European IVD Regulations and Risk Based Classification

An Overview for Global Quality Professionals

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Caution

• The new regulations are draft and subject to change

• Further details will be added later pre and post application through implementing and delegating legislation
Why?
Background to the changes

- Discovery of a 16 year fraud in PIP breast implants using low quality “industrial grade” silicon oil
- Stress test performed by EU Commission
- Determine that changes were needed to improve early detection and prevent this type if incident
- Other high profile vigilance cases with hips, pelvic floor meshes, pacemaker leads, etc.

Outcome

- Short term changes proposed to the system:
  - Increased market surveillance
  - Additional unannounced visits on top of regular audits
  - Identify a person who is responsible for regulatory compliance
What?
IVDD will become a regulation

**Impact of becoming a regulation**

- Direct entry into force
- No Transposition period
  - No need for transposition into national law
- There will be a transition period 3 years reduced from 5 in the first draft
- There has been some discussion to reduce this to 3 years in line with the MDR
- A regulation should result in more consistent application
- The regulation identifies areas which can be updated in the future using additional implementing acts according to Article 84(3)
Structure of the IVDR

**Chapters** 10

**Articles** 90

**Annexes** 14

**Annex I**  General Safety and Performance Requirements

- Equivalent to the current essential requirement
- Broadly similar with additional clarification
- New sections for software and requirements for use with mobile platforms
- Requirements for self tests are extended to include near patient testing

**Annex II**  Technical documentation

- Significantly more detail regarding the expectations for technical documentation

**Annex III**  Declaration of Conformity

**Annex IV**  CE marking

**Annex V**  Registration and UDI

**Annex VI**  Requirements for Notified Bodies

**Annex VII**  Classification

**Annex VIII**  Conformity Assessment based on Full QA or Design Examination

**Annex IX**  Conformity Assessment based on Type Examination

**Annex X**  Conformity Assessment based on Production QA

**Annex XI**  Notified Bodies Certificate content

**Annex XII**  Clinical Evidence and Post Market Follow up

**Annex XIII**  Interventional Clinical Performance Studies

**Annex XIV**  Correlation table

More detailed consistent with the proposed MDR
When?
Legislative process - overview

September 2012 – October 2013

Agreement: Legislation into force

First reading discussions close

Q4 2014

Rejected: Second reading in Council or removed

September 2012 – December 2014

26 September 2012
Legislative process – Scenario One

26 September 2012
European Commission submits proposal to EP and Council

18 June 2013
IMCO vote*

18 Sep 2013
ENVI vote*

Q4 2013 – Q2 2013
Intensified discussions and analysis in the Council

Q4 2014
Legislation finalised

Sep 2012 – May 2013
EP review

21 June 2013
EMPL vote*

22 Oct 2013
Plenary vote on final EP

May 2014
Consensus reached – end of First Reading

* IMCO and EMPL vote only on their own amendments, the ENVI Committee votes on all amendments.
Legislative process – Scenario Two

- **26 September 2012**: European Commission submits proposal to EP and Council
- **18 June 2013**: IMCO vote*
- **18 Sep 2013**: ENVI vote*
- **Q4 2013 – Q2 2014**: Discussions and analysis in the Council
- **Q3 2014 – Q1 2015**: Council discussions continue
- **Q3 2015**: Legislation finalised

**Timeline:**
- **Sep 2012 – May 2013**: EP review
- **21 June 2013**: EMPL vote*
- **Oct/Nov 2013**: Plenary vote on final EP
- **May 2014**: Consensus NOT reached
- **Q1 2015**: Consensus reached - end of 1st Reading
Timeline

ENVI Vote → Plenary Vote → Council → Second Reading

Adoption → Implementing Acts → Transition → Enforced

2014-2015 → 3 Years → 2018-2020
Managing the transition

Entry into Force

- NB designation (6 months)
- Implementing measures (12 months)
- Cooperation Between Authorities (12 months)
- Unique Device Identification Systems (UDI) (18 months)
- New Vigilance Procedures (24 months)
- New conformity assessment procedures, including use of clinical evidence (TBD)
The Basics of the IVDR
Classification and Conformity
Classification

Class D (Blood screening)

- Devices intended to be used to detect the presence of, or exposure to,
  - a transmissible agent in blood, blood components, cells, tissues or organs, or in any of their derivatives, in order to assess their suitability for transfusion or transplantation.
  - a transmissible agent that causes a life-threatening disease with a high or currently undefined risk of propagation
- Blood grouping ABO, Rhesus, Kell, Kidd and Duffy systems

Class C

Devices intended for

- detecting the presence of, or exposure to, a sexually transmitted agent;
- detecting the presence in cerebrospinal fluid or blood of an infectious agent with a risk of limited propagation;
- detecting the presence of an infectious agent, if there is a significant risk that an erroneous result would cause death or severe disability to the individual or foetus, or to the individual's offspring;
- pre-natal screening of women in order to determine their immune status towards transmissible agents;
- determining infective disease status or immune status, if there is a risk that an erroneous result would lead to a patient management decision resulting in an imminent life-threatening situation for the patient or for the patient's offspring;
Classification

Class C (Continued)

- selection of patients, *i.e.*
  - Devices intended to be used as *companion diagnostics*; or
  - Devices intended to be used for disease staging; or
  - Devices intended to be used in *screening for or in the diagnosis of cancer*.
- *human genetic testing*;
- *monitoring of levels of medicinal products, substances or biological components, when there is a risk that an erroneous result will lead to a patient management decision resulting in an imminent life-threatening situation for the patient or for the patient's offspring*;
- management of patients suffering from a *life-threatening infectious disease*;
- screening for congenital disorders in the foetus
- Devices intended for *self-testing* are classified as class C, except those devices from which the result is not determining a medically critical status, or is preliminary and requires follow-up with the appropriate laboratory test in which case they are Class B.
- devices intended for blood gases and blood glucose determinations for *near patient testing* are class C.

Other devices that are intended for near-patient testing shall be classified in their own right.

*Companion diagnostic* means a device specifically intended to select patients with a previously diagnosed condition or predisposition as eligible for a targeted therapy

*Device for near-patient testing* means any device that is not intended for self-testing but is intended to perform testing outside a laboratory environment, generally near to, or at the side of, the patient;
Classification

Class B
• Any IVD not listed under Classes D, C or A.
• Controls without an assigned value.

Class A
• Reagents, other articles with specific characteristics.
• Instruments intended specifically for use in IVD procedures.
• Specimen receptacles.

There will be clarification to the classification but no substantial change
Note Class D devices regardless of whether they are used in a single healthcare institution must meet the regulation with the exception of the requirements for economic operators unless there is no CE marked device. Class A, B + C devices used within a single healthcare institution which have a single quality management system compliant with ISO 15189 (Medical laboratories - Particular requirements for quality and competence) may be exempt from the majority of the regulation; however, they must report adverse incidents.
Designation of Notified Bodies and Special NBs

Notified Body
Class B
& Class C

No Notified Body
Class A

Special Notified Body
Class D
Additional Requirements for Class D Devices

Summary of safety and performance
High risk devices (Class C and D) devices will require a summary of safety and performance which will be available to the public and should be clear to the intended user.

SUBJECT TO DISCUSSION
• Highly likely to be some form of scrutiny for selected high risk devices
• Changed from the Medical Device Coordination Group (MDCG) to the Assessment Committee of Medical Devices (ACMD)
• There will be delays compared to the current process
• There may be additional fees
Quantum Leap

**IVD Directive**
- Require a Notified Body
- Do not require a Notified Body 80-90%

**IVD Regulation**
- Require a Notified Body 80-90%
- Do not require a Notified Body
Latest Changes and Hot topics
Latest Changes introduced by the amendments

- Transition Period
- Clinical expectations including Ethics & Informed consent
- Transparency
- Control Notified bodies
- In house testing
- Control of the supply chain
- Unannounced visits
Clinical Expectations
Clinical Evidence

- Increased expectation for clinical requirements
- Clinical evidence is to be kept up to date during the life time of the device

![Diagram showing relationships between Clinical Evidence, Scientific Validity, and Clinical Utility]
Interventional studies

• New requirements for interventional clinical performance studies and other performance studies involving risk’s for the subjects of the studies
• In the IVDD there was an assumption that IVD studies did not create a risk to the patient.
• Due to the advent of Companion Diagnostics and genetic testing this is no longer the case
• IVDR includes requirements for ethics committee approvals
• New requirements detailing the requirements to protect the rights of minors and the incapacitated during such studies which could impact prenatal and neonatal testing
• New requirements addressing the need to supply genetic counselling especially to minors for genetic diseases which do not develop till adulthood. These requirements are directed to the members state not industry or the notified bodies
Transparency

- There was a huge loss of confidence post PIP
- There are measures throughout the IVDR to increase transparency including
  - Summary of safety and performance to be publically available for class C + D devices
  - Lists of manufacturers subcontractors to be available on the registration database
  - Audit reports of Notified Bodies to be publically available
  - Some notified body procedures to be publically available
  - Lists of notified body sub contractors and external experts including their declarations of interest to be publically available
Control of Notified Bodies

- 2 types of notified body
- Increased requirements for in-house staff
- Increased training requirements
- Joint audits by the Commission and more than one CA
- Unannounced visits by the CA of notified bodies
Person Responsible for Regulatory Compliance

• Manufacturers shall have available within their organisation at least one person responsible for regulatory compliance who possesses the requisite expertise in the field of in vitro diagnostic medical devices.

• This will include:
  • a degree or equivalent in natural sciences, medicine, pharmacy, engineering or law
  • or 3 years of professional experience in regulatory affairs or in QMS relating to IVDs

• The person responsible for regulatory compliance is responsible for ensuring:
  • that the conformity of the devices is appropriately assessed before a batch is released;
  • that the technical documentation and the declaration of conformity are drawn up and kept up-to-date;
  • that vigilance requirements have been fulfilled.
  • for performance evaluation for interventional studies

• If compliance is share between more than one person responsibilities will be defined in writing

• This person should suffer no disadvantage by performing their role

• Authorised representatives will also be required to have a person responsible for regulatory compliance within their organisation.
Increased Control of the Supply Chain

Manufacturer

Crucial Suppliers
OEM’s
Sub contractors

Distributers
Importers
Authorised Representatives
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 as well as significant subcontractors including unannounced visits
- Changes to contracts will be required
- Increased role in vigilance and recall for Importers, Distributors and Authorised Representatives
- Required to have a Person responsible for regulatory compliance
- Manufacturers now have to have liability insurance but importers required to check this is adequate or take out their own
Final Summary

• This is happening
• There is no grandfathering
• Requirements and expectations are increasing
• Keep up to speed and understand the impact to organisations
• Take into consideration your notified body’s plans for designation and resource
• Classify devices
• Look at clinical data held, is it enough?
• Discuss at management reviews
Any Questions
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