Glass-Laser Multiplexed Biosensor

Regulatory framework for Medical Devices

Sandra Ferretti

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1. Medical Device Regulation (MDR)

2. In Vitro Diagnostics Regulation (IVDR)

The Medical Device Regulations (1 of 2)

REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT

AND OF THE COUNCIL

of 5 April 2017

on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC

The Medical Device Regulations (2 of 2)

REGULATION (EU) 2017/746 OF THE EUROPEAN PARLIAMENT

AND OF THE COUNCIL

of 5 April 2017

on *in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU*

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WHEN ? Date of Application (DoA)

- MDR : 26th May 2020
- IVDR : 26th May 2022

...But...

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Transitional periods

- Various transitional periods
- E.g. : The UDI carrier to be placed on the label & higher levels of packaging (Article 27.4):
  - From 26 May 2021 for Implants & Class III devices
  - From 26 May 2023 for Class IIa and IIb devices
  - From 26 May 2025 for Class I devices
  - The UDI carrier on the devices itself 2 years after the above dates for reusable devices

  => All certificates will have to be renewed

WHAT ? Main changes (1 of 3)

- Wider definition of medical devices and in-vitro diagnostics (larger scope)
- New risk classification system for in vitro diagnostic medical devices
- Stricter requirements for manufacturers - person responsible for regulatory compliance
- Stricter role and requirements for authorised representatives - person responsible for regulatory compliance

WHAT ? Main changes (2 of 3)

- Stricter control for high-risk devices - pre-market approval by experts group at EU level (scrutiny mechanism)
- Stricter designation criteria and monitoring by authorities over Notified Bodies
- Stricter rules on clinical evidence and EU-wide notification for clinical investigations authorizations

WHAT ? Main changes (3 of 3)

- EU registration database on medical devices and device Unique Device Identification (UDI) traceability system
- Stricter post-market surveillance requirements for manufacturers
- Better vigilance and market surveillance coordination between member-states

IVD Scope

The IVDR widens scope:

- genetic tests and companion diagnostics providing information essential for safe and effective use of a corresponding therapeutic product

- IVD testing services offered online (‘information society services’) or by other means of communication, directly/through intermediaries, not placed on the market but used in the context of a commercial activity, free or paid

IVD Scope

- New sections for software and requirements for use with mobile platforms
- IVDs for near-patient testing: Requirements are included for self test IVDs
- A part or component that significantly changes the performance or safety characteristics of an IVD device shall be considered an IVD device in its own right

New risk classification for IVD

Class A (low risk), Class B, Class C or Class D (High risk)

- Class D:
  - High Public health and Personal risk
  - **i.e.** Screening for transmissible agents and for high risk blood grouping for transfusion, transplantation, cell administration; life-threatening transmissible agents : Screening where possible high risk of propagation, and detection of infectious load where monitoring determines patient management e.g. Blood groups ABO, Rh, Kidd, Duffy, Kell; HIV1 and 2, HTLV I/II, Hep B and C, Chagas, screening blood for syphilis

New risk classification for IVD

Class A (low risk), Class B, Class C or Class D (High risk)

- Class C:
  - Public health risk moderate – low;
  - Personal risk low
  - **i.e.** Testing for compatibility for transfusion, transplantation, cell administration, excluding high risk blood grouping; tests for Infectious disease / STI agents / cancer biomarkers / Companion diagnostics / genetic testing / TORCH screening / congenital disorders / monitoring high risk medicines/substances e.g. blood glucose / most self test IVDs

New risk classification for IVD

- Class B:
  - Public health risk Low
  - Personal risk moderate to low
  - e.g. clinical chemistry tests, some specific self-test IVDs
  - Class B = default ruling if no other Rule applies.

- Class A:
  - Public health and personal risk low
  - e.g. Specimen receptacles; products for general lab use, accessories with no critical characteristics, buffers, washes, culture media, histological stains if intended for specific test; instruments intended for IVD procedures

New risk classification for IVD

- Before IVDR : **20 %** NB certificates required **-** 80% **NO** NB certificate required

>< After IVDR : **80 % NB certificate required**

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PRCC (Person Responsible for regulatory compliance)

- Manufacturers shall have permanently and continuously at their disposal at least one **person responsible for regulatory compliance** who possesses the requisite expertise regarding the regulatory requirements for medical devices in the Union.

- The responsibilities of the Responsible Person for the manufacturer are specified (Art 15.3).

PRRC (Person Responsible for Regulatory Compliance)

- “The person responsible for regulatory compliance shall suffer no disadvantage within the manufacturer's organisation in relation to the proper fulfilment of their duties, regardless of whether or not they are employees of the organisation”.

⇒ No pressure from management, no conflicting of interest ?

Stricter over Notified Bodies

- 5 years ago : about 80 NB
- Today : about 40 NB
- Tomorrow : ?
- Notified Bodies:
    - Obtain re-designation under the Regulation for all categories of devices
    - It is unlikely that all current NBs will be approved, some manufacturers will need to start with a new (tougher?) NB
    - Employ the additional staff required to meet all their additional obligations
    - Re-issue all certificates in accordance to the transition arrangements
    - NB charges will increase.

Will manufacturers be able to bear those additional costs for all devices currently on the market?

=> Start as early as possible !

Stricter rules on clinical evidence

- The MDR (article 61 and Annex XIV) reinforces clinical data and evaluation process.

- Manufacturers shall provide sound clinical data and evaluation to confirm the device conformity with essential health and safety requirements.

- The clinical evaluation proves and/or assesses:
  - –device safety
  - –device performance according to its intended purpose,
  - –undesirable side effects
  - –acceptability of the benefit-risk ratio.

Stricter rules on clinical evidence

•Manufacturers shall plan, conduct and document a clinical evaluation in accordance with Article 61 and Part A of Annex XIV.

Clinical data source:

- Published data on clinical experience with the device or equivalent
- Clinical investigation
- Clinical investigation with similar device
- Combination of the above

Stricter rules on clinical evidence

- Any medical device must go through clinical evaluation :
  - –Assessing clinical data
  - –Data shall be in conformity with the harmonized standards and essential requirements that have been established by the European Union.

- For all class IIb (Article 54(1)) and III devices, the manufacturer may, prior to its clinical evaluation and/or investigation, consult an **expert panel** with the aim of reviewing the manufacturer's intended clinical proposals for clinical investigation.

Stricter rules on clinical evidence

The clinical evaluation must follow a certain procedure based on either.

•A critical evaluation of the relevant scientific literature currently available evaluating the design characteristics, safety, and performance of the device all based on its intended use where:

1. there is demonstration of equivalence of the device to the device to which the data relates and
2. the data adequately demonstrates compliance with the relevant safety and performance requirements

Stricter rules on clinical evidence

•A **critical evaluation** of results of all clinical investigations made with a consideration of **alternative treatment** options currently available.

•When a clinical data not deemed appropriate, there must be **adequate justification based on risk management** output and under consideration of the specifics of the device/body interaction, the performances intended and claims of the manufacturer.

PMCFU

- The clinical evaluation shall be **updated**
- throughout the life cycle of the device
- with clinical data obtained from the implementation of the manufacturer's **PMCF plan** (Part B of Annex XIV) and the **post-market surveillance plan** (Article 84).

Scrutiny mechanism for high risk devices

•For all class IIb (Article 54(1)) and III devices, the manufacturer may, prior to its clinical evaluation and/or investigation, consult an **expert panel** with the aim of reviewing the manufacturer's intended clinical proposals for clinical investigation.

•For class III and implantable devices, a PMCF evaluation report shall be updated yearly, and a **summary** of the safety and clinical performance shall be **uploaded to the EUDAMED** and updated yearly.

EUDAMED & UDI

- Before placing a device, other than a custom-made device, on the market, manufacturers must register on the EUDAMED database
- The CA will verify the data submitted
- The data entered in the electronic system shall be accessible to the public.
- The competent authority may use the data to charge a fee to the manufacturer, the authorised representative or the importer !!!

EUDAMED & UDI

- EUDAMED database to be available to the general public

- EUDAMED will :
  - Allow registration of operators and devices (SRN & UDI)
  - Allow registration of NB certificates
  - allow direct reporting of incidents
  - include clinical investigation submissions

EUDAMED & UDI

- Assign Basic UDI-DI code (Unique Device Identification – Device Identification) in EUDAMED before applying to the NB for Conformity assessment (Art 29, registration requirements Art 29 + 31)

- Before placing a device on the market, the manufacturer must verify that the UDI is in the database and up to date

- Devices designed or manufactured by a 3rd party, that person must be identified in Eudamed (Art 30.1)

Stricter post-market surveillance requirements

- The clinical evaluation shall be updated throughout the life cycle of the device

Better vigilance and market surveillance coordination between member-states

- With EUDAMED
- With Competent authorities

The Manufacturers have much to do 1 of 5

- Appoint an AR if they have no registered place of business in the EU
- The manufacturer (& AR) must appoint :
  - at least one person with the requisite qualifications as responsible for regulatory compliance
- Manufacturers shall :
  - proportionate to the risk class, type of device and the size of the enterprise,
  - have measures in place to provide **sufficient financial coverage** in respect of their potential liability

The Manufacturers have much to do 2 of 5

- Greatly expanded clinical evaluation
- Vigilance and reporting of incidents (Art 87 and 88)
- Post Marketing Surveillance (Art 83)
- Post Market Clinical Follow-Up
- Labelling (Annex I.23)

The Manufacturers have much to do 3 of 5

- The manufacturer of implantable devices (except sutures, staples, dental fillings, dental braces, tooth crowns, screws, wedges, plates, wires, pins, clips and connectors) shall provide together with the device the following:
  - information allowing the identification of the device, including the device name, serial number, lot number, the UDI, the device model, as well as the name, address and the website of the manufacturer

=> Traceability !

The Manufacturers have much to do 4 of 5

Continuing implant requirements. The manufacturer shall provide:

- Intended purpose
- any warnings, precautions or measures to be taken by the patient or a healthcare professional with regard to reciprocal interference with reasonably foreseeable external influences, medical examinations or environmental conditions;
- any information about the expected **lifetime** of the device and any necessary follow-up;
- any other information to **ensure safe use** of the device by the patient, including the overall qualitative and quantitative information on the materials and **substances** to which patients can be **exposed** (Annex I, Section 23.4 (u))
- Clinical Evaluation

The Manufacturers have much to do 5 of 5

- Revise / Re-write
  - Technical Documentation (update references to the Regulation, new requirements, retain for 10 years or 15 years for implants after last device placed on the market)
  - Expanded Essential Safety & Performance Requirements (Annex I)
  - Risk Analysis
  - Clinical Evaluation
  - Declaration of Conformity
  - QMS

The Manufacturers have much to do 5 of 5

- Submit their data and that of the device to the database so the CA can verify it and obtain a Single Registration Number (SRN)
- This is required before the manufacturer can apply to the NB
- Obtain new certificates from the NB

Quality Management System (QMS)

- To set-up procedures ensuring production conforms with the requirements of the Regulation.

- Constantly take into account changes in design or characteristics and changes in the relevant harmonised standards or CS.

The QMS Includes 1 of 5

(a) a strategy for regulatory compliance, including compliance with conformity assessment procedures and procedures for management of modifications to the devices covered by the system;

(b) identification of applicable general safety and performance requirements and exploration of options to address those requirements;

The QMS Includes 2 of 5

(c) responsibility of the management;

(d) resource management, including selection and control of suppliers and sub-contractors;

(e) risk management (Annex I Section 3);

(f) clinical evaluation in accordance with Article 61 and Annex XIV, including PMCF;

The QMS Includes 3 of 5

(g) product realisation, including planning, design, development, production and service provision;

(h) verification of the UDI assignments made for the devices and ensuring consistency and validity of information provided (Article 27.3, Article 29);

(i) setting-up, implementing and maintaining a post-market surveillance system (Article 83);

The QMS Includes 4 of 5

(j) handling communication with competent authorities, notified bodies, other economic operators, customers and/or other stakeholders;

(k) processes for reporting of serious incidents and field safety corrective actions in the context of vigilance;

(l) management of corrective and preventive actions and verification of their effectiveness;

(m) processes for monitoring and measurement of output, data analysis and product improvement.

ISO 13485

- THE quality management system standard for medical devices (including IVDs)

=> Will the QMS requirements in the MDR - IVDR be in line with ISO 13485 ?

Challenges & Priorities 1 of 3

- Eudamed
- UDI system
- NBOG codes
- Reference labs
- Expert panels
- Implementing / delegated acts (43 in total),
- Guidance
- Common Specifications
- Re-Harmonise the standards after updating

Many Questions Remain

- Which NBs will be accredited under the new Regulation?
- NBs will have so many devices to re-certify before the deadline and are known to be short staffed, will some devices fail to meet the deadline in the given time?
- Will the many changes to EUDAMED be completed in time?
- No devices can be made available under the Regulation until the manufacturer has received its Single Registration Number (SRN)
- Manufacturers need to upgrade the technical documentation

=> PLAN !

Conclusions

- Still a lot of unknown factors (implementing and delegated acts)
- Time to market might be longer !
- Innovation ?...

OBELIS SERVICES for MDR - IVDR – H2020

- Person Responsible for Regulatory Compliance
- Regulatory strategy and conformity assessment route
- Quality management system (preparation and internal auditing).
- Technical documentation including clinical evaluation and risk management
- Manufacturer & devices registration
- Notified body selection and handling
- CE declaration of conformity

Thank you for your attention!

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