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IVD Regulation 2017/746

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Recast-symposium
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IVD medical device Regulation
Points covered

* From Directives to Regulation
* Key points
    - Horizontal aspects
    - IVD specific aspects
* Clinical performance and clinical evidence
* Companion diagnostics
* Timelines
* End notes

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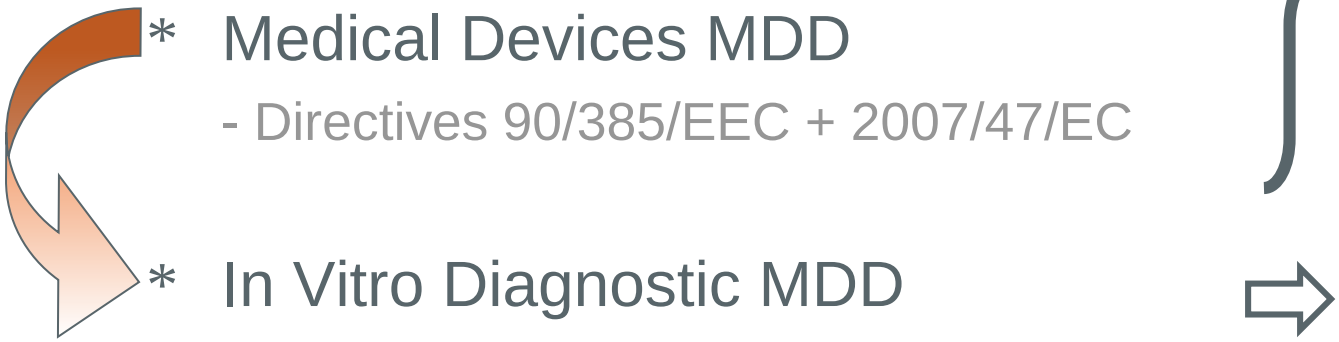
EU Medical Device Legislation

three Medical Device Directives

* Active Implantable MDD
  - Directives 90/385/EEC + 2007/47/EC

* Medical Devices MDD
  - Directives 90/385/EEC + 2007/47/EC

* In Vitro Diagnostic MDD
  - Directive 98/79/EC



Regulation 2017/745

⇨ ***Regulation 2017/746***

From Directives to Regulation (1)

Public consultation 'Recast' 2008

Public consultation 'IVD' 2010

- Questions: input from *Ad hoc* group
  → analysing the specific needs
  → technical aspects of IVD medical devices

Special MDEG meetings 2012

Recast mirror group

- *Ad hoc* group from CAMD

From Directives to Regulation (2)

Proposal for an IVD Regulation by Commission

26-09-2012

Amendments adopted by the European Parliament

22-10-2013

Council Working Party reached General Approach

05-10-2015

Consolidated compromise text

15-06-2016

IVD Regulation 2017/746

Regulation (EU) 2017/746 on in vitro diagnostic medical devices

and

repealing Directive 98/79/EC and Commission Decision 2010/227/EU

Official Journal of the European Union, L 117, **5 May 2017**

http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:L:2017:117:TOC

IVD medical device Regulation
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IVD medical device Regulation
Key points

Horizontal aspect:

- alignment IVD and MD Regulation

Specific modifications

- taking account of the specificities of the IVD

IVD medical device Regulation
Horizontal aspect

- Notified bodies
- Economic operators
- Post-Market surveillance
- Vigilance
- Market surveillance
- Traceability, UDI and registration
- Summary of safety and performance
- Transparency

IVD medical device Regulation
Horizontal aspect - what is new ?

- Notified bodies
- Economic operators
- Post-Market surveillance
- Vigilance
- Market surveillance
- Traceability, UDI and registration
- Summary of safety and performance
- Transparency

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IVD medical device Regulation
IVD: Definition

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

IVD medical device Regulation
IVD: Definition (cont.)

… 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.

IVD medical device Regulation Scope (1)

Scope and definitions

- Enlargement
  - **to define** or monitor therapeutic measures

- Clarification
  - **software** ... for the purpose of providing information…
  - **predisposition** to a medical condition or disease
  - to predict **treatment response or reaction**
  - **service** providers

IVD medical device Regulation Scope (2)

'In house' - home brew devices

Manufacture and use within single EU health institution

Not manufactured on an industrial scale

* **Annex I is applicable**
  = general safety and performance requirements

* **Class D: document- manufacturing facility,**
  - manufacturing process,
  - design and performance data

IVD medical device Regulation
Specific for IVD

Provisions taking into account specific risks

- Classification rules
  - class D > class C > class B > class A
- Conformity assessment
  - reference laboratory / experts / medicines agency
  - technical documentation examination
- Devices for self-testing
- Devices for near-patient testing
- Companion diagnostics

IVD medical device Regulation
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IVD medical device Regulation
Clinical evidence - Recital (61)

To ensure a high level of safety and performance, demonstration of compliance with the general safety and performance requirements laid down in this Regulation should be based on clinical evidence. It is necessary to clarify the requirements for the demonstration of the clinical evidence, that is

based on data on scientific validity, and the analytical performance and clinical performance of the device.

To allow for a structured and transparent process, generating reliable and robust data, sourcing and assessment of available scientific information and data generated in performance studies should be based on a performance evaluation plan.

IVD medical device Regulation
Scientific validity

Definition **(38)**:

“the association of an analyte with a clinical condition or a physiological state”

IVD medical device Regulation
Analytical performance

Annex I, point 9.1 (a)

such as, analytical sensitivity, analytical specificity, trueness (bias), precision (repeatability and reproducibility), accuracy (resulting from trueness and precision), limits of detection and quantitation, measuring range, linearity, cut-off, including determination of appropriate criteria for specimen collection and handling and control of known relevant endogenous and exogenous interference, cross- reactions

IVD medical device Regulation
Clinical performance

Annex I, point 9.1 (b)

such as diagnostic sensitivity, diagnostic specificity, positive predictive value, negative predictive value, likelihood ratio, expected values in normal and affected populations

IVD medical device Regulation
Clinical evidence - Recital (61)

To ensure a high level of safety and performance, demonstration of compliance with the general safety and performance requirements laid down in this Regulation should be based on clinical evidence. It is necessary to clarify the requirements for the demonstration of the clinical evidence, that is based on data on scientific validity, and the analytical performance and clinical performance of the device. To allow for a structured and transparent process, generating reliable and robust data, sourcing and assessment of available scientific information and data generated in performance studies should be **based on a performance evaluation plan**.

IVD medical device Regulation
PMPF - Recital (63)

Post-Market Performance Follow-up PMPF

It is necessary to ensure that the clinical evidence of devices is updated throughout their lifecycle. Such updating entails the **planned monitoring of scientific developments and changes in medical practice by the manufacturer**. Relevant new information should then trigger a reassessment of the clinical evidence of the device thus ensuring safety and performance through a continuous process of performance evaluation.

IVD medical device Regulation PMPF - Recital (63)

Post-Market Performance Follow-up PMPF

It is necessary to ensure that the clinical evidence of devices is updated throughout their lifecycle. Such updating entails the planned monitoring of scientific developments and changes in medical practice by the manufacturer. Relevant new information should then **trigger a reassessment** of the clinical evidence of the device thus ensuring safety and performance through a **continuous process** of performance evaluation.

IVD medical device Regulation
Clinical evidence

Performance evaluation

- performance evaluation report
  - scientific validity
  - analytical performance
  - clinical performance
  - **clinical evidence**

- post market performance follow-up

Chapter VI, Art 56.3 – Annex XIII
Performance evaluation – plan –

a defined and methodologically sound procedure

to demonstrate

scientific validity	**analytical performance**	**clinical performance**
		
analyte ⟺ information IVD	*correctly detect / measure*	*patient ⟺ information IVD*

Clinical evidence ???

scientific validity

analytical performance

clinical performance

conclusions drawn from the assessment

Chapter VI, Art 56.3
Clinical evidence

… such as to **scientifically demonstrate**, by reference to the **state of the art in medicine**, that, under normal conditions of use:

- intended **clinical benefit(s)** will be achieved
- device is **safe**
- general safety and performance requirements of **Annex I** are fulfilled

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IVD medical device Regulation
Companion diagnostics - definition

a device which is essential for the safe and effective use of a corresponding medicinal product to:

- identify, before and/or during treatment, patients who are most likely to benefit from the corresponding medicinal product; or

- identify, before and/or during treatment, patients likely to be at increased risk of serious adverse reactions as a result of treatment with the corresponding medicinal product

IVD medical device Regulation
Companion diagnostics - recitals

Additional information

- quantitative or qualitative determination
- specific biomarker(s) in healthy subjects or patients

Not considered companion diagnostics:

- monitoring a treatment with a medicinal product in order to ensure that the concentration of relevant substances in the human body is within the therapeutic window

IVD medical device Regulation
Companion diagnostics – classification

Annex VIII, Rule 3

Devices are classified as **class C** if they are intended:

(f) to be used as companion diagnostics

If Annex VIII, Rule 1 and 2

- multiple intended purposes
- several classification rules apply

→ classified as **class D**

IVD medical device Regulation
Companion diagnostics – conformity

QMS + assessment of the technical documentation

or

production quality assurance + type examination

+ opinion medicinal products authority
* Member State
* EMA

<u>If</u> class D

+ EU reference laboratories +/- experts opinion

IVD medical device Regulation
CDx - performance evaluation studies

Performance studies on left over samples *notification*

- comply with the general requirements apart aspects studied
- correct design and conduct
- data protection

Other performance studies with CDx *authorisation*

+ ethical considerations
+ performance study plan (design/objectives/hypotheses)
+ performance study report

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IVD medical device Regulation Timelines

25/05/2017

26/05/2022

IVD medical device Regulation Interpretation requested

* Article 110 – Transitional provisions
* Article 112 – Repeal
* Article 113 – Entry into force and date of application

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IVD medical device Regulation
End notes

- clear scope and delineation
- provisions with sufficient level of detail
- defining the responsibilities
- cooperation
- clear classification rules
- intended use - performance - clinical evidence
- trust in products
- trust in conformity assessment
- transparency

Thank you

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