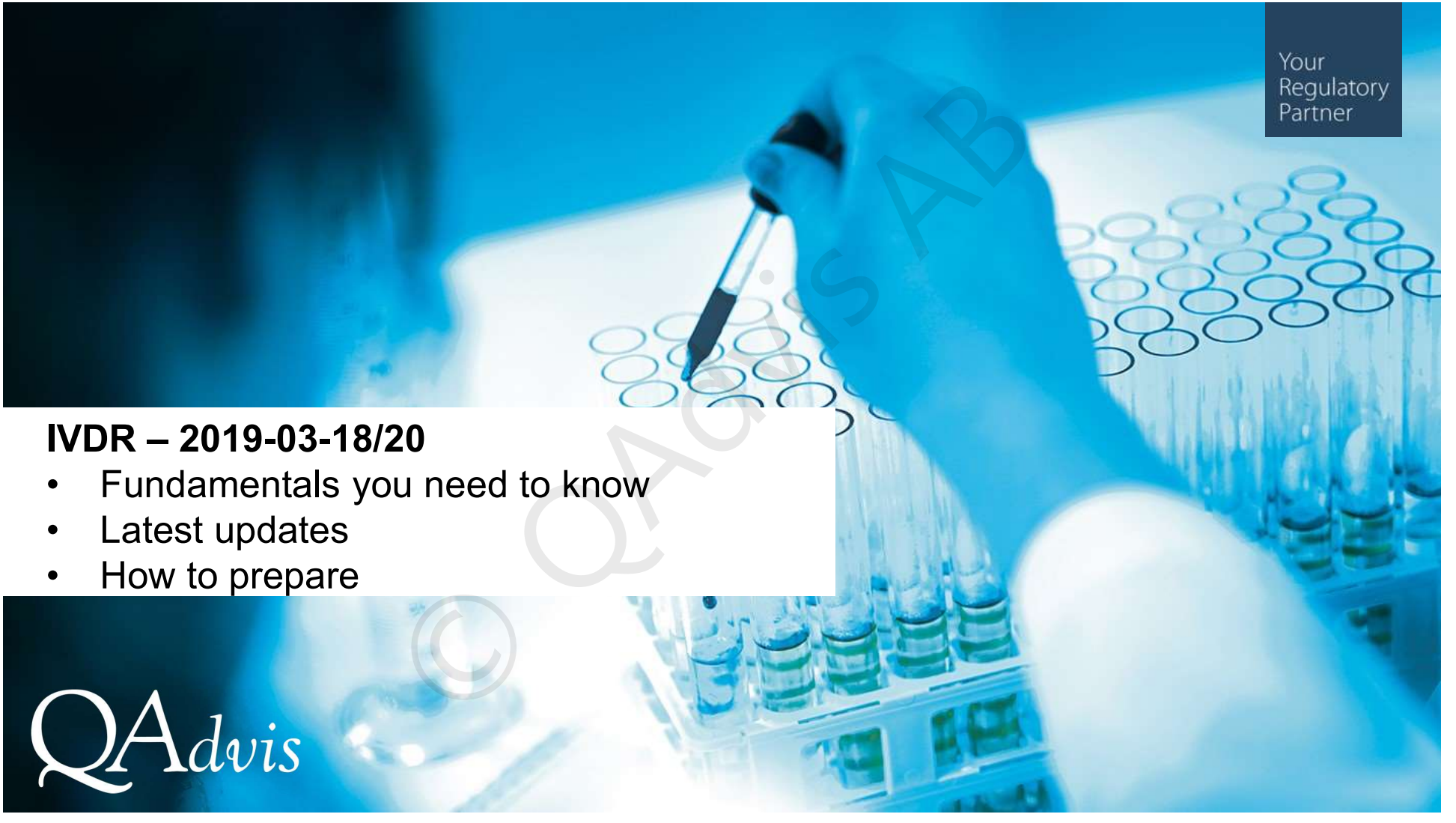

IVDR – 2019-03-18/20

- Fundamentals you need to know
- Latest updates
- How to prepare

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QAdvis – Key competence areas

QMS In-the-cloud

Turn Key QMS
Digital Signatures
Efficient and Lean

System Development

Product Software Validation
Computer Systems Validation
Risk Management
Verification and Validation
Process Validation

European Authorised Representation

Providing European representation for non-EU MedTech companies
Active member of EAAR (European Association of Authorized Reps)

Training/Courses

CE-Marking, MDR, IVDR
ISO 13485 & QSR & MDSAP
IEC 62304 & IEC 82304-1
IEC 60601-1
IEC 62366-1
Risk Management
And more…

Agile, Lean and Six Sigma

Training and consulting in cooperation with US partner

QA&RA/Clinical Consulting

Interim Management, Expert Advise
Audits/Mock audit/Due Diligence
Warning Letters, Compliance Projects
PMA, 510k, CE-Marking, Tech Files
Global Regulatory Support
Vigilance, Recalls, PMS
Clinical Evaluation and Clinical Studies

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Presentation of the speaker – Anna-Karin Areskog

Senior Quality and Regulatory Consultant

Experiences within

- QA Manager
- IVDD/IVDR and MDD/MDR
- GMP, ISO13485, QSR 21CFR 820
- Internal and external audits

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Presentation of the speaker - Emma Axelsson

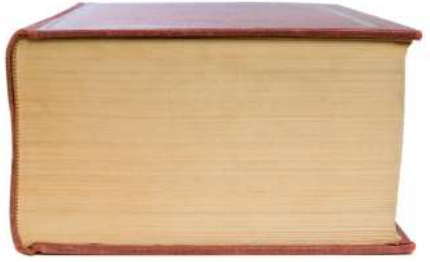
- Quality and regulatory consultant for medical devices and in vitro diagnostics
- Quality and Regulatory Manager medical device company
- Quality management system (ISO 13485:2016)
- Medical Device Directive (MDD) and Medical Device Regulations (MDR)
- In Vitro Diagnostic Regulation (IVDR)

BACKGROUND

Background

- MDD, AIMDD and IVDD old
- Technological and scientific development
- Different interpretations in Member States
- Scandals
- Product traceability

Background



- Directives
  - AIMDD
    (90/385/EEG, LVFS 2001:5)
  - MDD
    (93/42/EG, LVFS 2003:11)

  MDR 2017/745
- Directive
  - IVDD
    (98/79/EG, LVFS 2001:7)

  IVDR 2017/746

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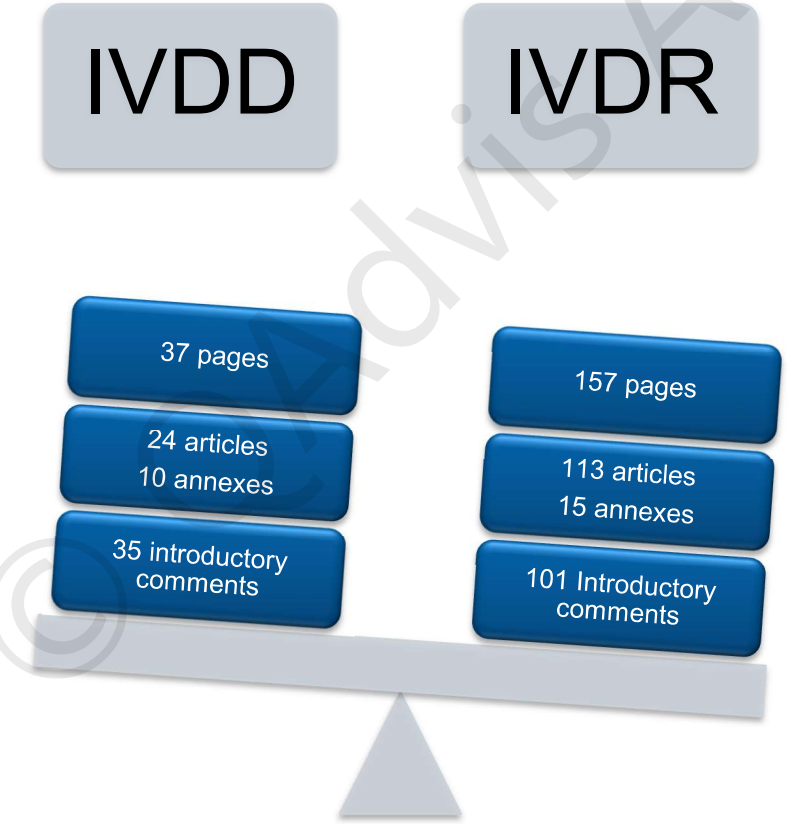
Overview



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Transitional provisions

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IN VITRO DIAGNOSTIC REGULATION (IVDR)

Definition
Common specifications (CS)

"*Means a set of technical and/or clinical requirements, other than a standard that provides a means of complying with the legal obligations applicable to a device, process or system.*"

When there are no harmonized standards or the harmonized standards are not sufficient, the Commission can adopt a common specification.

(MDR Article 2 (71) / IVDR Article 2(74))

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Definition
Delegated and implementing acts

Delegated acts

Acts used to modify and explain the WHAT in regulation implementation.

Implementing acts

Acts used to clarify and explain HOW the regulation should be interpreted and used.

(MDR/IVDR)

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Definition
Person Responsible for Regulatory Compliance (PRRC)

Manufacturer shall have available within their organization at least one person responsible for regulatory compliance.

"The person responsible for regulatory compliance shall suffer no disadvantage within the manufacturer's organization in relation to the proper fulfilment of his or her duties, regardless of whether or not they are employees of the organization."

(MDR/IVDR Article 15)

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Definition
Economic operator

- Responsibilities and authorities
- Control of each other
- Eudamed
- Importers – name and address on device, packaging or accompanying documentation

(MDR/IVDR Article 10, 11, 13, 14)

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Technical Documentation - Overview

- General Safety and Performance Requirements (GSPR) (Annex I)
- Technical Documentation (Annex II)
- Technical Documentation on PMS (Annex III)
- Declaration of Conformity (DoC) (Annex IV)
- Performance evaluation, performance studies and post-market performance follow-up (Annex XIII)
- Interventional clinical performance studies and certain other performance studies (Annex XIV)

(IVDR Annex I, II, III, IV, XIII, XIV)

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General Safety and Performance Requirements (GSPR)

- Change from IVDD Essential Requirements (ER) to General Safety and Performance Requirements (GSPR)
- Checklist recommended
- Method of compliance
- Reference to evidence of compliance

(IVDR Annex I)

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General Safety and Performance Requirements (GSPR)

- General Requirements (GSPR 1-8)
- Requirements regarding Performance, Design and Manufacture (GSPR 9-19)
- Requirements regarding information supplied with the device (GSPR 20)

(IVDR Annex I)

Classification rules - 7 rules and 4 classes

A. Low individual risk and low public health risk
B. Moderate individual risk and/or low public health risk
C. High individual risk and/or moderate public health risk
D. High individual risk and/or high public health risk.

Based on intended purpose for the device.

(Annex VIII)

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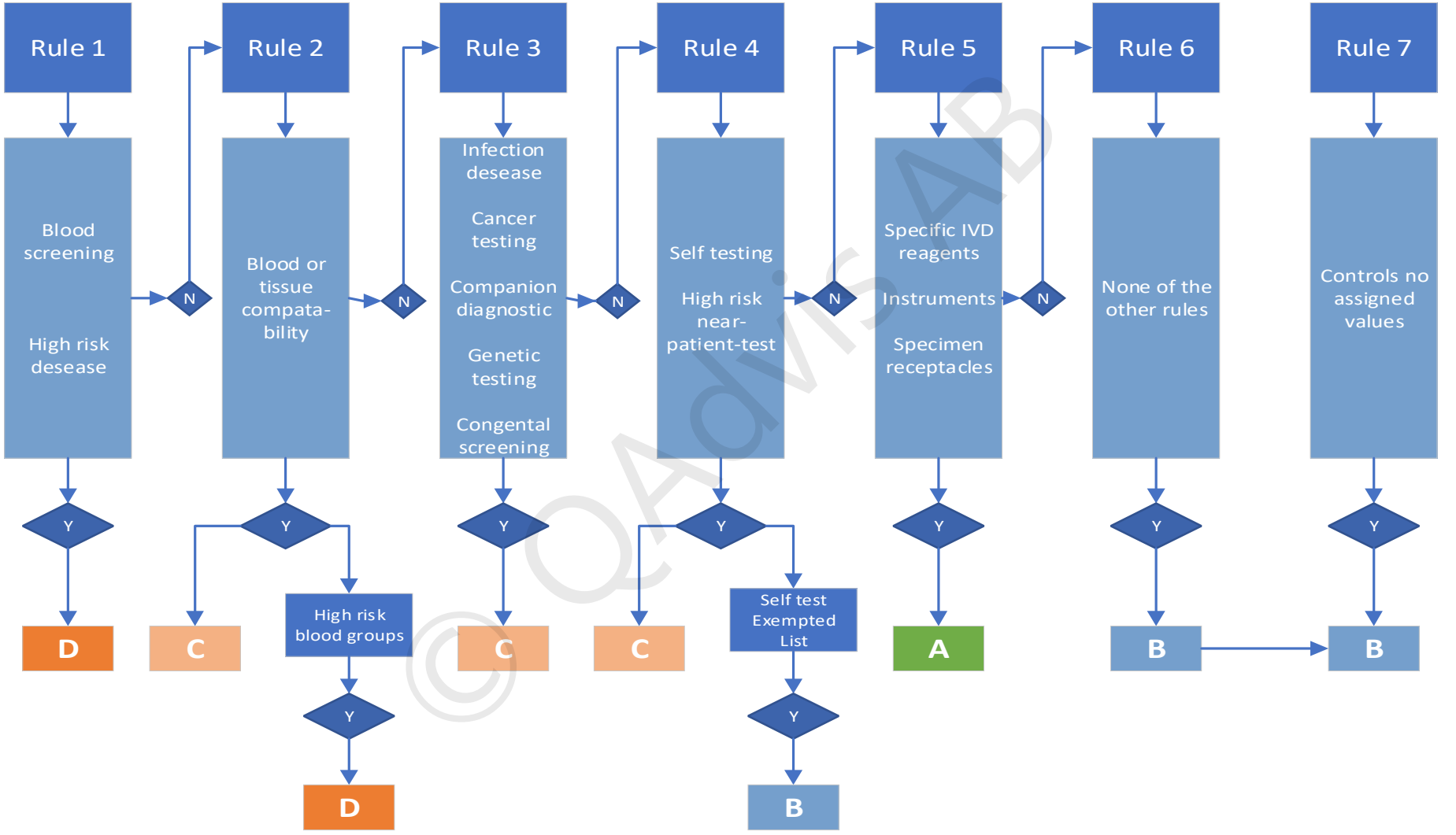
Rule 1
Blood screening
High risk desease
N
Y
D
Rule 2
Blood or tissue compata-bility
N
Y
C
High risk blood groups
Y
D
Rule 3
Infection desease
Cancer testing
Companion diagnostic
Genetic testing
Congental screening
N
Y
C
Rule 4
Self testing
High risk near-patient-test
N
Y
C
Self test Exempted List
Y
B
Rule 5
Specific IVD reagents
Instruments
Specimen receptacles
N
Y
A
Rule 6
None of the other rules
Y
B
Rule 7
Controls no assigned values
Y
B

Conformity route

- Conformity route to be selected for each device category – different routs to chose between depending on classification and type of device
- Involvement of Notified Body differs depending on assessment route and device classification

(MDR Article 52 / IVDR Article 48)

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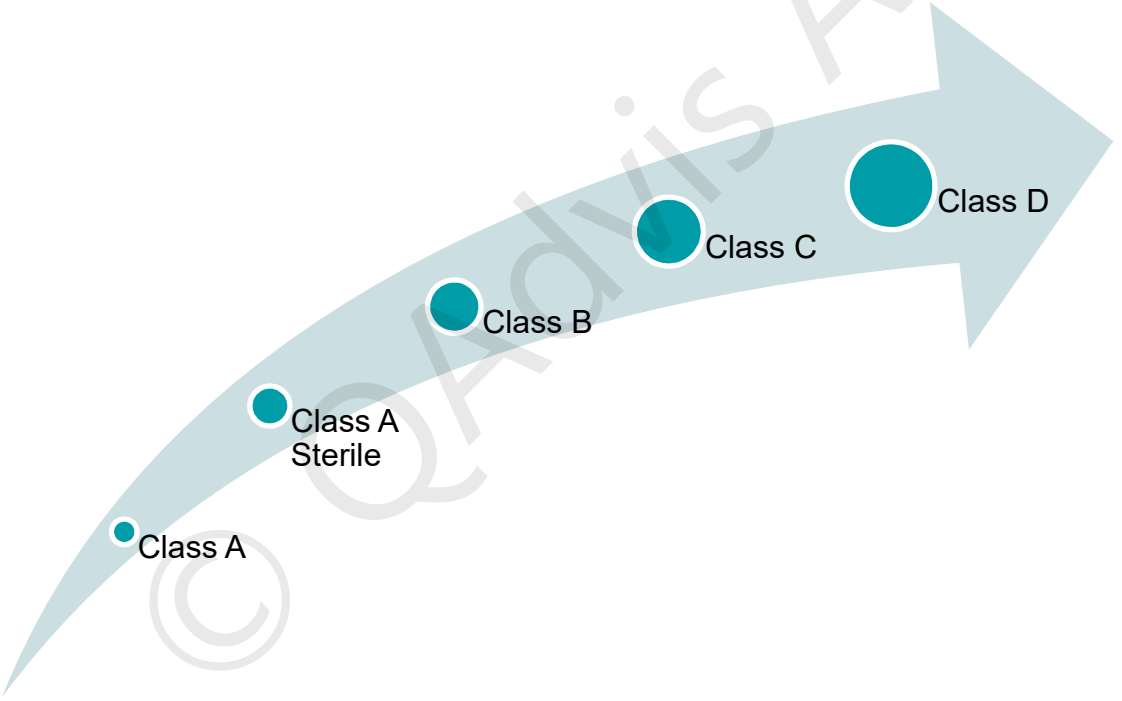
Conformity route – involvement of Notified Body



(IVDR Article 48)

Performance evaluation

- Intended purpose and intended use
- Regulatory context
- Performance evaluation – general
- Clinical performance evaluation – what's new?
- Where to start?

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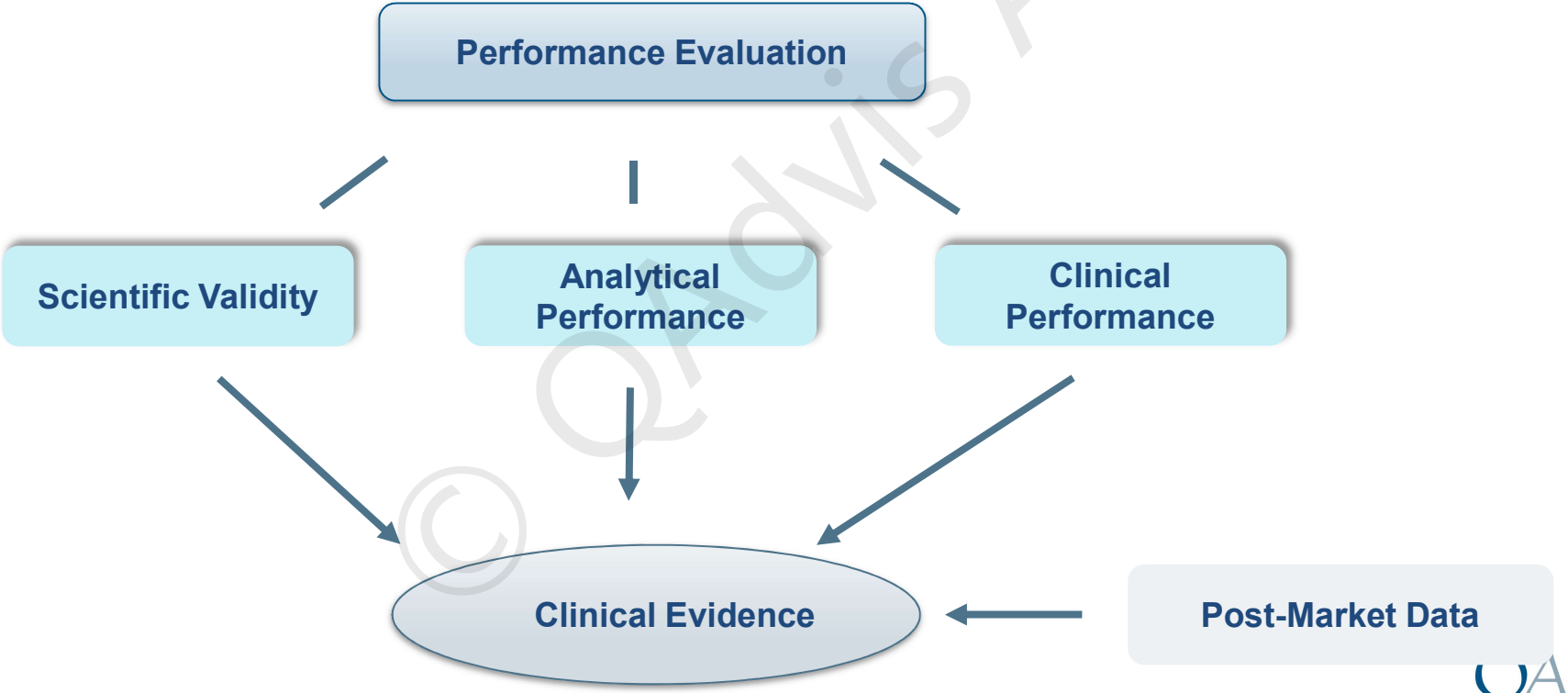
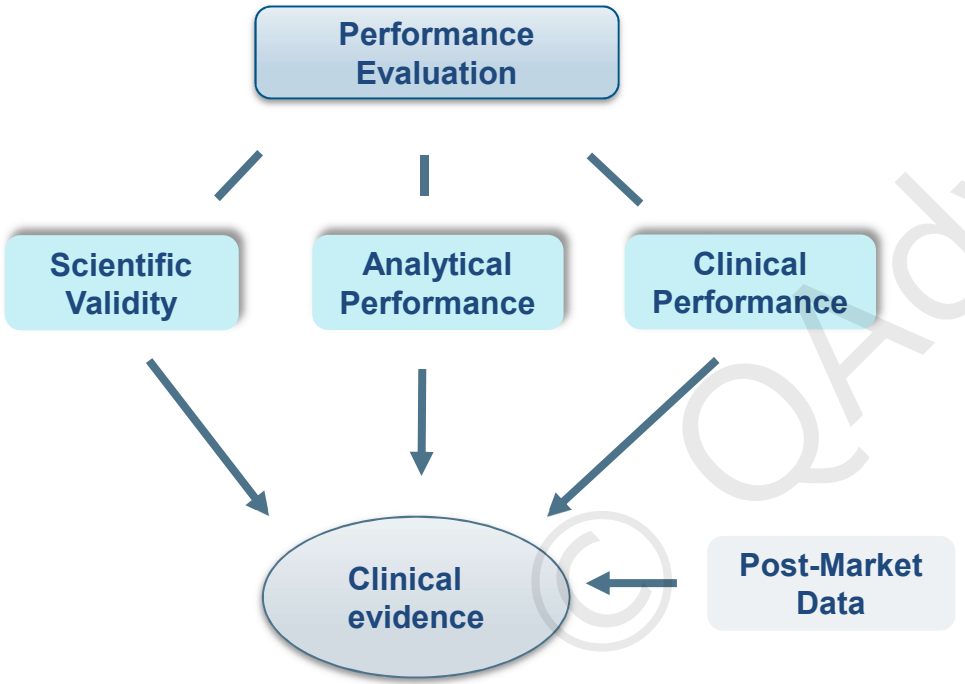
Performance evaluation - concept overview



Performance evaluation - concept overview



- Assessment and analysis of data to establish or verify the scientific validity, the analytical, and, where applicable, the clinical performance of a device
- A continuous process
- Extent according to e.g. risks, device classification and intended use

(IVDR Annex XIII)

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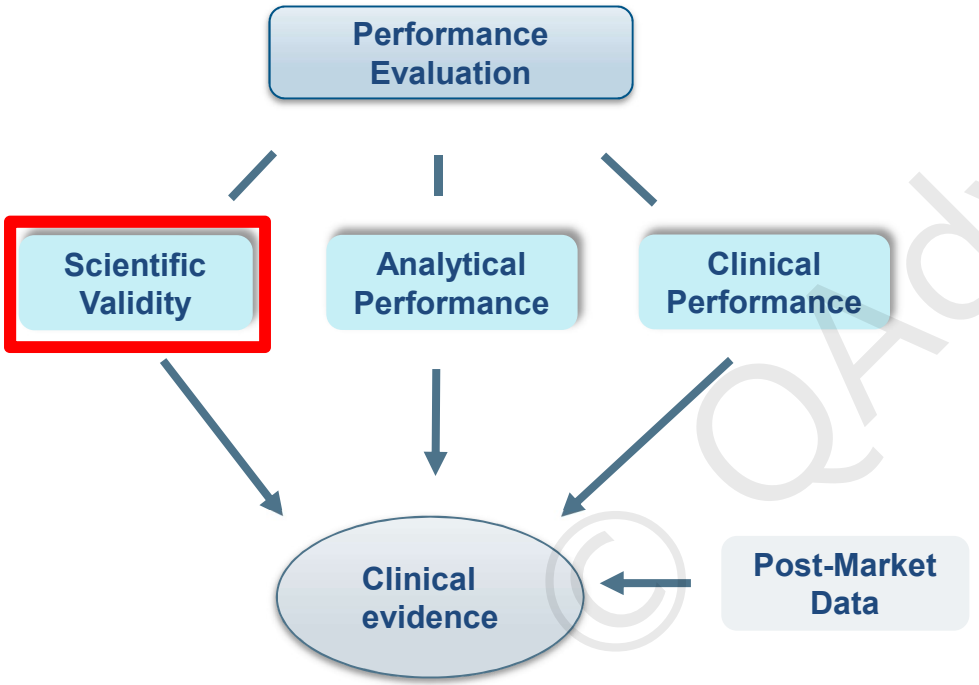
Scientific validity - Definition



- The association of an analyte with a clinical condition or a physiological state
- Potential sources:
  - devices measuring the same analyte
  - scientific literature
  - consensus expert opinions
  - proof of concept studies
  - clinical performance studies

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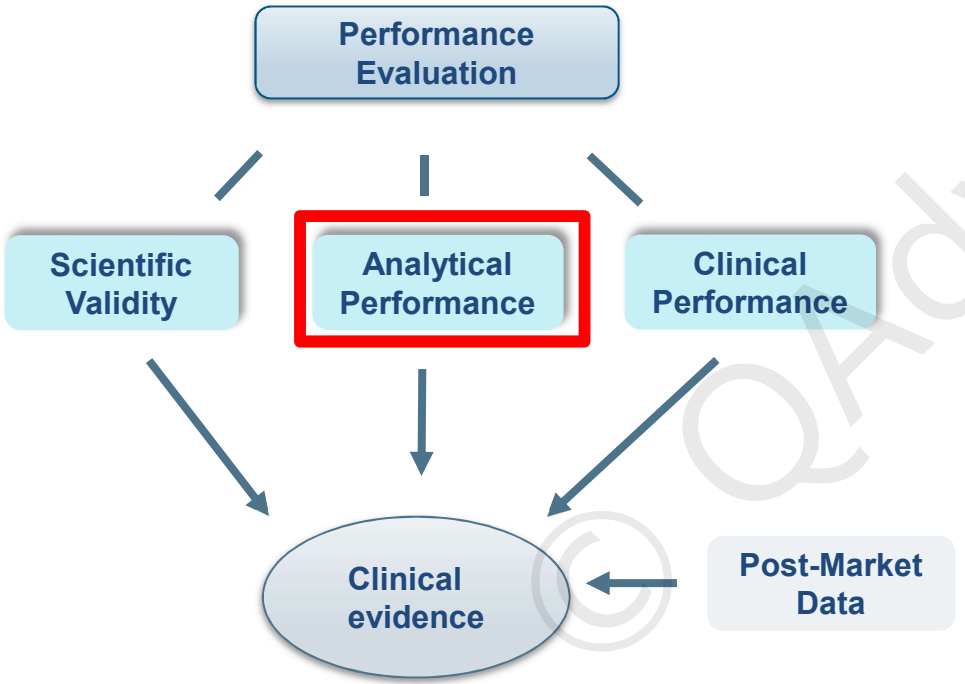
Analytical performance - Definition



- The ability of a device to correctly detect or measure a particular analyte, e.g.
  - analytical sensitivity
  - analytical specificity
  - trueness
  - precision
  - measuring range
  - linearity

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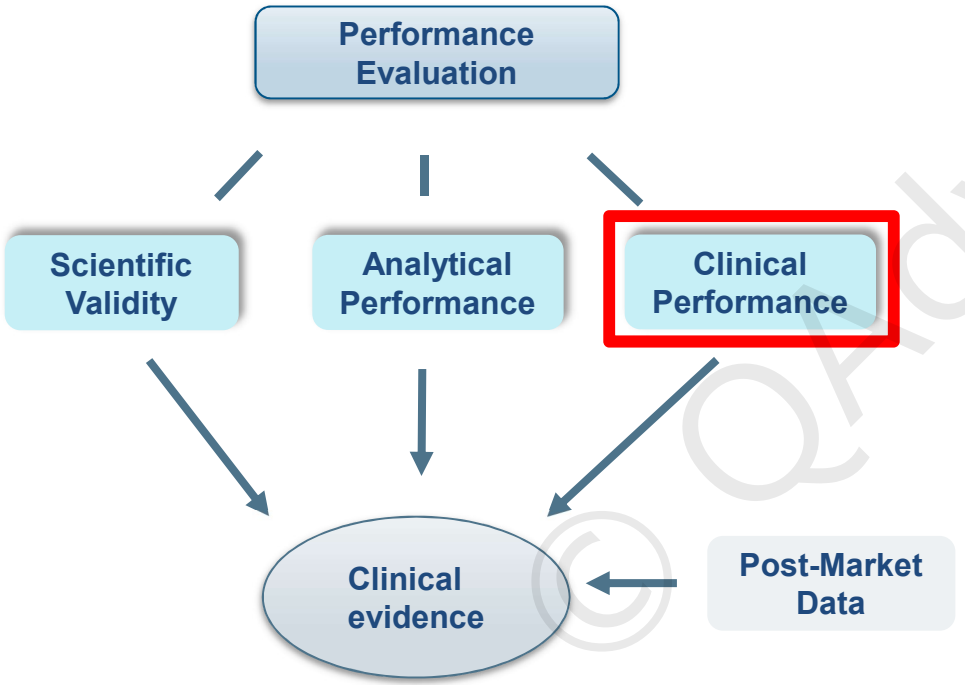
Clinical performance - Definition



- The ability of a device to yield results that are correlated with a particular clinical condition or a physiological or pathological process or state in accordance with the target population and intended user, e.g.
  - diagnostic sensitivity
  - diagnostic specificity
  - positive / negative predictive value
  - expected values in normal and affected populations

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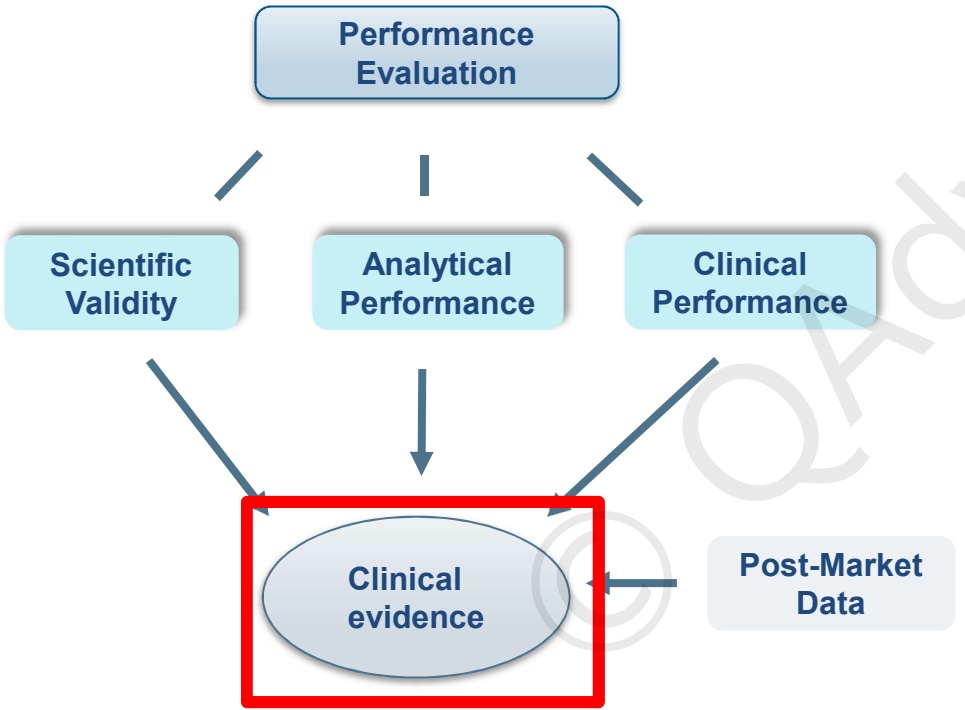
Clinical evidence - Definition



- Clinical data and performance evaluation results of sufficient amount and quality to allow a qualified assessment of whether the device is safe and achieves the intended clinical benefit(s) when used as purposed

(IVDR Annex XIII)

Performance evaluation – Content according to IVDR

1. Performance evaluation plan
2. Demonstration of scientific validity
3. Demonstration of analytical performance
4. Demonstration of clinical performance
5. Performance evaluation report = documentation of the clinical evidence

(IVDR Annex XIII)

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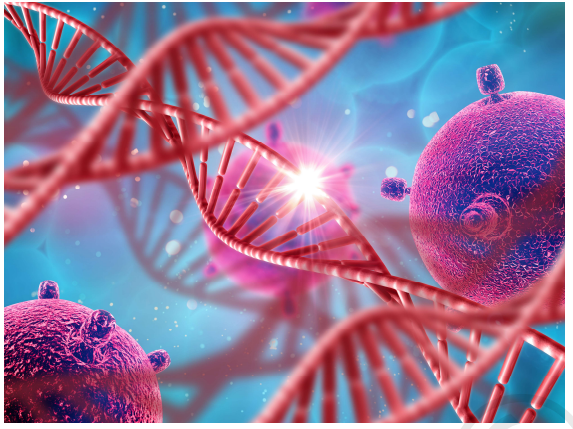
Post-market surveillance (PMS)



For each device the manufacturer shall

- plan,
- document,
- implement,
- maintain and
- update a post-market surveillance system
- proportionate to the risk class of the device and appropriate for the device type.

(MDR Article 83 / IVDR Article 78)

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In Vitro Diagnostic Regulation (IVDR)

- Many SaMD will get a classification of Class B or higher
- Need of a Notified Body
- No transition time for Class General

Warning for confusion between IVDR classification A/B/C/D and Software Safety Classification A/B/C in IEC 62304

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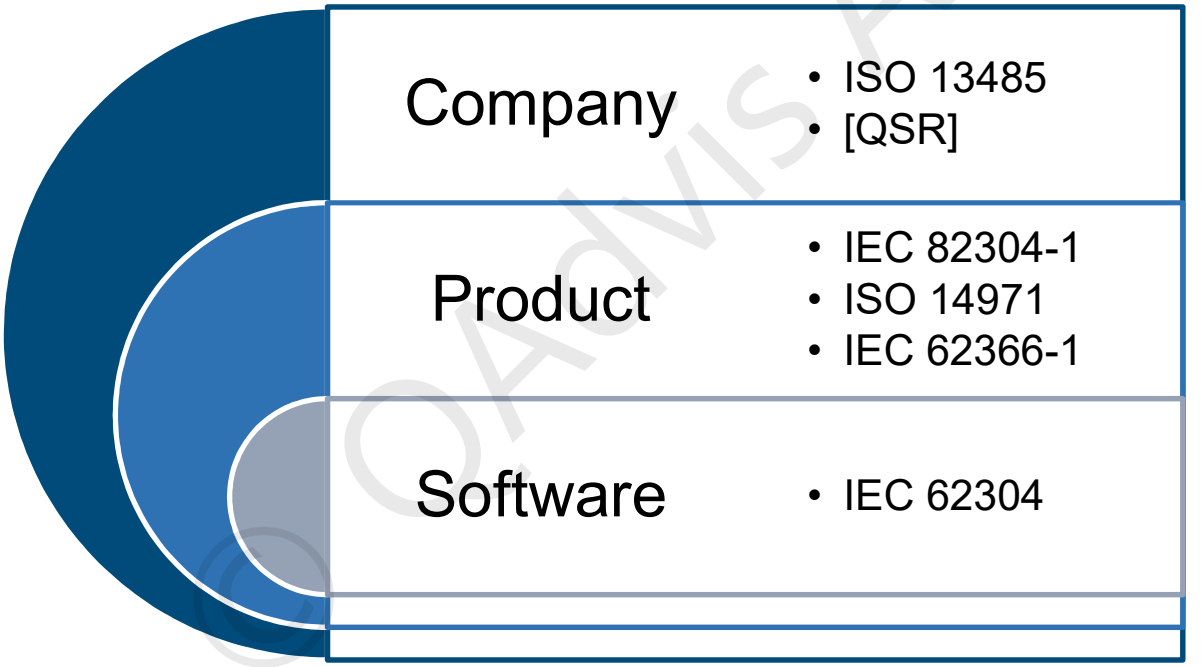
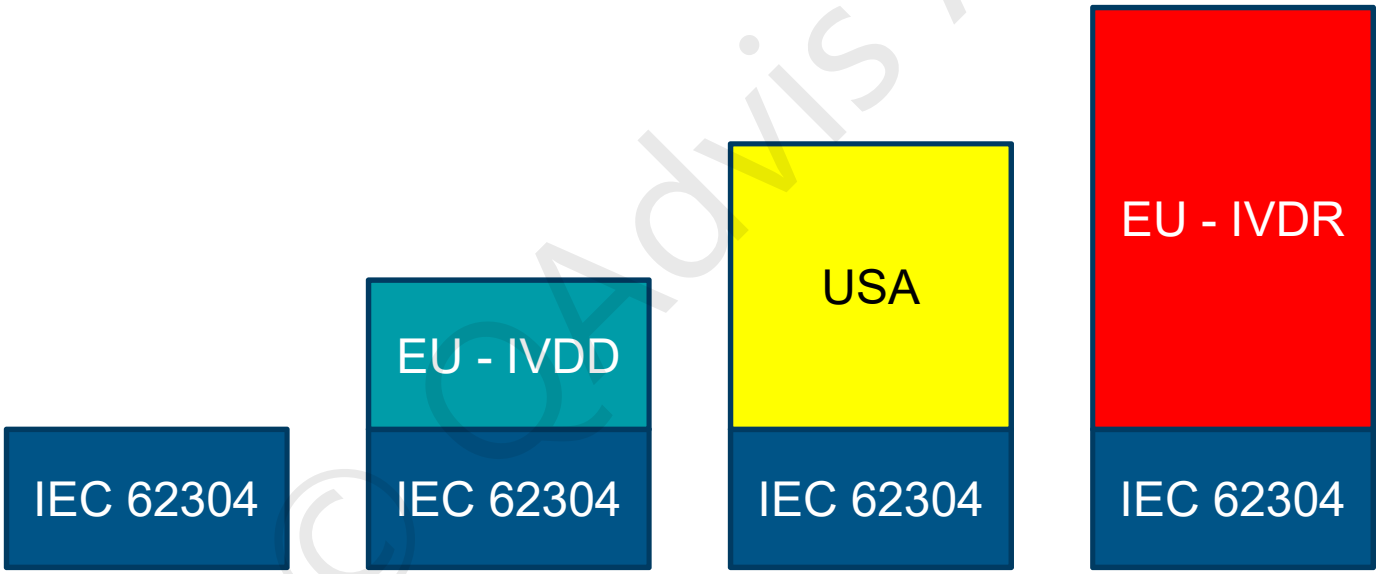
Relevant standards for SaMD according to IVDD



IEC 82304-1: Health Software – Part 1: General requirements for product safety

ISO 14971 and IEC 62304 are only setting a minimum level of requirements for software



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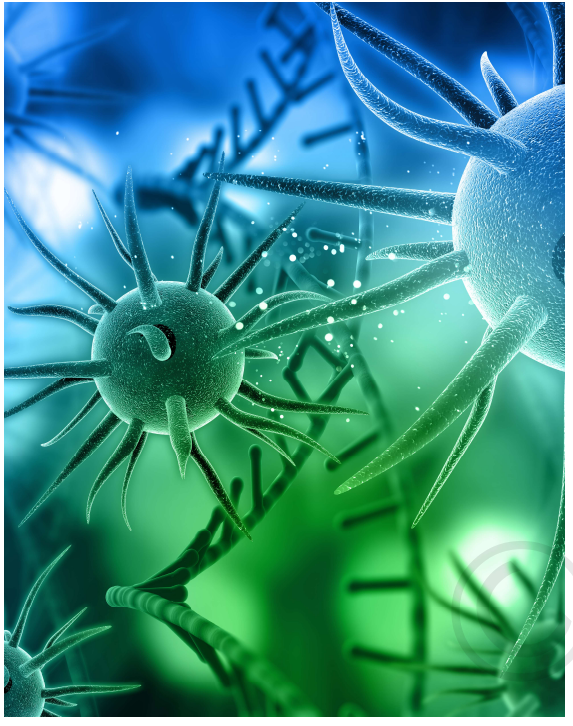
General obligations of manufacturers



Requirements on

- QMS
- Manufacturing and design
- Clinical evaluations / Performance evaluation
- UDI system
- Risk management
- Technical documentation and DoC
- Vigilance
- Post market surveillance system

(MDR / IVDR Article 10)

Unique Device Identification (UDI)

- Placed on packaging or labels for all devices placed on the market (except custom made devices)
- Used to report serious incidents and field safety corrective actions
- Basic UDI-DI shall be included in the DoC
- Reported in to Eudamed
- UDI database implementing act need to be developed for assignment of responsibility to assign UDIs

(MDR Article 27 / IVDR Article 24)

Eudamed

- European database for medical devices
- Registration of all devices by economic operators
- Accessed by
  - Economic operators
  - Competent Authority
  - Notified Body
  - The general public
- Regularly updated with post-market data and vigilance

(MDR Article 28 / IVDR Article 25)

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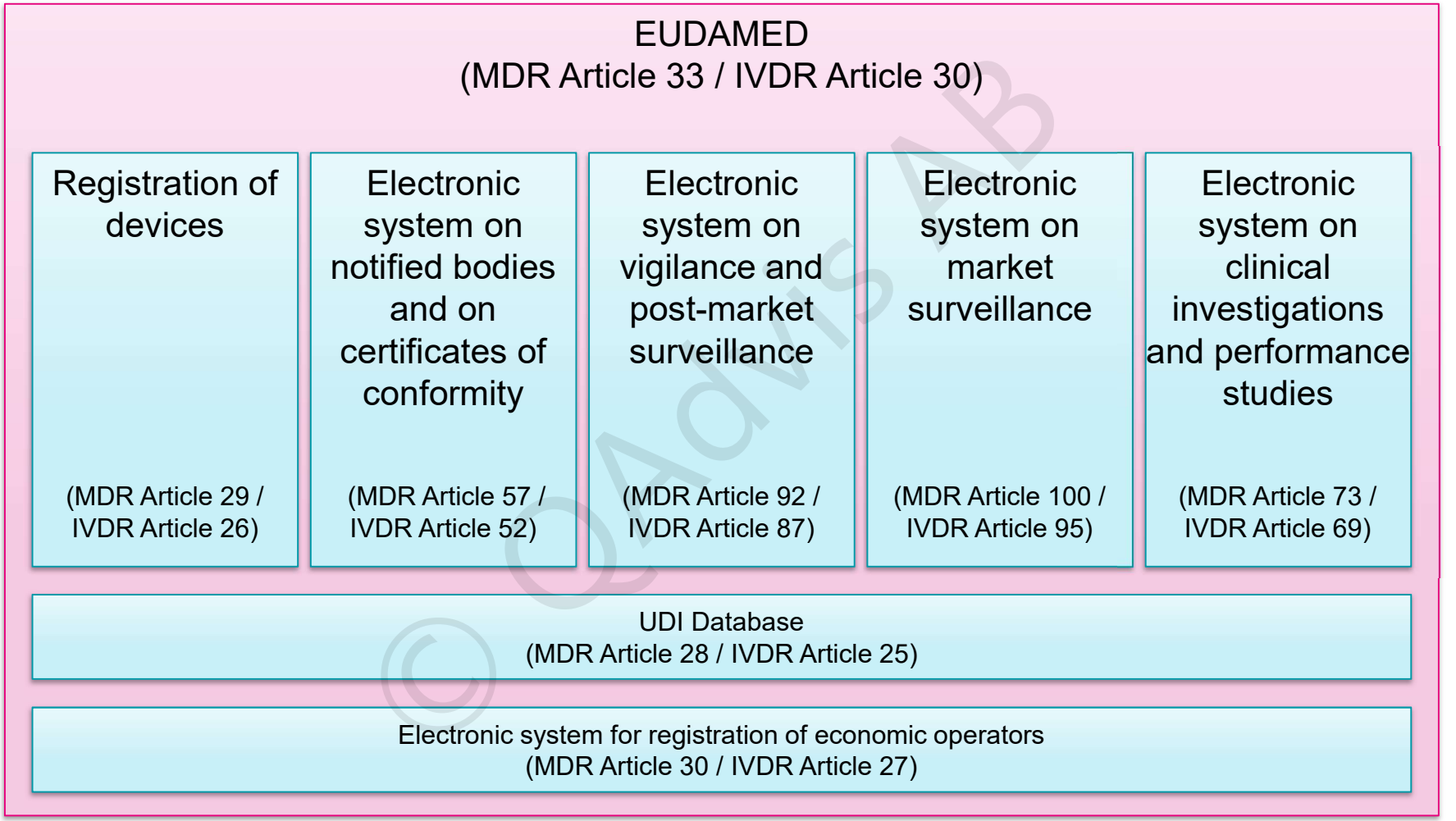
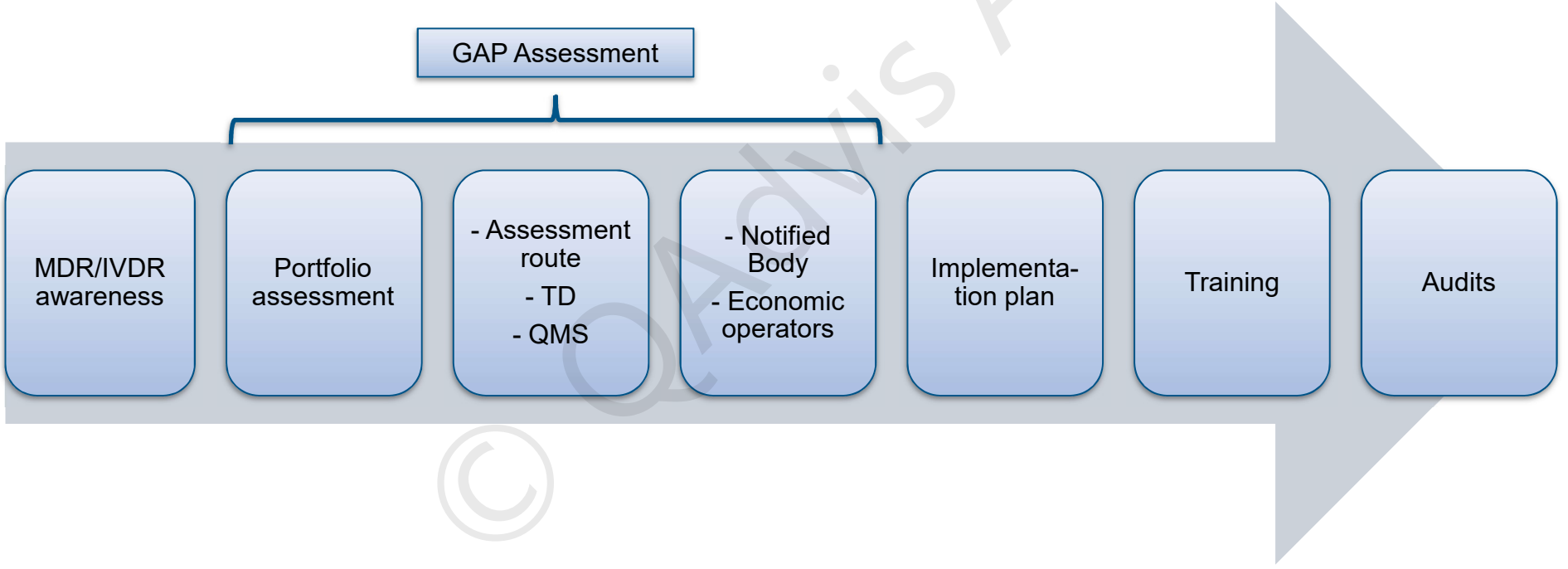

EUDAMED
(MDR Article 33 / IVDR Article 30)
Registration of devices
(MDR Article 29 / IVDR Article 26)
Electronic system on notified bodies and on certificates of conformity
(MDR Article 57 / IVDR Article 52)
Electronic system on vigilance and post-market surveillance
(MDR Article 92 / IVDR Article 87)
Electronic system on market surveillance
(MDR Article 100 / IVDR Article 95)
Electronic system on clinical investigations and performance studies
(MDR Article 73 / IVDR Article 69)
UDI Database
(MDR Article 28 / IVDR Article 25)
Electronic system for registration of economic operators
(MDR Article 30 / IVDR Article 27)

IMPLEMENTATION

Implementation



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Additional information – Concerns

- A lot of work for Notified Bodies
- Decreasing number of Notified Bodies
- More devices and manufacturers in need of a Notified Body
- EUDAMED not running in time
- Common Specifications necessary for implementation not published in time
- Necessary Implementing Acts not ready in time
- Brexit
  - NB in UK not possible
  - EAR in UK not possible

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Conclusions

- A lot of work – start now!
- No grandfathering:

  Not ready in time = products can not be placed on the market
- Stricter requirements on all players (Authorities, Notified Bodies and Manufacturers)
- Sufficient clinical data necessary
- Many products will be up-classified

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Thank you for your attention!
Questions & Answers

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QAdvis services

- Courses
  - IVDR / MDR
  - Risk management,
  - SW risk management
  - ISO 13485:2016
- Product specific workshop
- Internal trainings
- GAP analysis and implementation plan
- Quality Management System
- Auditing
- Risk management
- Clinical evaluation

Kurs IVDR
2019-05-06 Malmö
2019-05-09 Stockholm

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