Ready or Not: The New Medical Device Regulations Are Here!

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Objectives

By the end of this session attendees will be aware of…

• The regulatory pathway to market authorization
  – Geography
  – Notified Bodies and Competent Authorities
  – CE Mark
  – Comparison *versus* US

• The regulatory framework involving MDRs
  – Device definitions
  – “Directives” *versus* “Regulations”
  – Timelines

• Examples of key changes imposed by MDRs

• Resources concerning MDRs
The Stage Is Set....

Directive (MDD) 93/42/EEC
Directive (AIMD) 90/385/EEC
Directive (IVDD) 98/79/EC

Regulation (EU) 2017/45
Regulation (EU) 2017/46

- MDR and IVDR strengthen the existing regulatory system by repealing the original Directives in place for ~ 25 years
Who Are the Players?

- EU Commission, Parliament, Council
- Member States, EFTA, EEC, Competent Authorities
- Notified Bodies
- Manufacturers, Sub-Contractors, Suppliers, Importers EU Authorized Rep
European Union = 27 Member States

“Brexit”
EU + [Iceland, Liechtenstein, Norway, Switzerland*] = EEA
European Economic Area

*Switzerland has bilateral agreements with EU

“Brexit”
Who Are the Players?

EU Commission, Parliament, Council

Member States, EFTA, EEA, Competent Authorities

Notified Bodies

Manufacturers, Sub-Contractors, Suppliers, Importers EU Authorized Rep

New Regulatory Framework
What is a Notified Body (NB)?

• NBs exert regulatory control over market authorization and quality systems for medical devices
  – NBs perform technical and medical reviews of marketing applications / renewals
    o NBs critically review device safety and performance as part of the regulatory package (Technical File or Design Dossier) submitted to obtain or maintain CE Marking

• NBs are independent, for-profit organizations – not manufacturers

• Not all NBs are designated for all medical devices
  – Per MDR, scope of NBs will be specified by 26 Nov 2017

• NBs are authorized / monitored by Competent Authorities
Find a Notified Body

EXAMPLE: Search for Notified Body accredited under 90/385/EEC (AIMD)

<table>
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<tbody>
<tr>
<td>TÜV NORD CERT GmbH</td>
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<td>POLSKIE CENTRUM BADAN I CERTYFIKACJI S.A.</td>
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Note: Manufacturers can use any Notified Body authorized to evaluate the specific device class
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Notified Bodies
Manufacturers, Sub-Contractors, Suppliers, Importers EU Authorized Rep

New Regulatory Framework
What are Competent Authorities?

- Competent Authorities, in each Member State, conduct market surveillance and enforcement
  - Monitor compliance at the national level
  - Approve clinical investigations
  - Protect public health and safety
  - Authorize, monitor, and audit NBs

EXAMPLES:
- Federal Institute for Drugs and Medical Devices (Germany)
- The Health Products Regulatory Authority (Ireland)
- Danish Health and Medicines Authority (Denmark)
- French National Agency of Medicine and Health Products Safety (France)
Regulatory Pathway to Market Authorization

- CE Mark…..
  - Symbolizes conformity with the relevant Essential Requirements for device safety and performance
  - Designates product registration and marketing approval in one country, followed by free trade across borders
    - Reimbursement varies by Member State
  - Is generally recognized across the globe
    - Australia and New Zealand
    - India
Comparison of Market Authorization for Medical Devices

- To achieve CE Mark, manufacturers submit to a **Notified Body**:
  - Technical File required for Class I, IIa, IIb devices
  - Design Dossier required for class III medical devices
  - Notified Body verifies whether medical device satisfies safety and performance requirements

- To achieve *clearance for a “substantially equivalent device”*, manufacturers submit 510k application to FDA

- To achieve *approval for a new medical device*, manufacturers submit PMA package to US FDA
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NEW Regulatory Framework

Official Journal of the European Union

Legislation

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5 May 2017

Contents

I Legislative acts

REGULATIONS


NEW Regulatory Framework: MDR

- Known as Regulation (EU) 2017/745
  - 175 pages
  - 101 “Whereas” = WHY
  - 10 Chapters of 123 Articles = WHAT
    - I: Scope and Definitions
    - II: CE Marking
    - III: Identification and Traceability
    - IV: Notified Bodies
    - V: Device Classification
    - VI: Clinical Evaluation
    - VII: Vigilance and Market Surveillance
    - VIII: Cooperation Among Member States
    - IX: Confidentiality, Data Protection, Penalties
    - X: Final Provisions
  - 17 Annexes = HOW
NEW Regulatory Framework

- Consolidates three prior Directives

- Directives versus Regulations
  - Directives = Legislation ratified by the EU Parliament and transposed into national law by each Member State
  - MDR = “Direct entry into force” with clear and defined rules that are binding across all Member States
NEW Regulatory Framework: MDR

- **EU Definition of Medical Device (2017):**
  - Any instrument, apparatus, appliance, material or other article, used alone or in combination with accessories or software, intended for:
    - Diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease ..... or injury
      - **NEW** - Does NOT necessarily have to be therapeutic
        - **EXAMPLE:** Tinted contact lenses
    - Control or support of conception
    - Cleaning, disinfection, or sterilization of medical devices
  - Does not achieve its intended action by pharmacological, immunological or metabolic means, but may be assisted in its function by such means
NEW Regulatory Framework: MDR

• **Implantable Medical Device EU Definition (2017):**
  - Any device, including those that are partially or wholly absorbed, intended:
    - To be totally introduced into the human body, or
    - To replace an epithelial surface or the surface of the eye
    - AND remains in place after clinical intervention for at least 30 days

• **Active Medical Device EU Definition (2017):**
  - Any device, the operation of which depends on a source of energy other than that generated by the human body, or by gravity, and which acts by converting that into energy
NEW Regulatory Framework: IVDR

• EU Definition of IVD (2017):
  – In vitro diagnostic medical device 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 for in vitro 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 more the following:
      - Physiological or pathological process or state
      - Congenital physical or mental impairments
      - Predisposition to medical condition or disease
      - Safety and compatibility with potential recipients
      - Treatment response or reactions
      - Monitoring or therapeutic measures
NEW Regulatory Framework: Timeline

- **2008**: EU Commission launches public consultation
- **2012**: EU Parliament reviews draft and proposes changes
- **2014**: EU Commission publishes proposal for MDR
- **2015**: EU Council reviews draft and proposes additional changes
- **2017**: Expected publication of MDR
- **2020**: Expected end of three-year transition period

*26 May 2020 MDR 26 May 2022 IVDD*

Updated from www.tuv-sud.com/mdr
True or False?

• Existing medical devices will be “grandfathered” automatically into the MDR without need for (new? additional?) clinical investigation or further documentation

FALSE !
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Examples of Key Changes Imposed by MDRs

- Strengthened device class designation
- More stringent and transparent clinical data will be required to demonstrate safety, performance, and clinical benefit
  - High-risk devices must be evaluated in clinical investigations
  - Mandatory unannounced audits conducted by Notified Body
- Most IVDs (~80-90%) will require involvement of Notified Body
- Unique Device Identifier ("UDI" = series of unique numeric or alpha numeric characters) will be required for unambiguous identification of specific devices on the market
- Recommendation for CE Mark can be reviewed by EC "Expert Panel"
- Post-market follow-up should be "proportionate to the device (risk) class and appropriate for the type of device"
- More frequent device re-certification will be required
Example of Key Change: Device Equivalence

• “Equivalence” can only be established using a single, CE-marked device that satisfies all clinical, technical, and biological requirements
Example of Key Change: Device Equivalence

- Manufacturer must confirm that any differences between the device under evaluation and the designated equivalent device does not affect safety, performance, and clinical benefit.
Difficulties with Device Equivalence Approach

- This approach may be limited by a lack of available, relevant clinical data pertaining to the designated equivalent device
  - The Notified Body shall have access to relevant pre-clinical data, drawings, diagrams, properties, and specifications, for the designated equivalent device
  - The only clinical data considered relevant are data obtained from CE-marked medical device(s) used in accordance with the approved labelling
Example of Key Change: PMCF

- Manufacturers must implement post-market clinical follow-up investigations after CE Marking
  - Device is used in accordance with approved labelling
  - Objective is to answer specific questions relating to clinical safety, usability, and performance
  - These studies may identify risks not observed during pre-market testing

- Describe planned or ongoing post-market clinical follow-up studies in the clinical evaluation

- In the event that post-market clinical follow-up data will NOT be collected, discuss with Notified Body *a priori* and justify in the clinical evaluation
Example of Key Change: PMS

- Post-market surveillance is required for all CE-Marked devices sold in the EU

- Manufacturers must execute pro-active PMS plans that are fully described in the clinical evaluation
  - Confirm safety and performance during expected lifetime of device
  - Determine acceptability of known risks within a large patient population
  - Detect emerging risks based on factual evidence

- Eudamed (European Databank on Medical Devices) proposed under MDRs

- Periodic safety reports required for device Classes IIa, IIb, III
Risk/Benefit Assessment

Intended Use

Safety Data

Performance/Clinical Data

Risk/Benefit Analysis
Risk / Benefit Assessment

- Risk / benefit
  - Known and foreseeable adverse health effects must constitute acceptable risk when weighed against intended clinical benefits
  - Evaluation of side-effects and risk / benefit profile must rely on clinical data
Resources to Help with CER Preparation

- Reg (EU) 2017/45 and Reg (EU) 2017/46
- MEDDEV Guidelines
  - 2.7.1/rev. 4 “Clinical Evaluation”
  - Other relevant MEDDEV guidelines
    - 2.7.4 “Clinical Investigations”
      - See also ISO 14155 (under revision)
    - 2.12.2/rev. 2 “Post-Market Clinical Follow-up”
- Notified Body guidance documents
  - Documents issued by the Notified Bodies themselves (NB-MED)
    - Bulletins from TÜV
    - CER checklist from TÜV
Concluding Thought:
Pay Attention to the Changing Regulatory Landscape
Thank You!