Medical Device Regulation Overview

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What is the issue?

- Existing EU Directives – dating back to the 1990s
  - Not in pace with the enormous technological progress in the past 20 years
- EU countries interpret and implement current rules differently
- Not always possible to trace medical devices back to their supplier
  - new rules on traceability are needed
- Patients, healthcare professionals and others do not have access to
  - essential information on assessment on medical devices
  - clinical evidence to show they are safe and effective
- Need for greater transparency highlighted by recent scandals
  - faulty silicone breast implants
  - problems with some metal-on-metal hip replacements

Who will benefit and how?

- Patients and public
  - all medical devices will have to undergo thorough, independent assessment of safety and performance before they can be sold on the European market
  - controls will not block or unduly delay access to innovative, cost-effective devices
- Healthcare professionals
  - better information on the benefits for patients, residual risks and overall risk/benefit ratio
  - make the best use of medical equipment
- Manufacturers
  - clearer rules, easier trading between EU countries and a level playing field
  - with penalties for those who don't play by the rules
  - new rules support patient-oriented innovation
  - take particular account of the specific needs of the many small and medium sized manufacturers in this sector

What will change?

- Wider, clearer scope for EU legislation on medical devices
  - extended to include, for example, implants for aesthetic purposes, and clarified as regards to genetic tests
- Stronger supervision of independent assessment bodies by national authorities
- More powers for assessment bodies
  - ensure thorough testing and regular checks on manufacturers,
  - unannounced factory inspections
- Clearer rights & responsibilities
  - for manufacturers, importers and distributors
  - apply to diagnostic services and internet sales
- Extended Eudamed database on medical devices
  - comprehensive information on products available on the EU market
  - non-confidential data will be publicly available

What will change?

- Better traceability of MD throughout the supply chain
  - enabling a swift and effective response to safety problems (e.g. recalls)
- Stricter requirements for clinical evidence to support assessments of MD
- Updated classification rules
  - New labelling rules
  - keep pace with technological and scientific progress
- Better coordination between national surveillance authorities
  - Commission provide scientific, technical & logistic support
- International guidelines to be incorporated into EU law

European Commission Expectation

- Increased patient safety
- Governance of system and transparency
- Criteria for designation, monitoring and obligations of notified bodies
- Risk classification of devices and the safety and performance requirements
- Obligations of economic operators
- Clinical evaluation, traceability and reprocessing of single-use devices

Delegated Entities under MDR

- European Commission (EC)
- EU Member States (MS)
- EU Competent Authorities (CA)
- Medical Device Coordination Group (MDCG)
- Medical Device Advisory Committee (MDAC)
- Assessment Committee for Medical Devices (ACMD)
- EU Reference Laboratories (EURL)
- European Medicines Agency (EMA)*
- Notified Bodies (NB)
- Special Notified Bodies (SNB)*

*EC – Need to carefully assess added value of EMA involvement

Governance

- Improved cooperation and coordination between Member States
- New Medical Device Coordination Group of MS
- EC coordinating role to assist MS manage the system
- Increased resources at EU level (DG SANCO, JRC)

EU Joint Action Plan for Immediate Action

- Notified Bodies
  - Competence and tasks
  - Reassessment of NB’s dealing with high-risk devices
  - Joint audits by MS and EC
- Coordination and Transparency
  - Coordinated inspections, trends and analysis
  - International coordination IMDRF
  - Traceability (UDI)
- Post Market
  - MS reinforcement
  - Vigilance coordination
  - EC analysis benchmarking

Standards & Guidelines

- Better management of development and harmonized implementation of EU guidance
  - now formal responsibility of the new MDCG
- Possibility of ‘Common Technical Specifications’ where no standards exist

EU MDR

- Merge of AIMDD and MDD
- Integration of contents of the GHTF and the MEDDEV
- Wider and clearer scope
  - include implants for aesthetic purposes
  - devices containing or being made of non-viable human tissues
- 10 chapters with 97 articles altogether (currently, the MDD contains 23 articles)
- More definitions, e.g.: Sponsor
- New assessment of classifications
  - Reclassification of Breast Implants
  - Reclassification of Hip, Knee and Shoulder
- Designation of a qualified person by the manufacturer and AR

EU MDR

- Relabeling and repackaging by parallel importers
- Distance sales
  - diagnostics/therapeutics and associated services
- Clarification re medical software
- Expansion of EUDAMED
- Class III devices: EUDAMED publication
- Animal tissue regulation
- Involvement of competent authorities and expert groups in class III devices
- Implementation of EU reference laboratories
- Implementation of the UDI
- Centralized system for safety reporting and vigilance
- Centralized submission process with multi-centric clinical investigations

10 chapters

- Ch I - Scope & definitions
- Ch II - Making available of devices, obligations of economic operators, reprocessing, CE marking, free movement
- Ch III - Identification and registration of devices and economic operators, summary of safety and clinical performance, EU medical device databank
- Ch IV - Notified bodies
- Ch V - Classification and conformity assessment
- Ch VI - Clinical evaluation and clinical investigations
- Ch VII - Post-market surveillance, vigilance and market surveillance
- Ch VIII - Cooperation between MS, MDCG, EU reference laboratories, device registries
- Ch IX - Confidentiality, funding, penalties
- Ch X - Final provisions

15 Annexes

- Annex I - General Safety & Performance Requirements
- Annex II - Technical Documentation
- Annex IIa Technical documentation on post-market surveillance
- Annex III - EC Declaration of Conformity
- Annex IV - CE Marking of Conformity
- Annex V - Information for Registration of Devices & Economic Operators & Data Elements UDI
- Annex VI - Requirements to be met by Notified Bodies
- Annex VII - Classification Criteria
- Annex VIII - Conformity assessment based on a quality management system and assessment of the technical documentation
- Annex IX - Conformity assessment based on type examination
- Annex X - Product Conformity Verification
- Annex XI - Conformity Assessment for Custom-Made Devices
- Annex XII - Certificates issued by a notified body
- Annex XIII - Clinical Evaluation and Post Market Clinical Follow-up
- Annex XIV - Clinical Investigations
- Annex XV - List of Non-Medical Products Included in Medical Device Definition

Definitions

- Medical Device
- Accessory
- Label
- Instructions for use / Unique Device Identification
- Manufacturer / Authorized Representative / Importer / Distributor / Economic Operator
- Health Institution / User / Lay Person
- Reprocessing / Fully Refurbishing
- Conformity assessment terms
- Clinical terms
- Vigilance and market surveillance terms

Economic operators

- Economic operators
  - manufacturer, authorised representative, importer and distributor
- Manufacturer
  - natural or legal person who manufactures or fully refurbishes a device
  - has a device designed, manufactured or fully refurbished, and markets that device under his name or trademark
- Importer
  - any natural or legal person established within the Union who places a device from a third country on the Union market
- Distributor
  - any natural or legal person in the supply chain, other than the manufacturer or the importer, who makes a device available on the market
- Inclusion of diagnostic services and internet sales

General obligations of manufacturer

- Design and manufacture devices in accordance with the regulation
- Draw up required technical documentation
- Complete an appropriate conformity assessment
- Prepare a declaration of conformity
- Make technical documentation available to CA's (STED)
- Operate a quality management system and maintain product conformity
- Conduct post market surveillance
- Supply instructions for use in a MS language
- Procedures for devices that do not comply – including vigilance
- Identify suppliers conducting device design & manufacture
- Liability insurance

Person responsible for regulatory compliance

- At least one qualified person possessing expert knowledge in the field of MD in manufacturer's organisation
  - a degree or equivalent in law, medicine, pharmacy, engineering or another relevant scientific discipline plus at least one year of professional experience in regulatory affairs or in QMS in MD or
  - four years of professional experience in regulatory affairs or in QMS relating to MD
- Responsible for ensuring
  - conformity of the devices is appropriately assessed before a batch is released
  - technical documentation and the declaration of conformity are drawn up and kept up-to-date
  - vigilance requirements have been fulfilled
  - subjects in clinical investigations or performance evaluation for interventional studies
- The qualified person should suffer no disadvantage by performing their duties

Obligations of AR, Importers, Distributors

- Manufacturer designates by written mandate a single AR confirmed in writing by the AR
  - Prescriptive requirements for AR
  - Written process for changing AR
- General obligations of importers
  - Confirm: manufacturer identifiable and competent, liability insurance, conformity assessment, authorized representative, technical documentation, devices CE Marked, labeled in accordance with regulation
  - Identify themselves, registration, storage & transportation, records, complaints, non-conformity/corrective action responsibilities

Increased control of the supply chain

- Increase expectation to hold or have quick access to technical documentation during audits
- Notified bodies can now audit
  - crucial suppliers
  - significant subcontractors including unannounced visits
- Changes to contracts will be required

Parts and Components

- New requirement for suppliers of parts or components
- Parts or components intended to replace parts or components that are defective or worn to maintain or re-establish performance of a device
- Responsibility to determine the part or component does not adversely affect the safety and performance of the device
  - Substantiating evidence available to CA
  - For implantable devices must cooperate with the manufacturer of the device
- Part or component that significantly changes the performance or safety characteristics of a device shall be considered a device in its own right

Traceability in the Supply Chain

- Introduction of Unique Device Identification (UDI) system to
  - enhance post-market safety
  - reduce medical errors
  - fight against counterfeiting
  - enhance purchasing and stock management by hospitals
- UDI
  - to facilitate traceability and recall devices will require a UDI
  - does not apply to devices for clinical investigation / performance evaluation
  - will appear on the label
  - need to be stored by the economic operators and the health institutions
  - approved systems will be designated by the Commission
    - Coherent if possible with a global regulatory approach to UDI

Traceability in the Supply Chain

- Extended database on MD
  - providing more information available on the quality and safety of devices on the market
- For devices, other than devices for clinical investigation or performance evaluation, economic operators shall identify the following, and will retain records for the 5 years after the last device has been placed on the market:
  - any economic operator to whom they have supplied a device;
  - any economic operator who has supplied them with a device;
  - any health institution or healthcare professional to whom they have supplied a device.

Eudamed: European Electronic Database

- UDI
- Registration of devices and economic operators
- Information of certificates
- Clinical investigations
- Vigilance
- Market surveillance
- Public access
  - Allow comparison of devices, economic operators, clinical investigations, vigilance

Implant card and information about implantable devices

- Manufacturers of implantable devices shall provide implant card for particular patients
  - implant card shall also be made available in an electronic format
  - identifies device implanted including UDI
  - warning, precautions, measures to be taken with reciprocal interference with external influences
  - potential adverse effects
  - information on expected life cycle and follow-up
  - principal characteristics of device including materials
- Exempted implants: sutures, staples, dental implants, screws, plates

Scrutiny process

- Article 44, scrutiny process
  - allow authorities to take a second look at the Notified Body's review of technical documentation prior to CE marking approval
  - require Notified Bodies to prepare a summary report of the technical review for an oversight group prior to approving CE Marking of high-risk devices
- The oversight group may request additional information and testing results
  - potentially delaying the submission process by several months
  - reducing the market advantage of launching products in Europe first

Declaration of Conformity

- Manufacturer name and address
- Statement that the manufacturer is taking responsibility for the device
- UDI
- Device identification – name, product code, catalog
- Statement of compliance with the regulation
- Risk classification
- Harmonized standards used for conformity
- Notified body, conformity assessment, certificate
- Place, date of issue
- Name and function of signature, indication of who on behalf of signs
- Continuously updated and issued in one of the official EU languages

Improvements in Notified Bodies

- More rigorous designation, audit and control by Member States and Commission
- Member States fees for designation and monitoring of NBs
- Joint audits of Notified Bodies by two Competent Authorities simultaneously
- NB enhanced compliance powers – rights and duty to carry out
  - periodic NB audits
  - unannounced inspections
  - physical or laboratory testing on MD
  - certificate suspensions, withdrawals or restrictions
- The increased workload created by unannounced audits
  - higher revenues for Notified Bodies and higher costs for manufacturers

Notified Bodies

- More prescriptive requirements
    - Must have permanent in-house staff: Administrative / Technical/Scientific / Medical / Pharmacological
- May use External Experts on ad hoc and temporary basis as needed
- Submission for designation of a Notified Body shall be overseen by three experts identified by the Commission and MDCG
- Better defined Scopes of Designation relative to competence
- Only Special Notified Bodies can assess high risk devices
  - Special Notified Bodies to meet in network, exchange good practice and convergence
  - In-house clinical experts
  - Two experts for each product category at least one in-house

Special Notified Body

- Special Notified Bodies are designated by EMA
- Only Special Notified Bodies shall conduct conformity assessment of high risk devices
  - MDR class III, implantable, class IIb intended to administer medicinal substance
- All applications for high risk devices shall be notified to the EC
  - Draft IFU
  - draft summary of safety and clinical performance
  - estimated date of completion of conformity assessment
- Notification will be communicated to MDCG
- Within 20 days MDCG may request prior to CE Marking SNB provide
  - clinical evaluation report
  - post Market Clinical Follow-up Plan
  - information on marketing or not in third countries (results of evaluations)

Special Notified Body

- MDCG will consult ACMD
  - At the latest of 60 days MDCG will issue opinion on documents submitted
  - Within that period <30 days ACMD may request additional information
  - Within 15 days of receiving MDCG opinion SNB will indicate whether it agrees
- If SNB disagrees it has 30 days to submit further information and request re-examination
- MDCG in consultation with ACMD has a further 30 days to re-examine opinion
- Following unfavorable opinion SNB shall not issue a certificate
- SNB can submit new information and MDCG may reassess application
- Following unfavorable opinion manufacturer can request from EC a hearing to discuss the scientific grounds for the unfavorable scientific assessment
- The EC will make MDCG opinions available to the public
- The manufacturer will not be charged for the additional MDCG assessment

Notified Bodies, Certificates and the Regulation

- Designations under AIMD, MDD and IVD
  - become void at the date of final application of the regulation
- AIMD, MDD and IVD EC Certificates issued before the regulation enters into force remain
  - valid until expiration date
- AIMD, MDD and IVD EC Certificates issued after the regulation enters into force
  - shall become void four years after the application of the regulation
- Certificates against the new regulation can be issued by notified bodies designated under the new regulation
  - before the date of application of the regulation

Medical Device Coordination Group (MDCG)

- MDCG – Article 78
- n=1 from each Member State MD

- Tasks of the MDCG – Article 80 Article 32 – Assessment of Applications of Notified Bodies
- Article 35 – Monitoring of Notified Bodies
- Article 41 – Classification Disputes
- Article 44 – Conformity Assessment of Class III Devices

Role of MDCG

- Contribute to
  - assessment of Notified Bodies
  - scrutiny of certain conformity assessment
  - development of guidance, in particular: designation and monitoring of Notified Bodies
- Apply general safety & performance requirements
- Monitor clinical evaluation by manufacturers and the assessment by Notified Bodies
- Assist Competent Authority in the coordination of
  - clinical performance studies
  - vigilance and market surveillance
- Provide advice and assistance to the Commission

CE marking of conformity

- New requirement – when CE Marking is used in promotional material the notified body number must also be identified
- The form of CE Marking “CE Medical Device”

Safety and Clinical Performance Report

- Clearer requirements for clinical evidence
- For all class III and implantable device
  - Evaluated on the basis of clinical investigation data
  - Based on data collected during the clinical investigation
  - Submitted to Special Notified Body for review
  - Special Notified Body will validate
- Must be understandable by users in the relevant local MS language
- The summary will be made available to the public through Eudamed
- Safety and clinical performance report shall be updated annually with clinical evaluation reports

Clinical Evaluation & Clinical Investigation

- New system of centralization of notifications and reporting system for severe adverse event
- Increased protection of subjects undergoing clinical investigations
- Extended post-marketing clinical follow-up
- Regulation combines and incorporates current guidance's on clinical evaluation and clinical investigation
  - significant requirements on clinical general requirements – sponsor responsibilities
  - application
  - registration
  - electronic system
  - post market clinical investigation requirements
  - substantial modification
  - sponsor information obligations regarding suspension / termination
  - event reporting

Common Technical Specification (CTS)

- CTS may be written where no Harmonised Standards exist to address General safety and performance requirements
- Technical documentation
- Clinical evidence and post-market follow-up
- Devices which are in conformity with the CTS shall be presumed to be in conformity with the requirements of the Regulation
- Manufacturers shall comply with the CTS unless they can duly justify
  - they have adopted solutions ensuring a level of safety and
  - performance that is at least equivalent

Vigilance & Market Surveillance

- Regulation combines and incorporates current vigilance guidelines Electronic system
- Better coordination between national surveillance authorities
- Centralised reporting
- Member State market surveillance activities Procedures for problem & non-compliant devices uniformly
- Action against economic operators
- Empowerment of healthcare professionals and patients to report serious incidents at Member State level

Post Market Requirements

- Increased requirements for Post Market Surveillance
- The post-market surveillance plan includes
  - the process for collecting, recording and investigating complaints and reportable incidents
  - keeping a register of non conforming products and product recalls or withdrawals
  - if deemed appropriate sample testing of marketed devices
- Where post-market follow-up is not necessary
  - to be duly justified and documented in the post-market surveillance plan
- There is a provision to create registries for certain devices to gain post market information