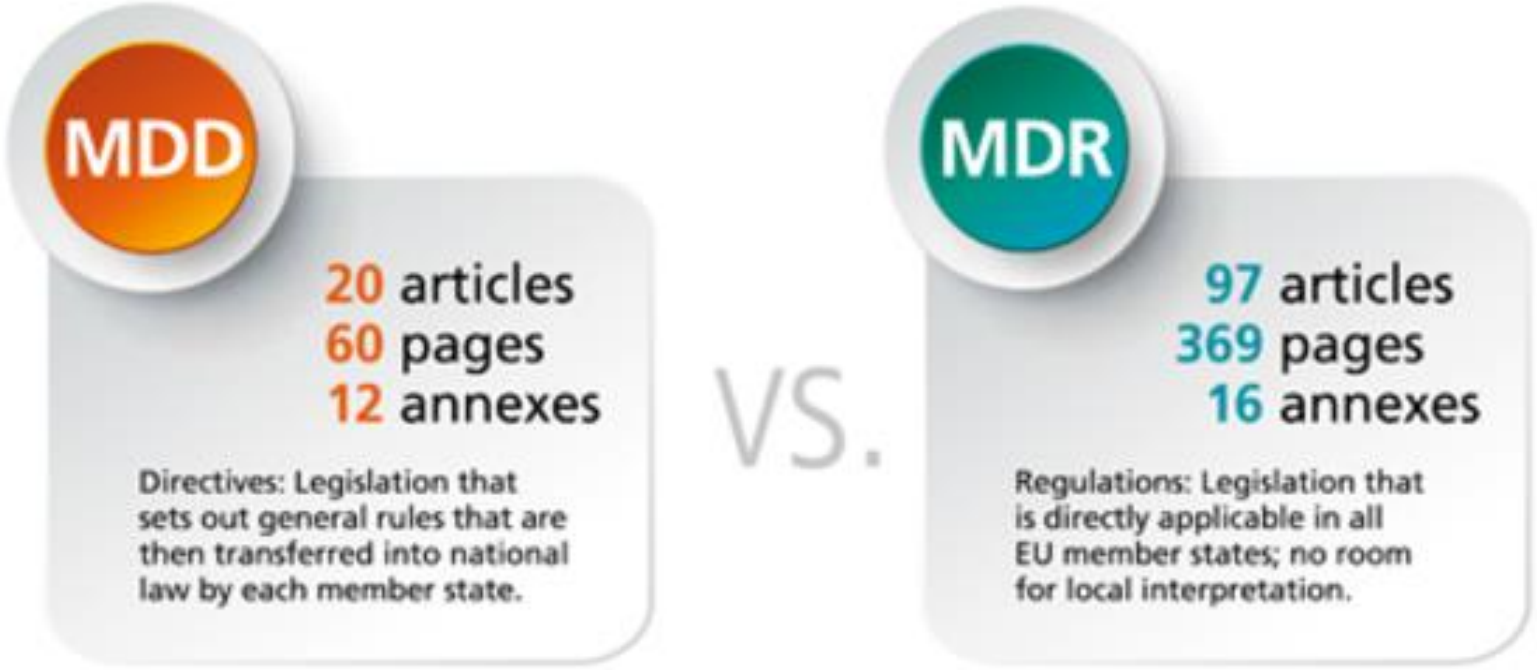
Where to start as a manufacturer?

There is plenty of work…



Next steps to manufacturers

- Still plenty of open questions – yet the work should be started
- Evaluate the shortcomings of your current documentation and processes compared to the requirements of the MDR / IVDR

  &
- Create a detailed road map how to bring your documentation and processes to the required level
- Feasibility of each device – is it worth to bring the documentation to the required level?
  - Especially the state of clinical data
- The more time you use in the planning phase, the easier is the implementation phase

Contacts

Medical Devices

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