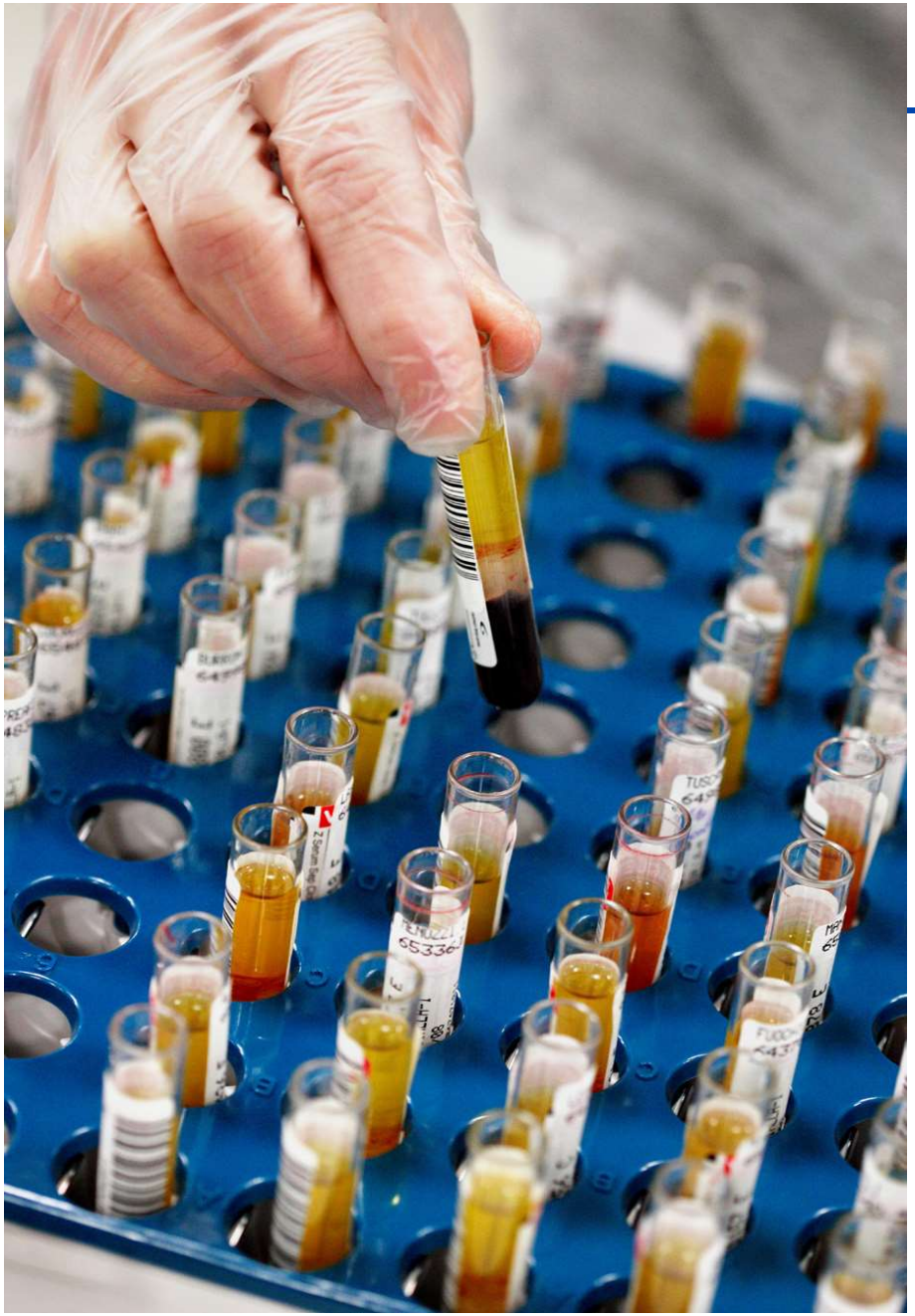


Product Service

Choose certainty.
Add value.

New EU-regulation for in vitro diagnostics

Interreg Stuttgart, January 30th, 2018

Thomas Theisen, MD, PhD
Director IVD
TÜV SÜD Product Services GmbH

TÜV SÜD Product Service as Notified Body under IVDD & IVDR

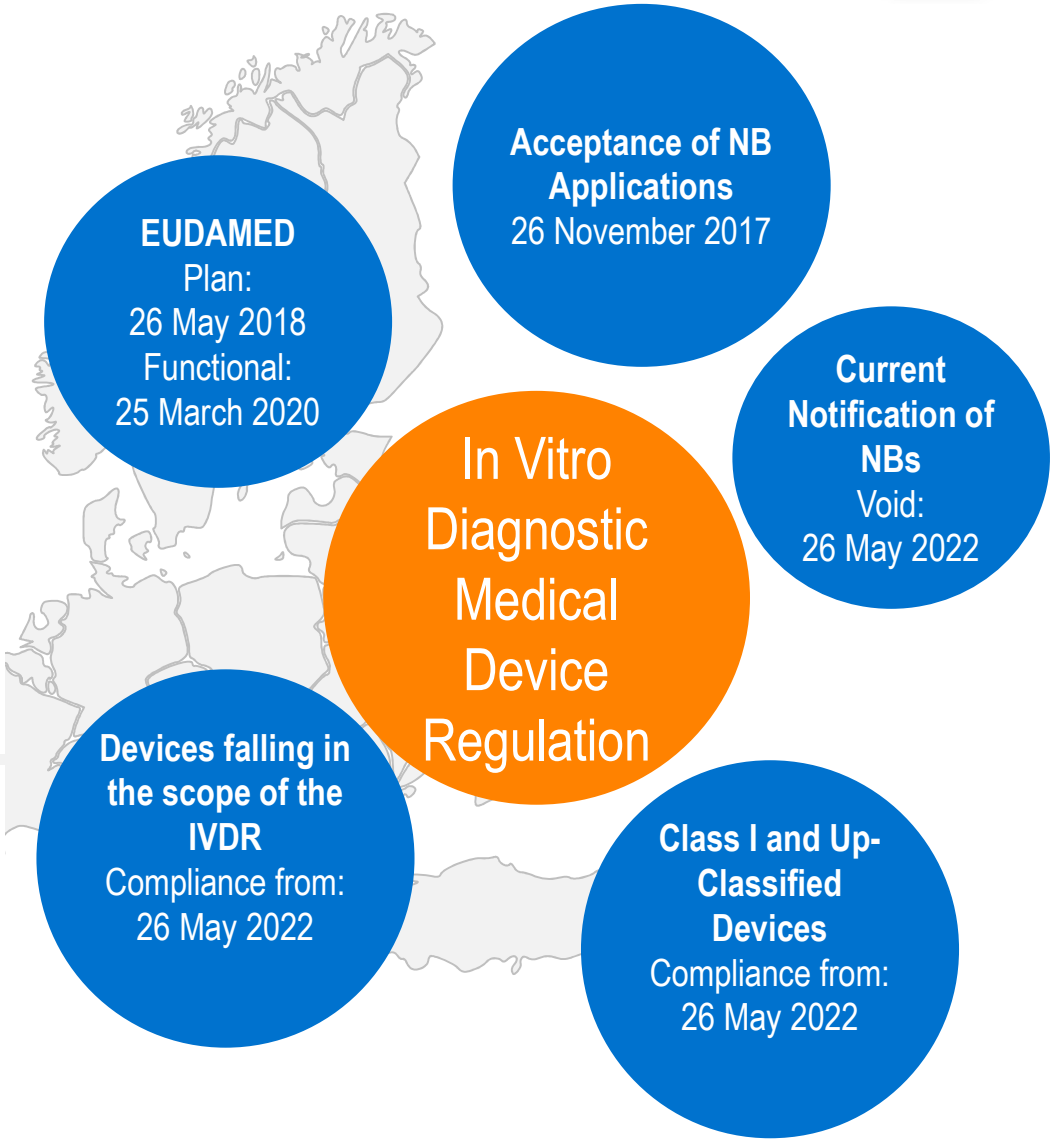
- Notified Body under IVDD since 2001, ID No. **0123**
- Notified for all IVD product categories
- Approx. 60 IVD experts worldwide
- Cooperation with IVD testing lab at Paul-Ehrlich-Institut, Langen, and the Centre National de Référence pour les Groupes Sanguins (CNRGS) at Institut National de la Transfusion Sanguine (INTS), Paris, for verification of manufactured products
- Application for designation under IVDR submitted on 26 Nov 2017 for all product categories

- Currently in total 22 Notified Bodies designated under IVDD

(http://ec.europa.eu/growth/tools-databases/nando/index.cfm)

EU's Milestones to the IVDR

2010	Commission: consultation on revision of IVD Directive
2012	Commission: proposal for new IVDR
2014 Q2	Parliament: position on IVDR
2015 Q3	Council position on proposed Regulation
2015 Q4	Trilogue: Commission, Parliament, Council
2017	IVDR published on May 26, 2017
2022	End of five-year transition on May 26, 2022



Disclaimer

Several important pieces of information are still missing due to inconsistencies in the text, corrections are to be expected

Issuance of **Delegated and Implementing Acts by Commission** to supplement and adapt the IVDR is foreseen in the text in several occasions

IVD Regulation 2017 / 746 (IVDR)

Selection of most important changes


Re-classification according to risk


Product scope expansion


Stricter requirements for Economic Operators

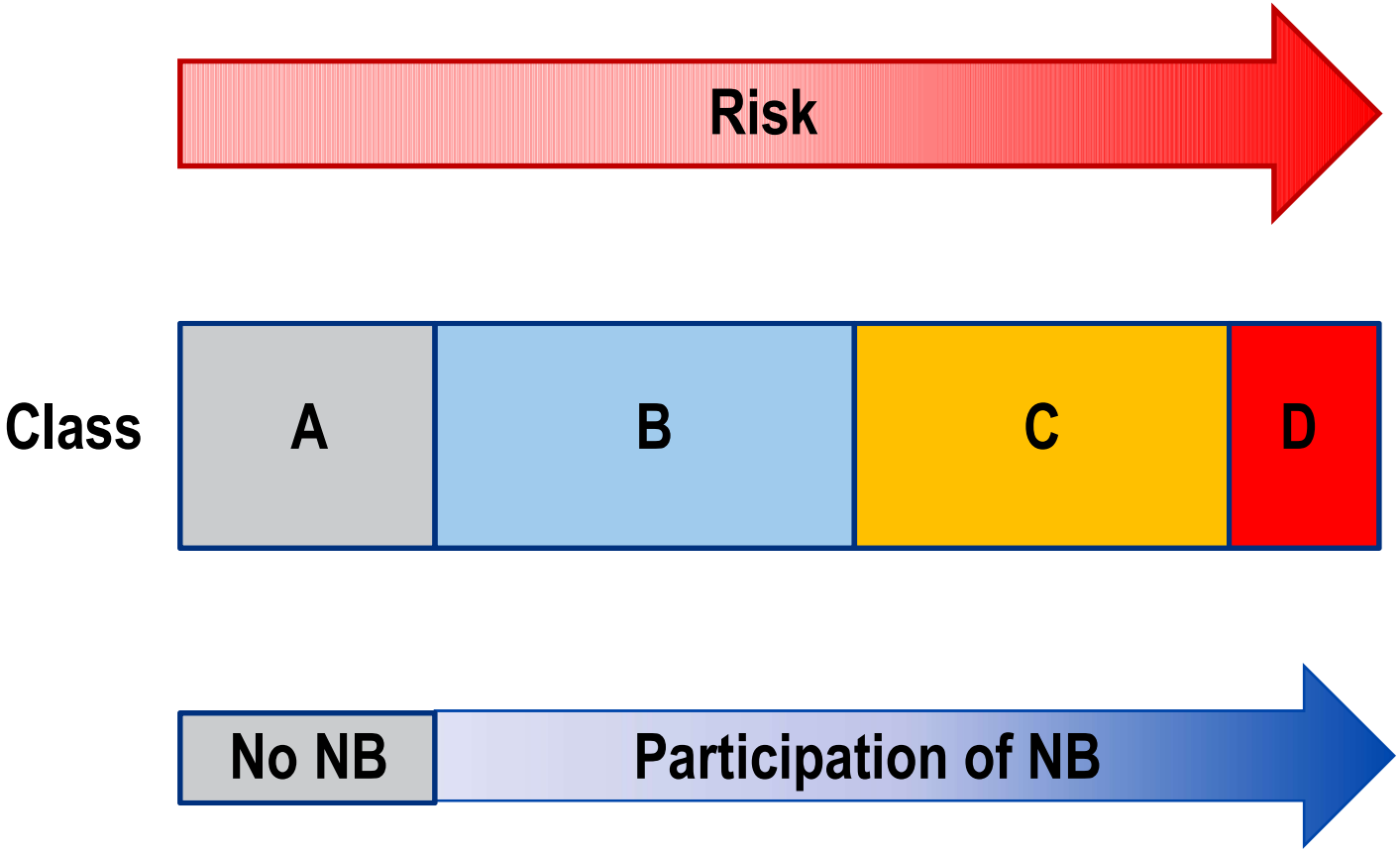

Greater scrutiny of Notified Bodies - Increased Notified Body involvement


Implementation of unique device identification


Stricter Requirements Technical Documentation and Clinical Evidence


Rigorous post-market oversight

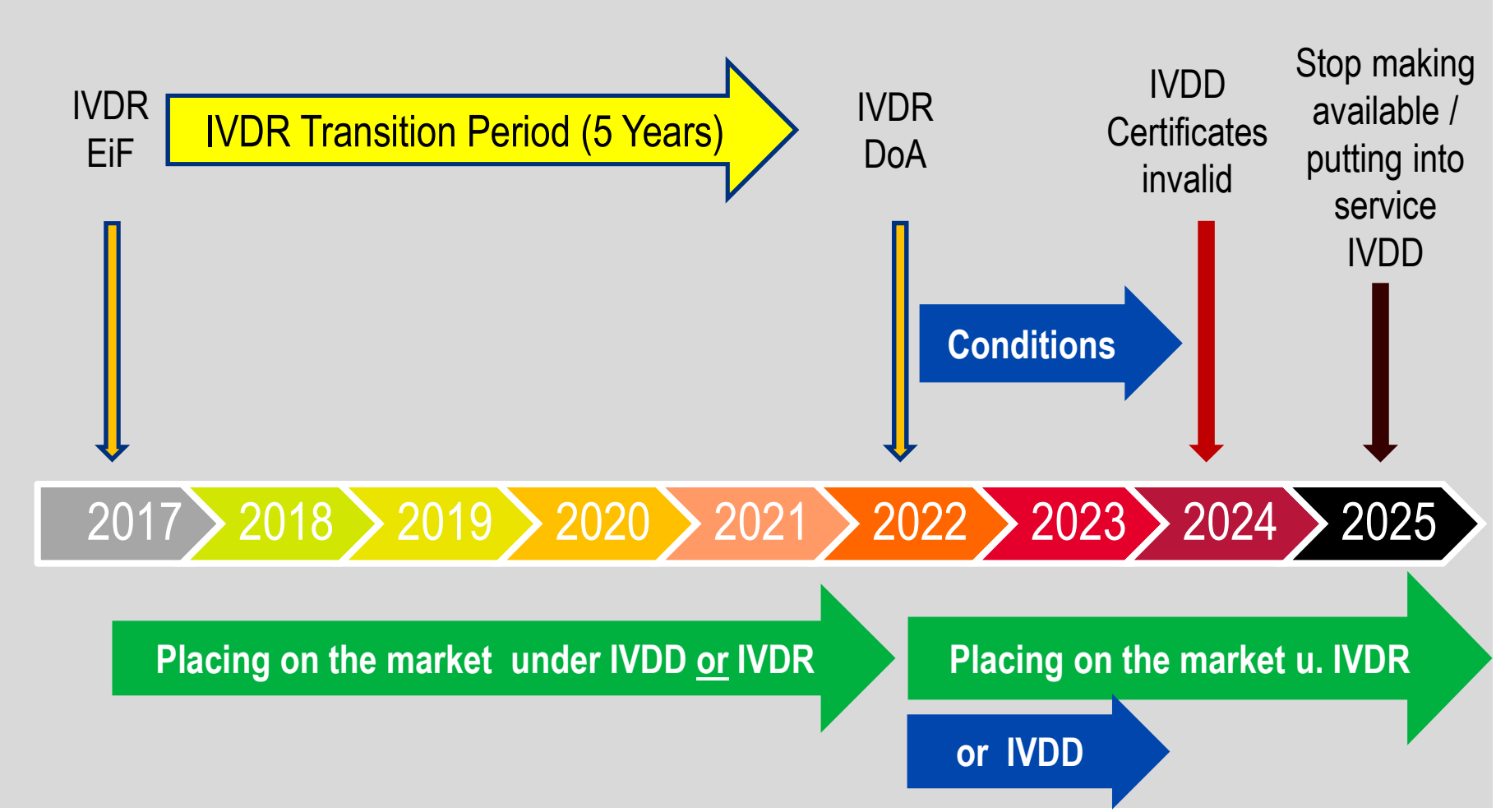
Risk based classification – Requirement for Participation of NB in CA



Timelines of IVD Regulation

Articles 110 and 113 – IVD Regulation (IVDR)

Transitional Provisions – Entry into Force and Date of Application



Timelines of IVD Regulation

Article 110 (3) IVDR

Conditions

for temporary placing on the market products already certified under IVDD after date of application of IVDR

Not applicable to currently self declared products !

- **Certification** according to IVDD is still **valid**
- The device continues to **comply with the directive**
- **No significant changes** in design and intended purpose

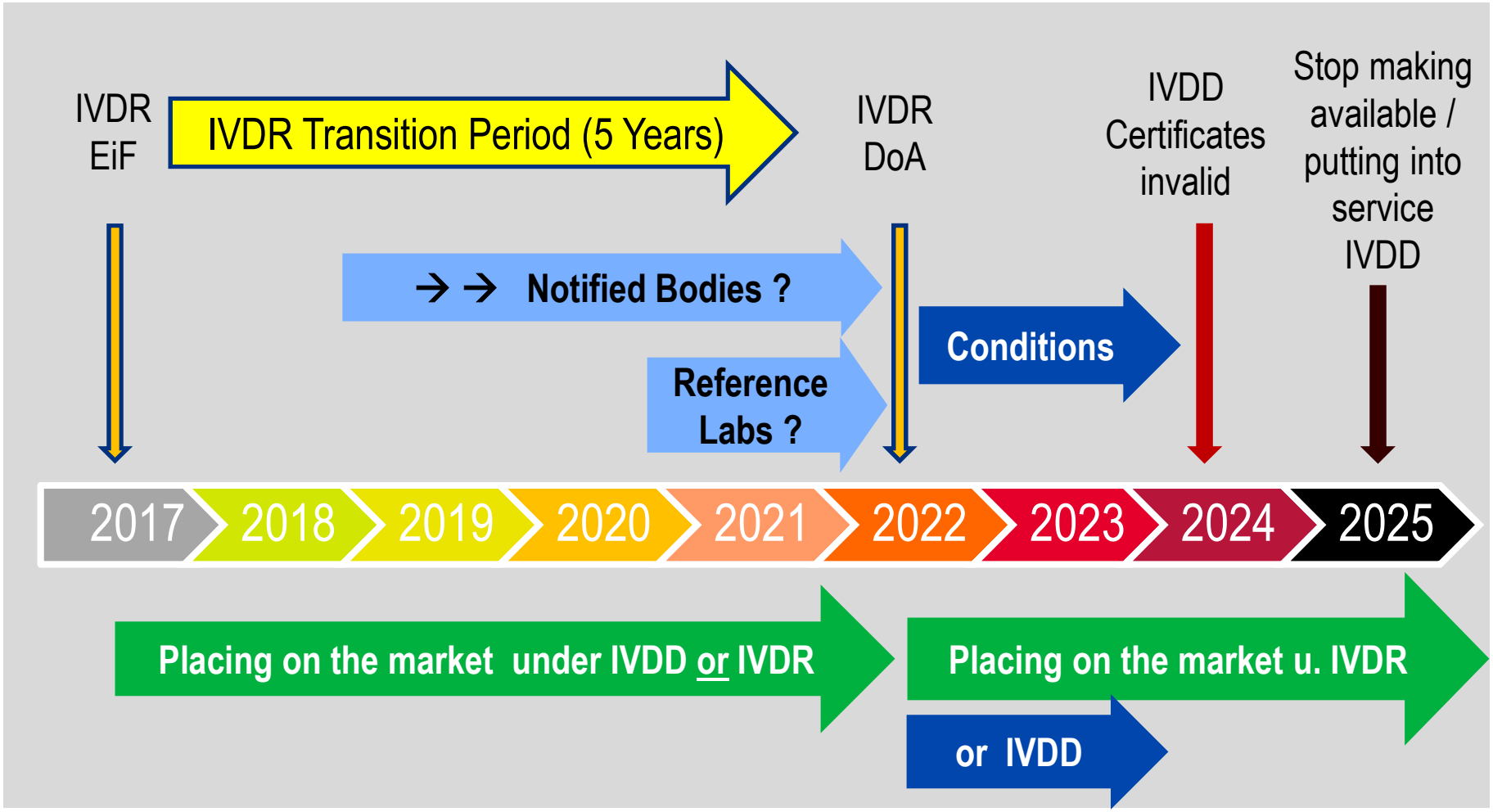
- Notified Body that issued the certificate according to IVDD ensures **appropriate surveillance**

- **IVDR requirements** are applied related to
  - post-market surveillance,
  - vigilance
  - registration of economic operators and of devices

Timelines of IVD Regulation

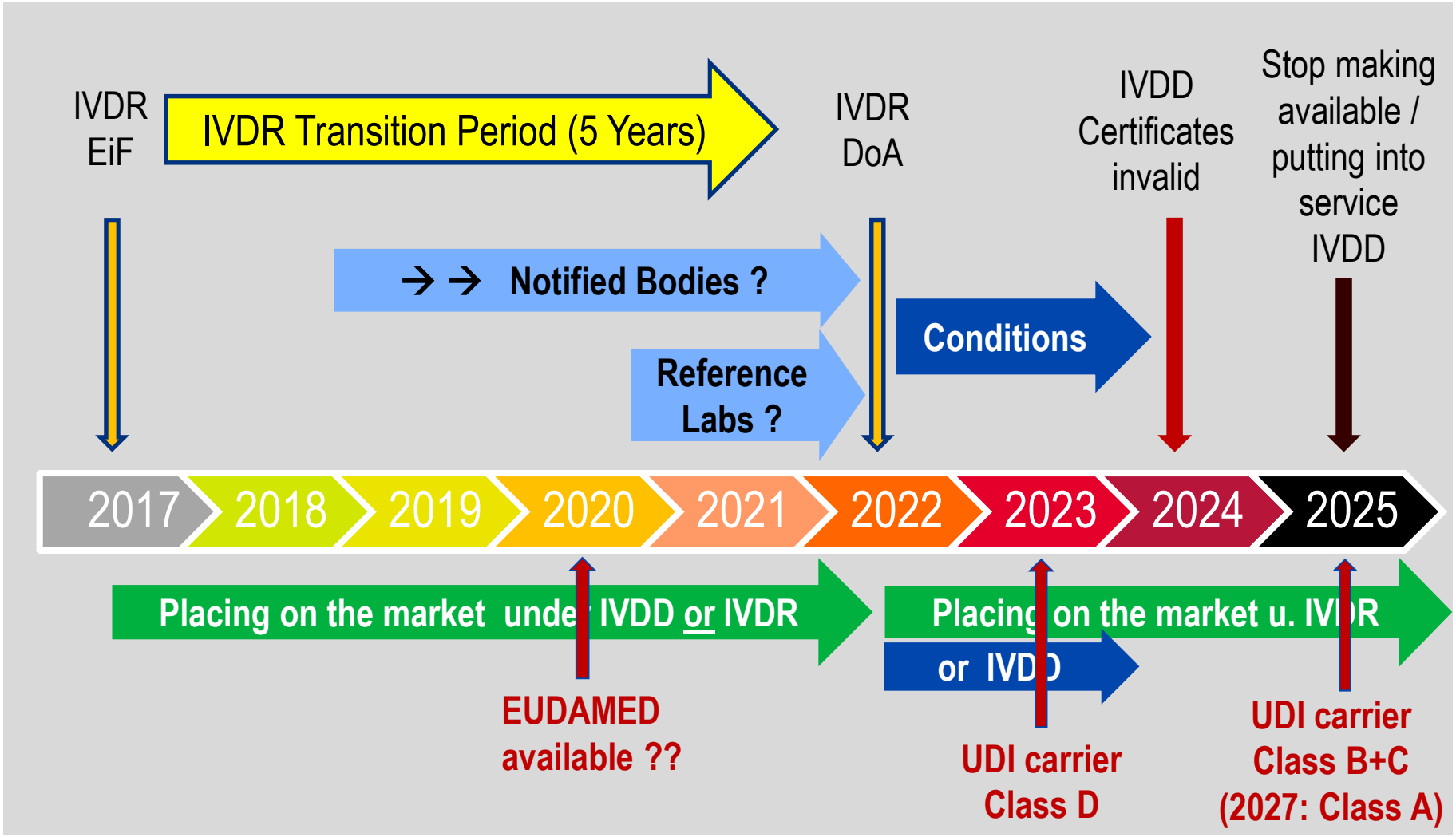
Articles 110 and 113 – IVD Regulation (IVDR)

Transitional Provisions – Entry into Force and Date of Application



Timelines of IVD Regulation 2017 / 746 – Traceability

Artikel 113 (3)



Resulting „active“ transition period is reduced

- What does this imply for the manufacturer?
  - Begin your preparations with self declared devices (or those devices, that under IVDR are classified in a higher risk-group than under IVDD)
  - Make sure you meet conditions to fully use „extended transition period“ for products already certified by NBs, especially current List A devices. This will give you the most flexibility

IVD Regulation

Articles 110 and 113 – IVD Regulations (IVDR)

Consequences for products already CE marked under the IVDD

- All devices need re-assessment according to IVD Regulation
  - ➢ **No grandfathering of currently existing approvals under IVDD**

Different impact on devices

- Devices classified to comparable risk class as under IVDD
  - ➢ Moderate impact
- Devices subject to “Re-“classification (up-classification) to a higher risk group
  - ➢ additional workload

What updates will be needed to place products furtheron on the market?

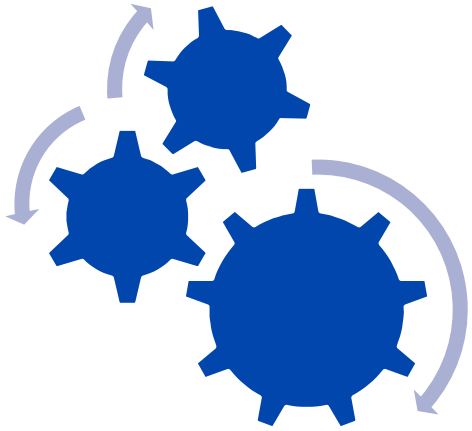
Product /Technical Documentation

- General Safety and Performance Requirements (replace ER)
- More detailed requirements regarding technical documentation (STED format required)
- Clinical Evidence:
  Scientific Validity + Analytical Performance + Clinical Performance Reports
  → Performance Evaluation Report
- Summary of Safety and Performance for Class C and D
- Information on postmarket surveillance (plan, reports, vigilance)
- Annual Periodic Safety Update Report (PSUR) for class C and D
- Post-market surveillance report for class A and B
- UDI to be integrated in label

The Technical Documentation consists of the elements listed in Annex II and Annex III.

What updates will be required to place products further on the market?

QMS wise



- Additional documentation and publication requirements
- Process of generation of Technical Documentation
- Single Registration Number
- Implementation of **Unique Device Identifier (UDI)** system
- Post Market Surveillance, Vigilance
- Relation with suppliers
- Relation with distribution chain
- (Relation with EU Representative)
- Upload of information into EUDAMED
- Appointment of a person responsible for regulatory compliance

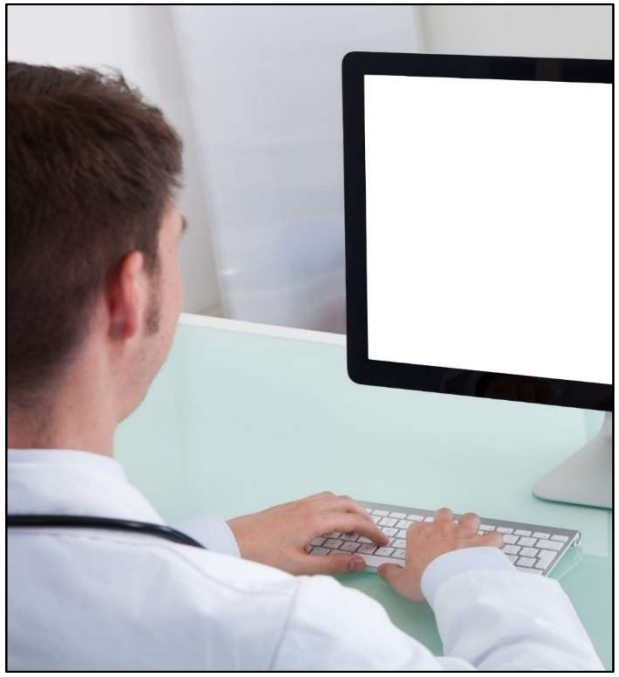
Requirements to Economic Operators

Article 15 – IVD-Regulation (IVDR)

Person responsible for regulatory compliance

Manufacturer

EU Representative (Authorized Representative)



- Check of device conformity before release
- Technical Documentation + DoC
- Post Market Surveillance
- Vigilance Reporting
- Statement for devices for interventional performance studies

Conformity Assessment Procedures acc. to IVDR (1)

Article 48 – IVD Regulation (IVDR)

Conformity Assessment Procedures

1. **Prior to placing a device on the market**, manufacturers shall undertake an assessment of the conformity of that device

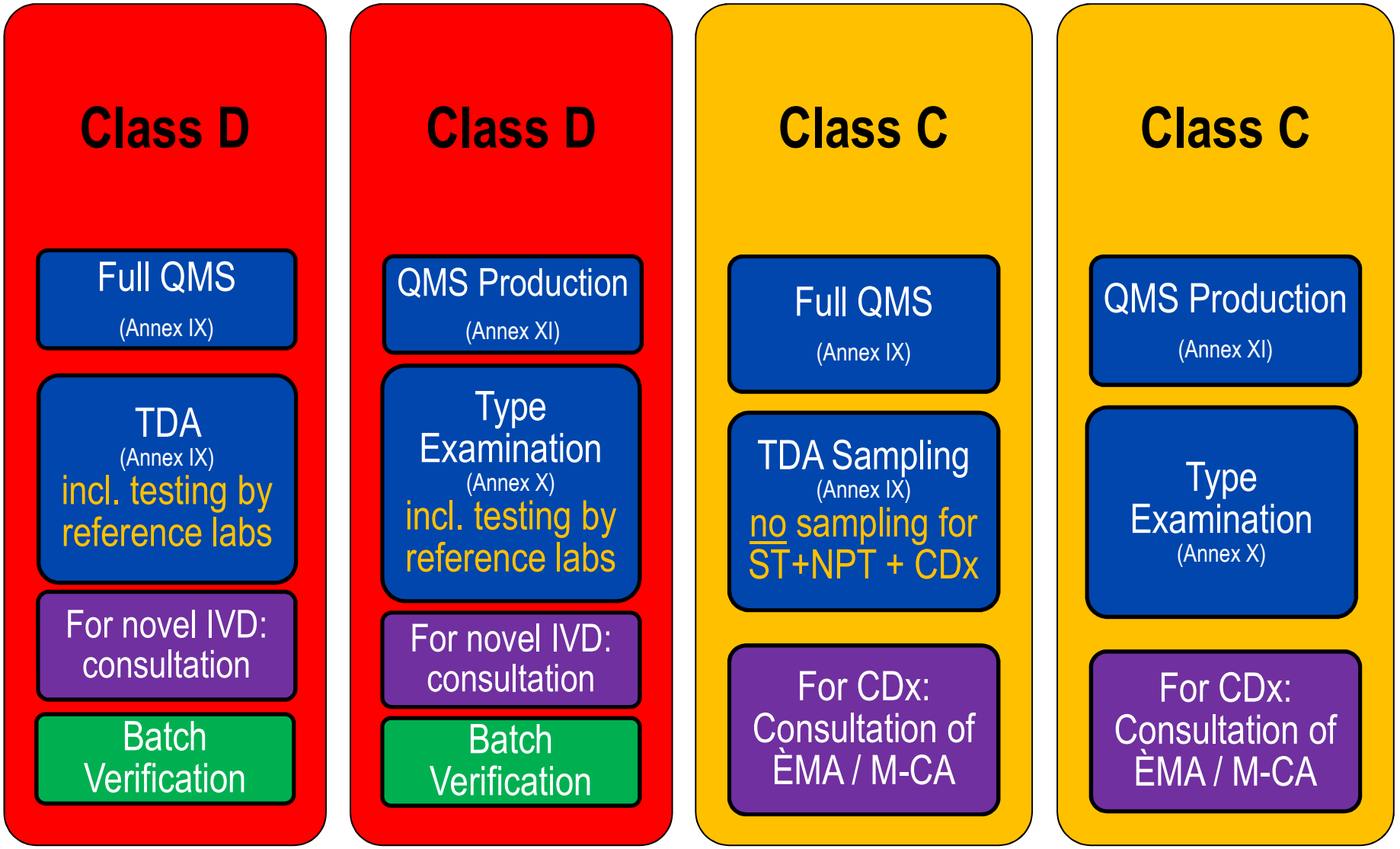
Annex IX	• Conformity Assessment based on a **Quality Management System** and on **Assessment of Technical Documentation**
Annex X	• Conformity Assessment based on **Type Examination**
Annex XI	• Conformity Assessment based on **Production Quality Assurance**
Article 48 (10)	• **Selfdeclaration by Manufacturer** **Class A *non-sterile* devices**

Participation of Notified Body for devices of

- **Class D**
- **Class C**
- **Class B**
- **Class A *sterile***

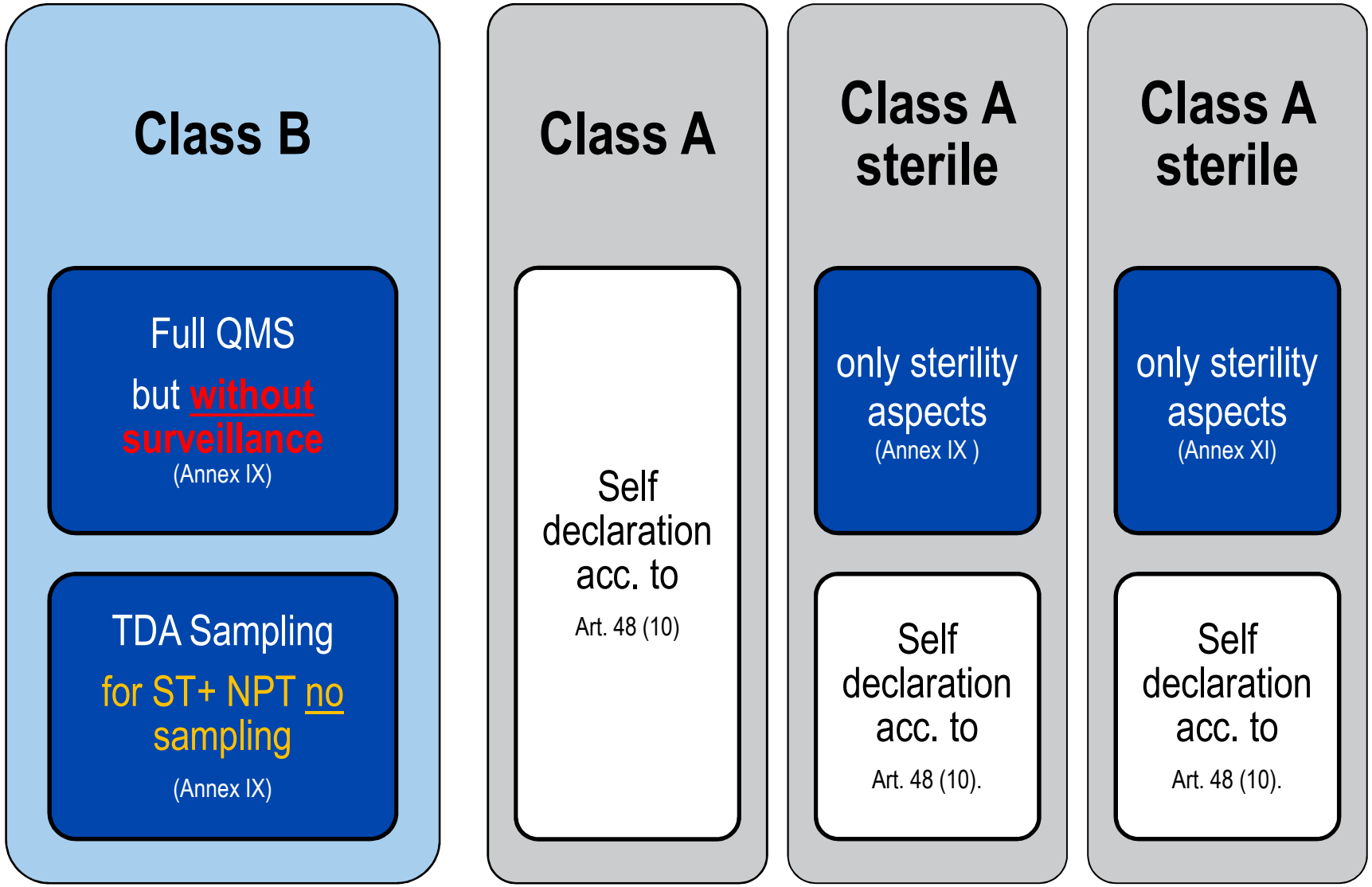
Conformity Assessment Procedures acc. to IVDR (2)

Article 48 – IVD Regulation (IVDR)



Conformity Assessment Procedures acc. to IVDR (3)

Article 48 – IVD Regulation (IVDR)



Important implication for self-testing/ near patient-testing devices and companion diagnostics:

Pre-market approval required (no sampling) !!!

Conformity assessments

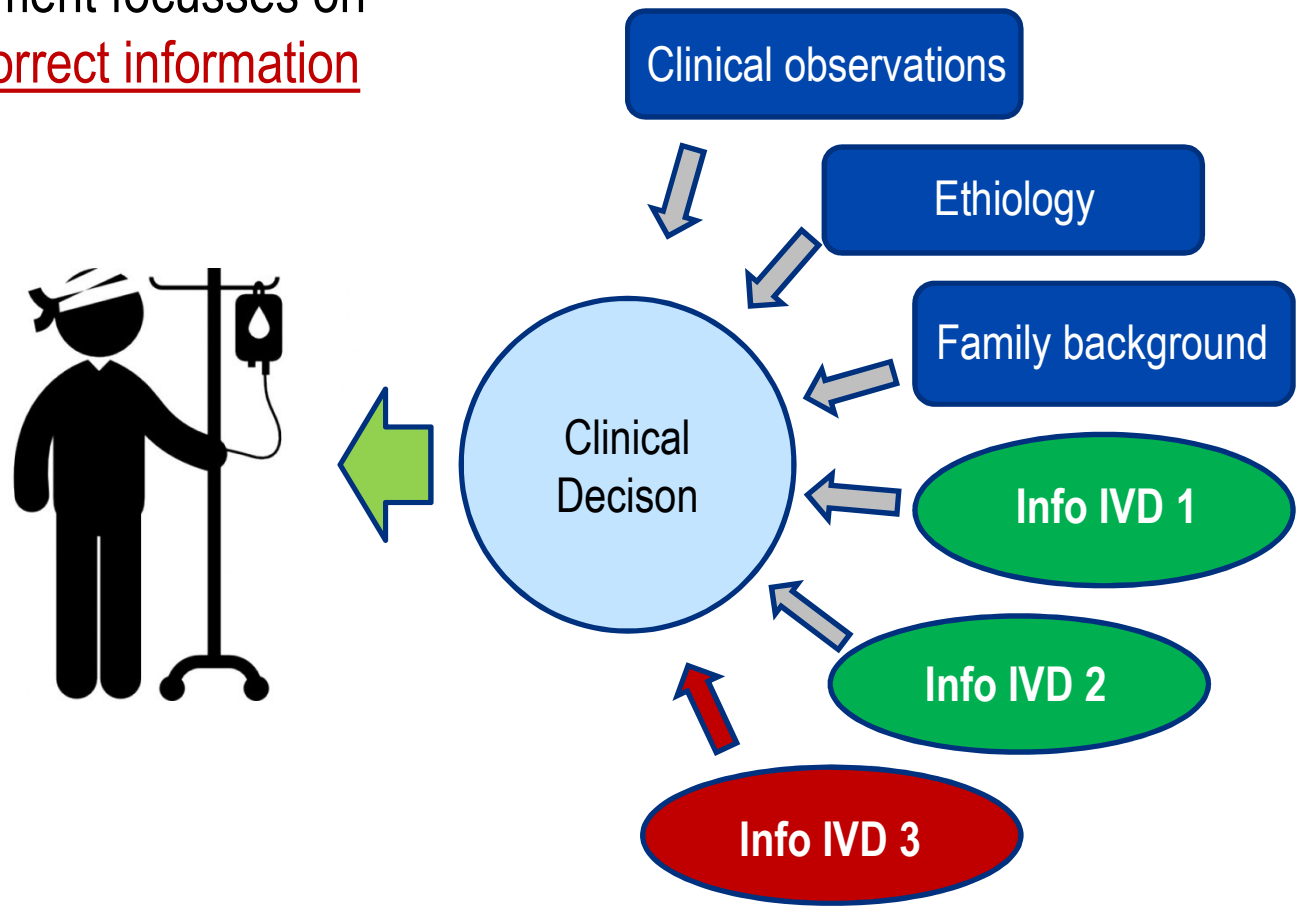
Open questions:

- Reasoning behind sampling of Technical Documentations for assessment?
  - Class B – how to differentiate product categories without examples at least?
  - Class C – how to unequivocally specify generic device groups without a respective list?

- No surveillance audits for class B devices for a period of 5 years?

Clinical decision making

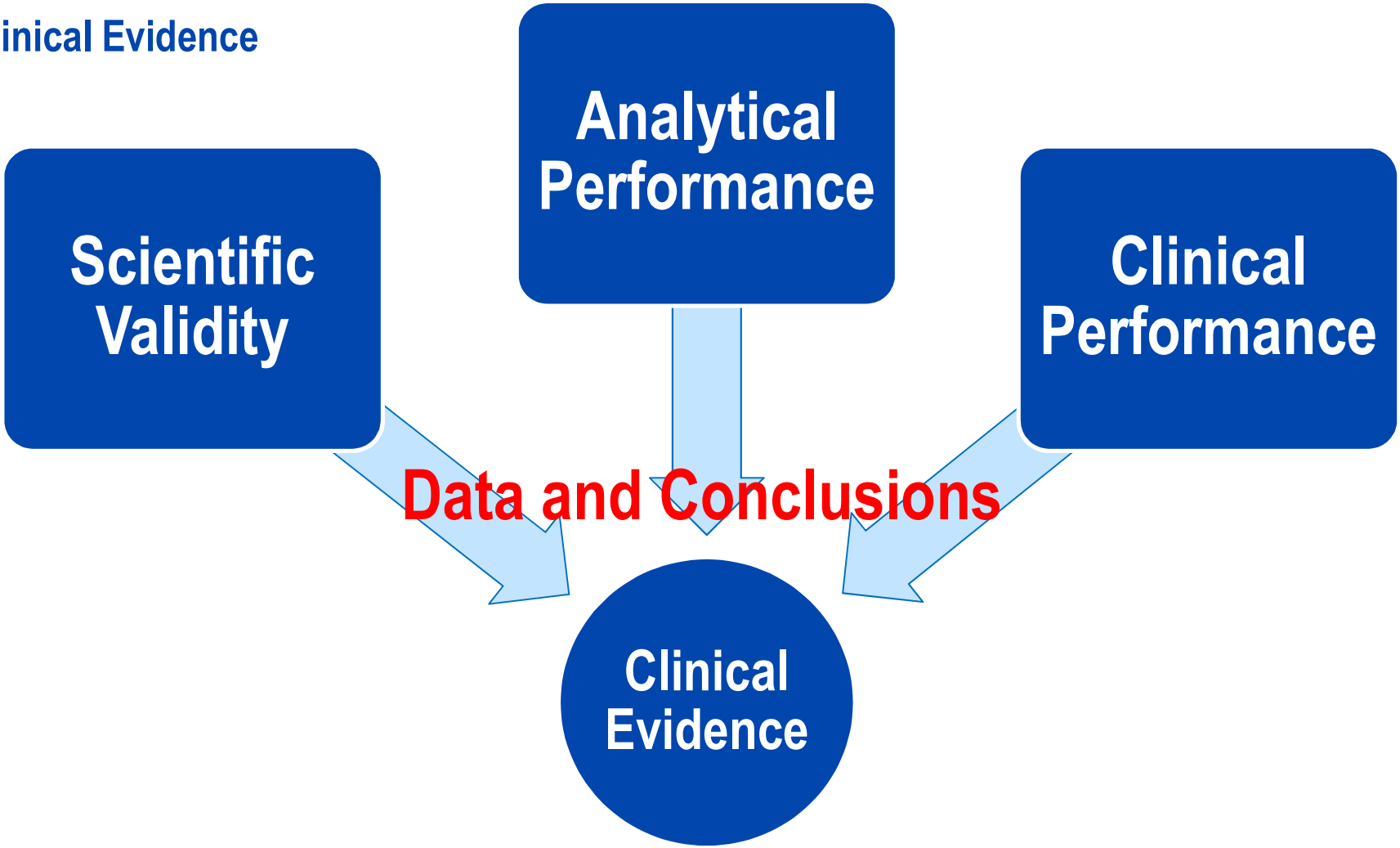
- Clinical evidence of the IVD device under assessment focusses on provision of correct information



Requirements regarding Performance Evaluations

Article 56 (3) – IVD Regulation

Clinical Evidence



Requirements regarding Performance Evaluations

Article 2 – IVD Regulation (IVDR)

Definitions

Scientific Validity	Analytical Performance	Clinical Performance
(38) 'scientific validity of an analyte' means the **association of an analyte to a clinical condition or a physiological state**	(40) 'analytical performance' means the **ability of a device to correctly detect or measure a particular analyte**	(41) 'clinical performance' means 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

Performance Evaluation

Clinical Evidence

Requirements regarding Performance Evaluations

Article 56 – IVD Regulation (IVDR)

Clinical Evidence

- shall scientifically demonstrate that the intended clinical benefit(s) and safety will be achieved according to the state of the art in medicine
- shall provide scientifically valid assurance, that the relevant general safety and performance requirements set out in Annex I, under normal conditions of use, are fulfilled.
- Clinical performance studies in accordance with Annex XIII, Part A Section 2 shall be carried out unless it is duly justified to rely on other sources of clinical performance data.
- Continuous process of performance evaluation

These requirements are not really new,
but more pronounced than in the IVDD !

Requirements regarding Performance Evaluations

Article 56 – IVD Regulation (IVDR)

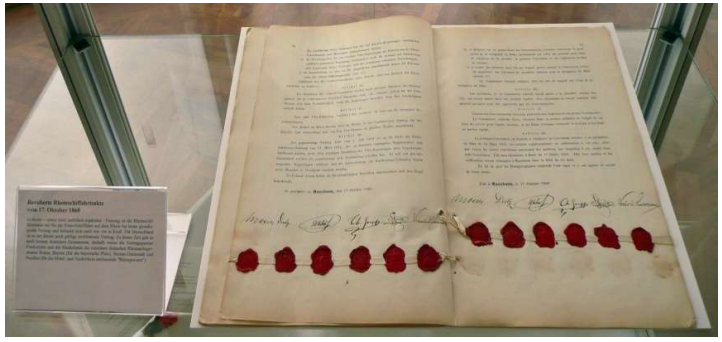
Reports regarding clinical evidence

(5) The scientific validity data, the analytical performance data and the clinical performance data, their assessment and the clinical evidence derived therefrom, shall be documented in the **performance evaluation report**

(6) Updates **throughout the life cycle** of the device with data obtained by post market follow-up according to respective plan

- Periodic Safety Update Report acc. to Article 81 when neccessary, at least annually for class C and D
- Summary of Safety and Performance Report (Article 29) to be updated soon as possible (class C and D)
- Post-market surveillance report for class A and B acc. to Article 80 when neccessary

➔ **Technical Documentation**



Challenges for Manufacturers

Legacy Products – clinical performance

- State of the art must be met – Overall benefit / risk ratio to be positive
- demonstration of clinical relevance and need for the device, if less sensitive /specific as comparative device e.g. via expert panel opinion
- Data from routine analysis, PMS and PPF reports might be used to close “gaps” analytical and clinical performance data (if suitable)

Scientific validity must be established also for “old“ products

Is scientific validity documented for the device still in line with current knowledge?

Preparation of scientific validity report for „multipurpose parameters“

Take home message

Don‘t rely on a long transition period of IVDR - consider

- High number of devices which might need revision of documentation
- Additional performance studies might be required
- Availability and Resources of Notified Bodies
- Late availability of Reference Laboratories
- Pre-market approval required for self and near patient testing devices
- Potential elongation of conformity assessment due to higher complexity of processes (e.g. for high risk products)
- Delayed availability of EDP systems (EUDAMED)
- Increased maintenance efforts for technical documentation

Get ready for the regulations without delay !

How to succeed transition to IVD-R ?

Communication	Increase awareness within your organization Discuss regulatory strategy for business with regard to IVD-R
Analysis	Analyze your product portfolio - Identify gaps in your Quality System and Technical Documentation
Partnership	Discuss and fine tune your approach with your Notified Body
Clear schedule	Develop plan to close gaps, execute tasks and verify the results
Information	Stay informed on further development of legislation, including implementing acts to come and adapt your activities
Resources	Ensure to acquire enough resources to cope with future regulatory burden
Timeliness	Be ready in time, significant changes on products covered by an IVDD certificate after date of application of IVDR will not be possible

? QUESTIONS ?

Thomas Theisen, MD, PhD
TÜV SÜD PS Munich
thomas.theisen@tuev-sued.com

www.tuv-sud.com/mhs
www.tuev-sued.de/mhs