



The New IVDR: Significant Changes for Industry

AMDM Focus Meeting

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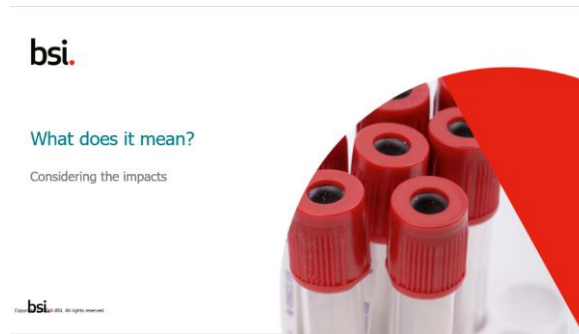
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Overview

Key impacts of the IVDR

1. Introduction and Timeline
2. Scope
3. Classification
4. Routes to Conformity
5. General Safety and Performance Requirements
6. Clinical Evidence
7. Post Market Activities
8. What does it mean – Assessing Impacts





1. Time line

IVD directive becomes a regulation

What's the difference

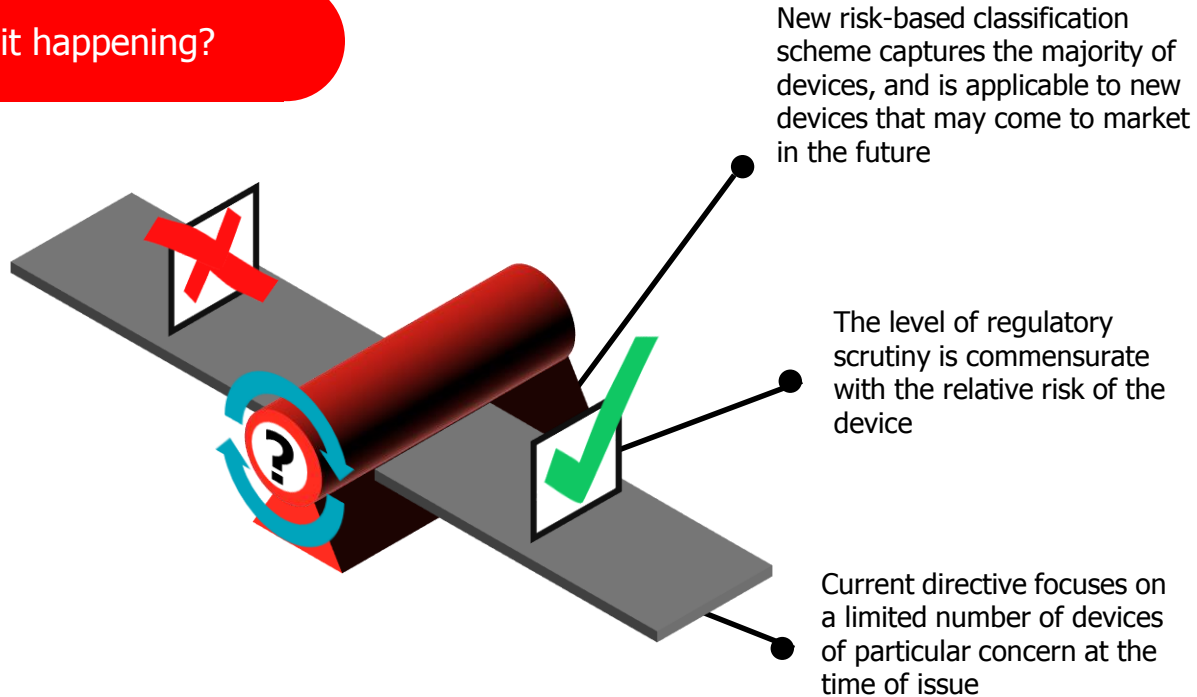
- A Directive is agreed by the European Parliament and Council and *directs* member states to pass national legislation to implement the directive
- A Regulation is a law agreed by the European Parliament and Council that takes effect directly in all member states

Impact of becoming a regulation

- The regulation is intended to result in more consistent application i.e. same text throughout EU
- Direct entry into force
- No Transposition period as it doesn't need transposing into Member State law
- There will be a transition period of 5 years
- The regulation identifies areas which can be updated in the future using additional implementing acts according to Article 84(3)

Advantages to the changes

Why is it happening?



Structure of IVDR

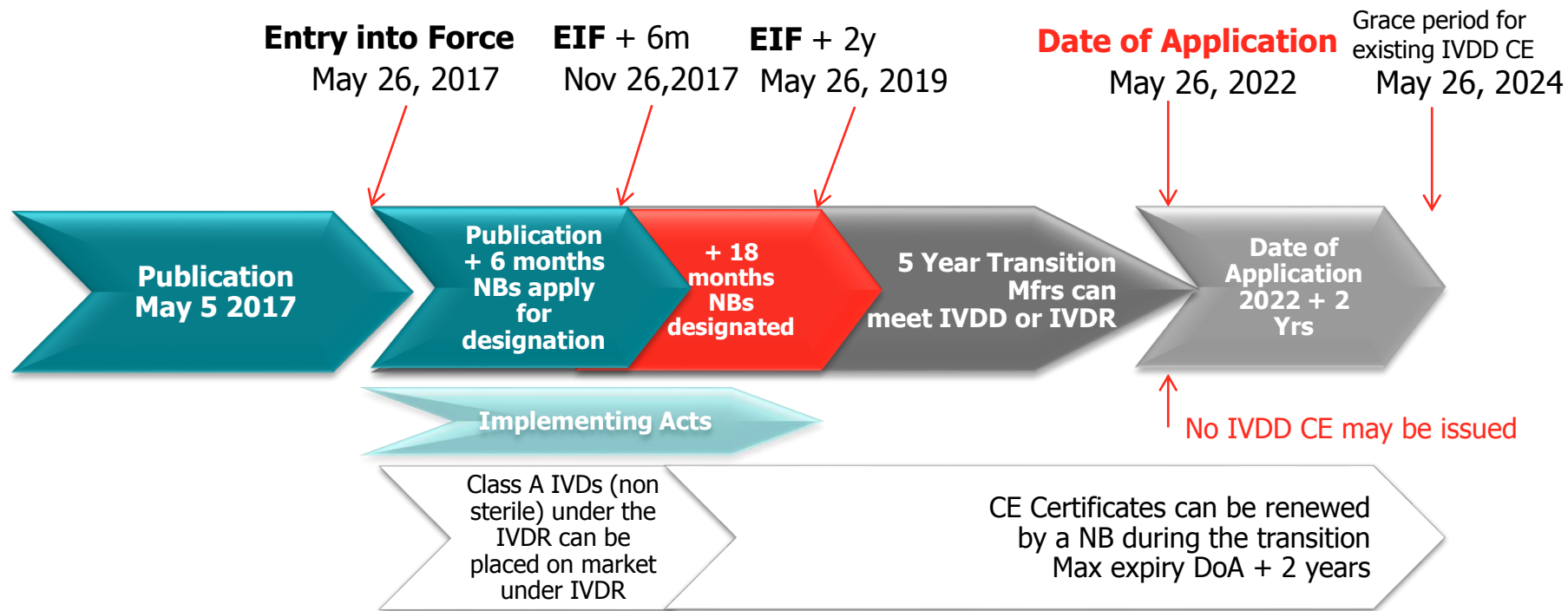
Chapters	10
Articles	113
Annexes	15

Annex I General Safety and Performance Requirements	
<ul style="list-style-type: none"> • 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
<ul style="list-style-type: none"> • Significantly more detail regarding the expectations for technical documentation 	

Annex III	Technical Documentation on Post-Market
Annex IV	Declaration of Conformity
Annex V	CE marking
Annex VI	Registration and UDI
Annex VII	Requirements for Notified Bodies
Annex VIII	Classification
Annex IX	Conformity assessment based on full QA or design examination
Annex X	Conformity assessment based on type examination
Annex XI	Conformity assessment based on production QA
Annex XII	Notified Bodies certificate content
Annex XIII	Clinical evidence and post-market follow-up
Annex XIV	Interventional clinical performance studies
Annex XV	Correlation table

More detailed and more prescriptive; consistent with the Medical Device Regulation

Transitional arrangements for IVDR





2. Scope

Scope – Definitions that apply

Medical Device

- 'medical device' means 'medical device' as defined in Regulation (EU) No 2017/745 [Regulation on medical devices].

Scope – Definitions that apply

Medical Device

- 'medical device/means medical device' as defined in the MDD [Regulation (EC) No 9026/2001]

In Vitro Diagnostic MD

- ...any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment, **software** or system,
- whether used alone or in combination, intended...to be used *in vitro* for the examination of specimens, including blood and tissue donations... from the human body,
- solely or principally for...providing information..

Scope – Definitions that apply

Medical Device

- 'medical device/means medical device' as defined in [Regulation]

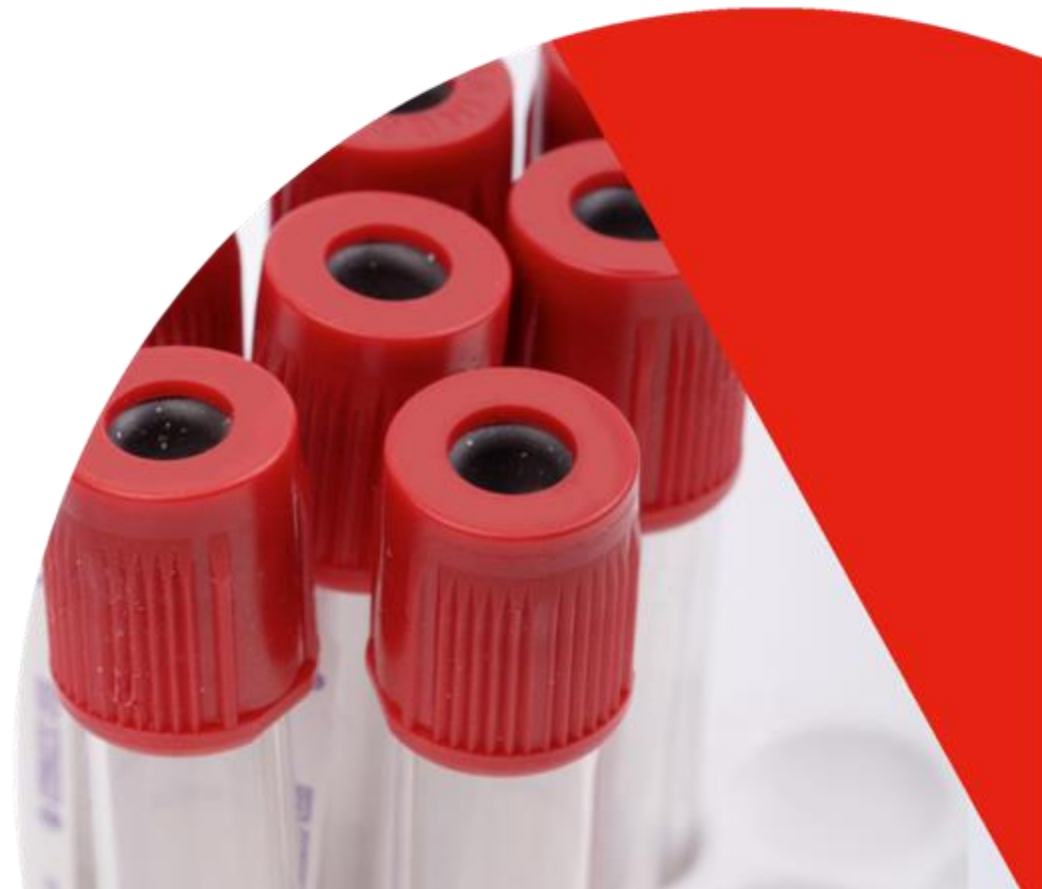
In Vitro Diagnostic MD

- concerning a physiological or pathological **process or** state;
- concerning congenital **physical or mental impairments**;
- **concerning the predisposition to a medical condition or a disease**;
- to determine the safety and compatibility with potential recipients;
- **to predict treatment response or reactions**;
- to **define or** monitor therapeutic measures.



What does it mean?

Considering the impacts



Impact

Planning

Implementation timelines are now established

Prepare a **transition plan** based on your product portfolio

Important factors to consider:

Notified body designation 2 years after entry into force – this means **only 3 years** to get all products reviewed

Some devices require **additional implementing acts** or establishment of EU Reference labs

Consider submitting a first product (which one?) and apply **lessons learned** to others

Notified body **gap analysis** or pilot review?

Scope

Do **changes in definition or scope** bring products under the IVDR that weren't considered under the IVDD?

Software?

Service Lab activities?



Classification

Reminder - IVDD Classification

Annex II List A

Highest Risk

- Detection of HIV, HTLV, and Hepatitis B, C, and D
- Blood typing for ABO system, Rhesus (C, c, D, E, e) anti-Kell

Annex II List B

High Risk

- blood groups Anti-Duffy and Anti-Kidd
- irregular anti-erythrocytic antibodies
- Rubella, Toxoplasmosis
- phenylketonuria
- Cytomegalovirus, Chlamydia
- HLA tissue groups DR, A, B
- tumour markers: PSA
- risk of trisomy 21 (includes software)
- self diagnosis for glucose

Self-test

Risk to lay user

All devices intended for self-test

Other

Risk level varies widely

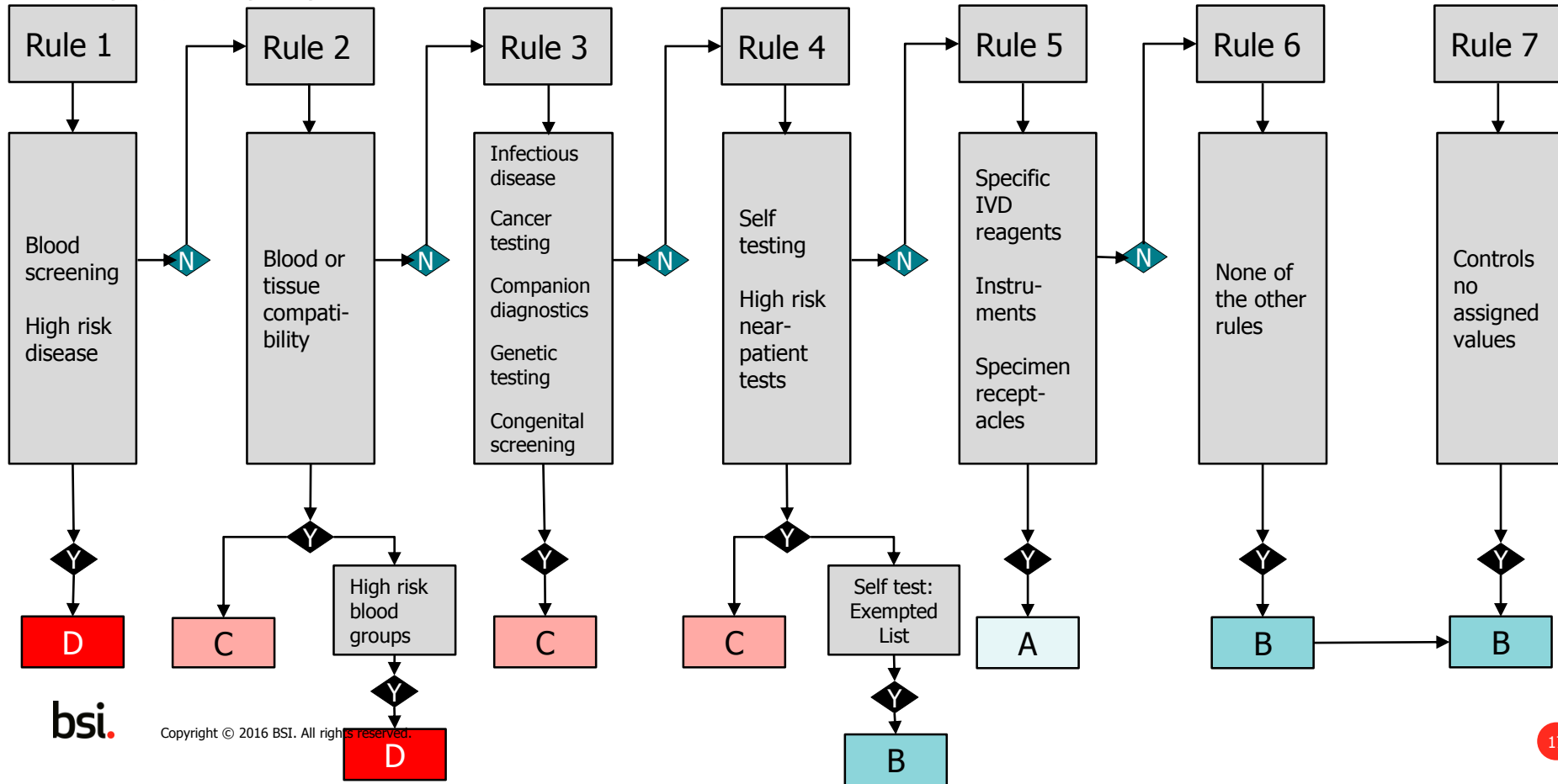
All other devices are self-declared, i.e. no notified body review

New Classification of IVDs by risk

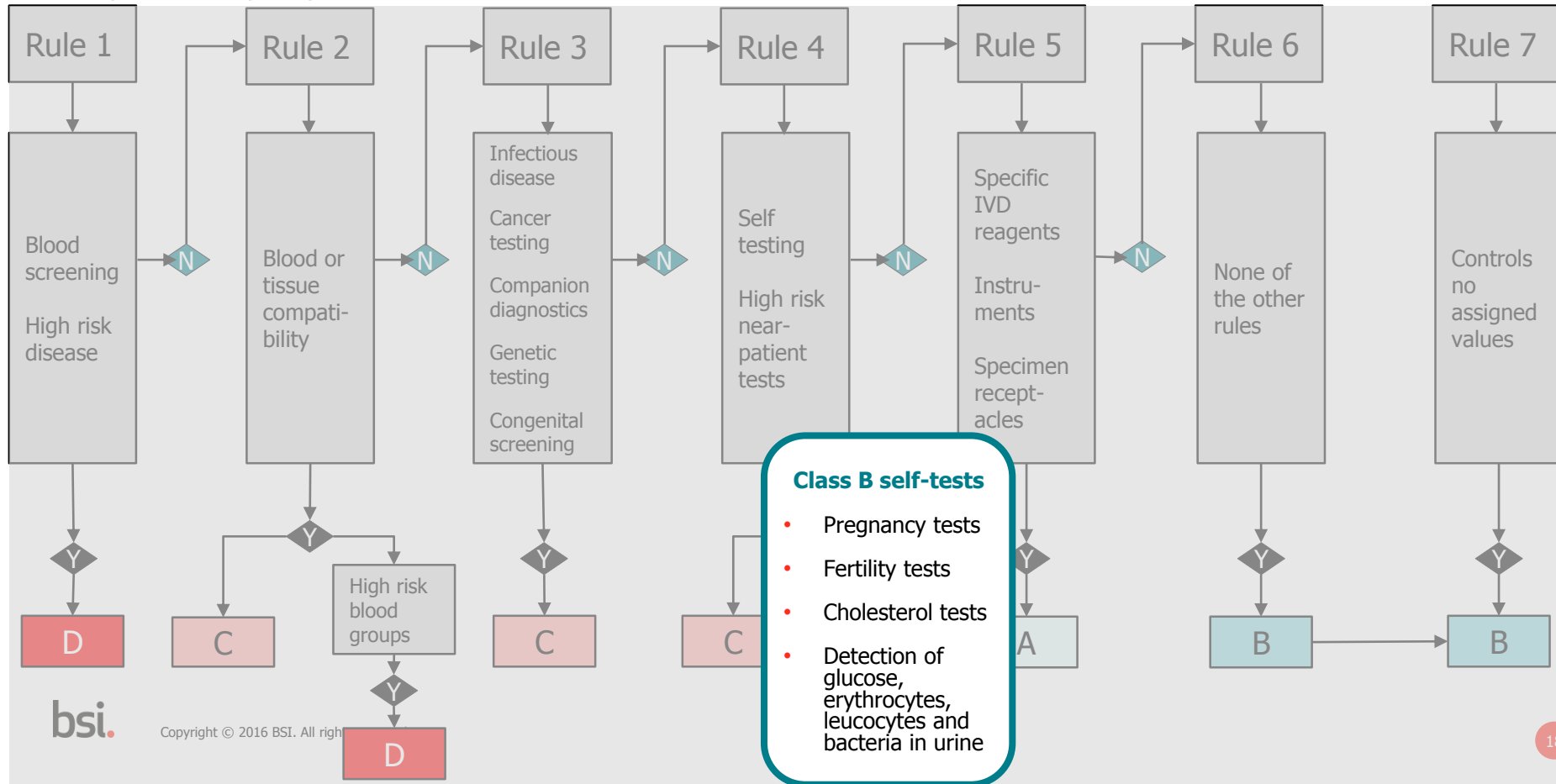


- Classification is based on the **intended use of the device**
- Risk classes A, B, C & D (where D is the highest) – Annex VIII
- Implementing acts and Guidance
- Borderline issues will be referred to the Competent Authority of the Manufacturer or Authorised Rep; if this is different to the CA of the NB, they will consult
- Role of Medical Device Coordination Group (MDCG)
- If there is more than one potential application for a test, and the intended use is of the lower classification, there must be a specific exclusion in the labelling
- Where more than one rule applies, the highest classification will be used.

Classification



Classification



New classes of IVD devices

Class D

**High public health risk,
high personal risk**

Examples

- HIV 1/2,
- Hepatitis C virus
- Hepatitis B virus
- HTLV I/II
- Blood grouping ABO, Rhesus (including RHW1), Kell, Kidd and Duffy systems
- CHAGAS
- Syphilis (used to screen blood donations)

Class C

**High personal risk,
moderate to low public health risk**

- Syphilis (diagnosis only)
- Neonatal screening for metabolic disorders e.g. PKU
- Rubella
- Cancer markers
- Genetic tests
- Companion diagnostics
- Blood glucose meters/strips
- Blood gas analysers
- Self tests

Class B

**Moderate to low personal risk,
low public health risk**

- Thyroid function
- Infertility assays
- Clinical chemistry
- Self-test devices listed as not Class C
- **'Near patient tests' are classified in their own right**

Class A

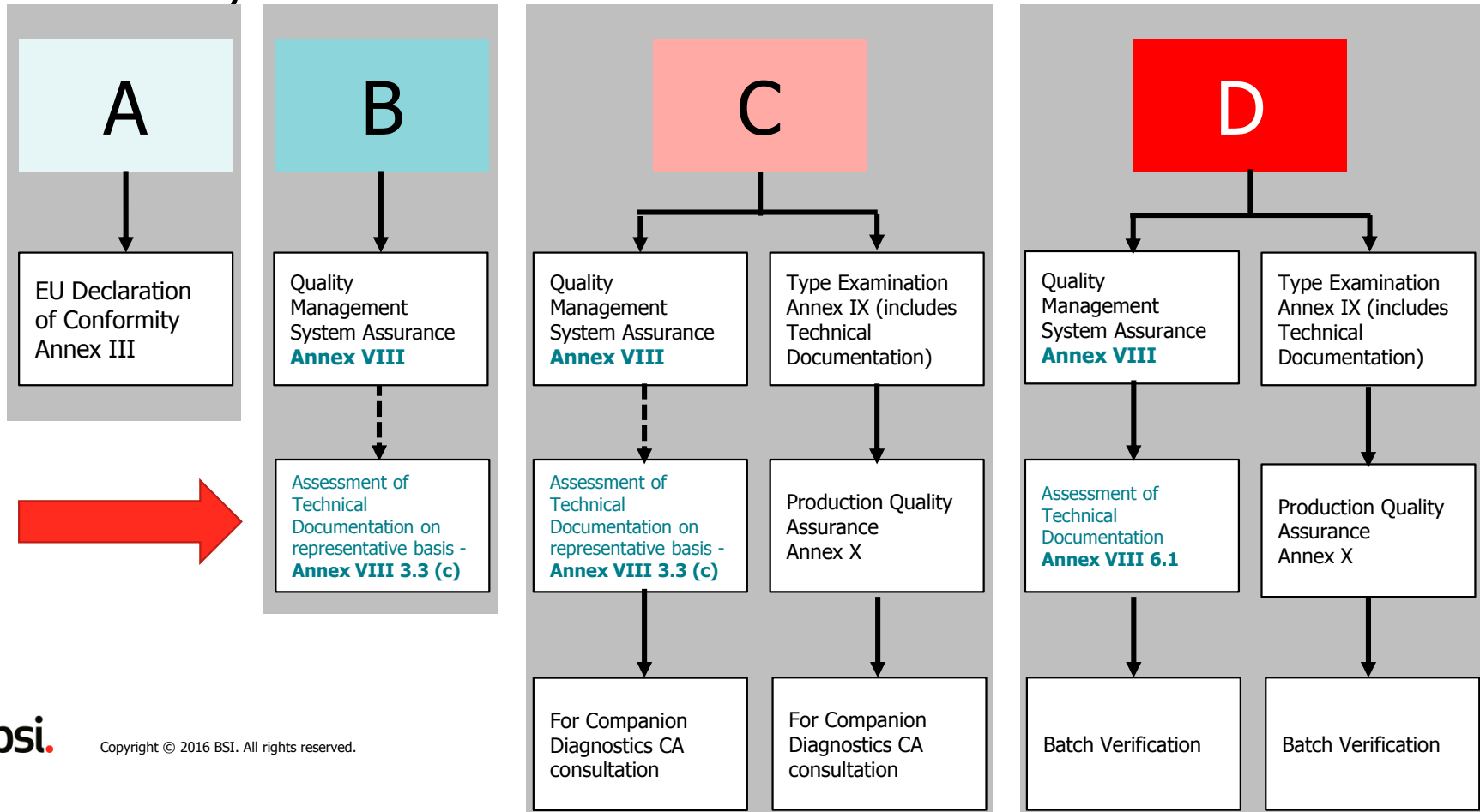
**Low personal risk, low
public health risk**

- Accessories
- Wash buffers
- Specimen receptacles
- Instruments
- Culture media



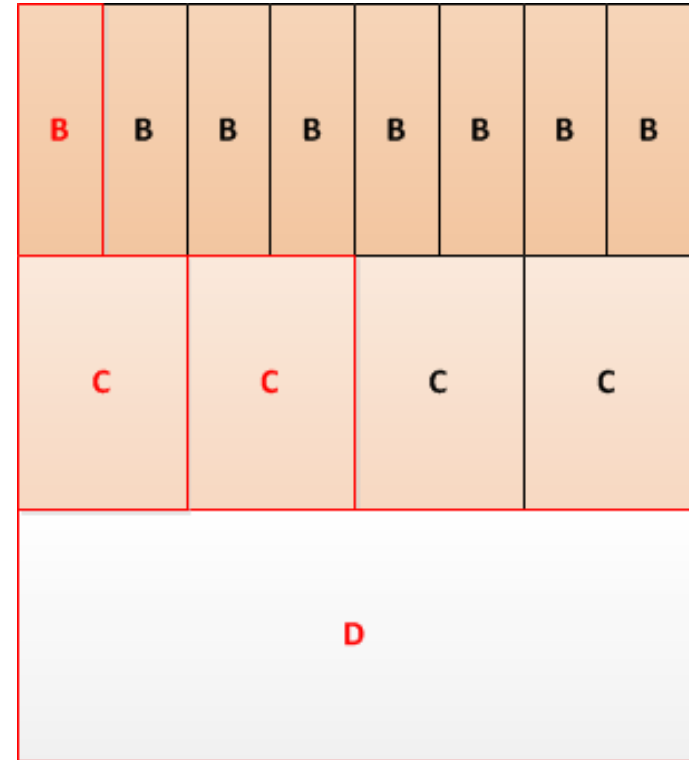
Conformity Assessment

Conformity Assessment

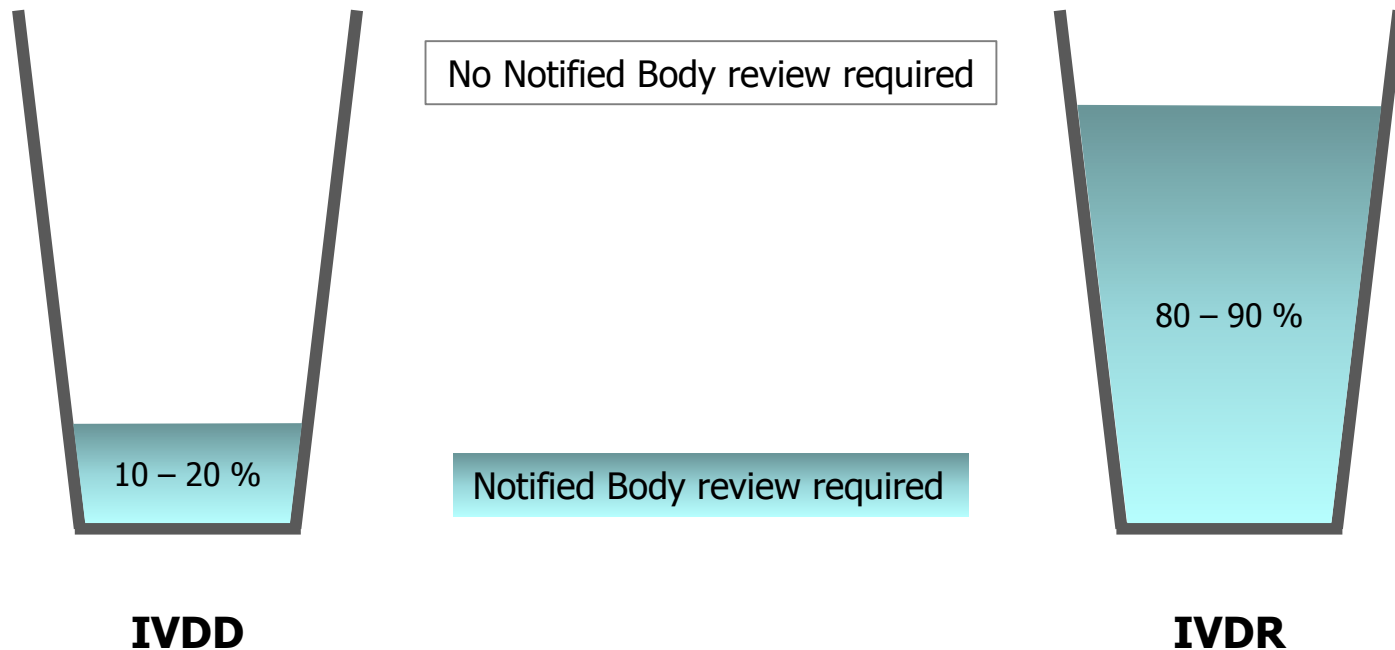


Sampling Plans

- All devices in Classes B – D will now get an in depth review
- Low risk devices will get less sampling

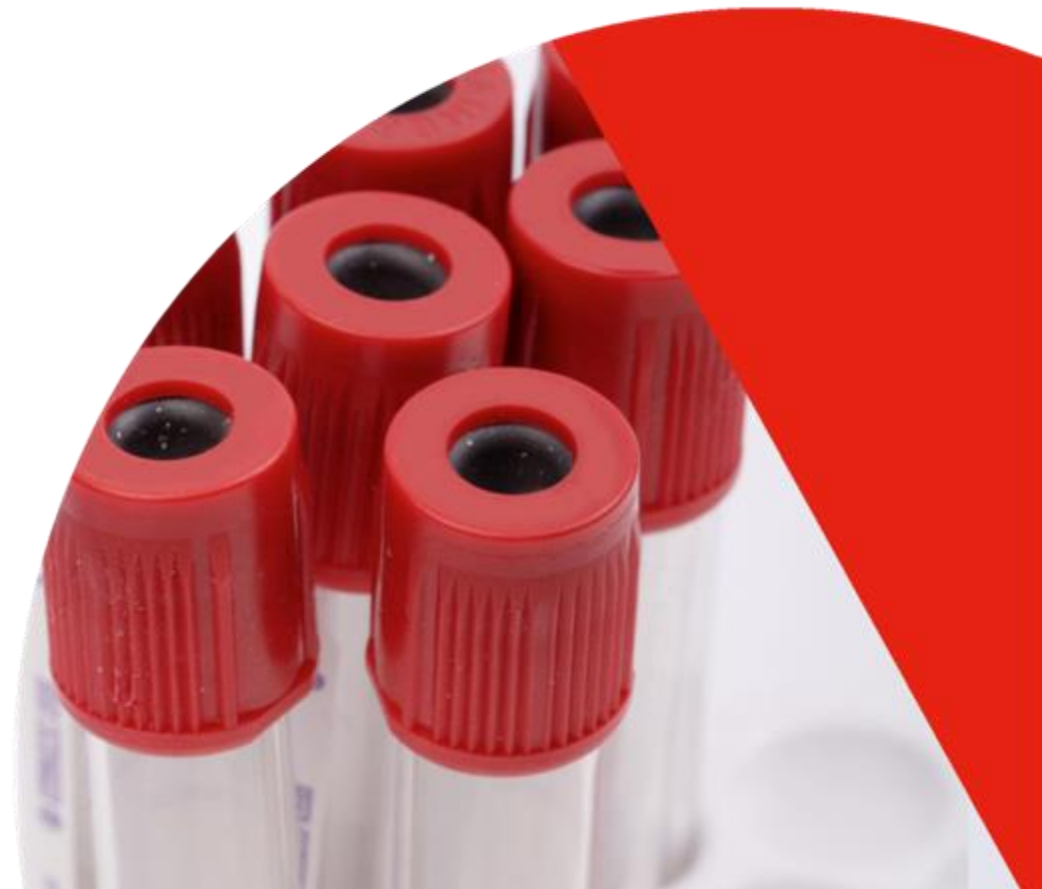


A sea change for industry and regulators



What does it mean?

Considering the impacts



Impact

Portfolio Analysis

Identify devices currently in your portfolio, and in the pipeline

Classify devices

Group into 'generic device groups' (Class C) and 'categories' (Class B)

More guidance will be needed to define these groups further

Define route to conformity

Planning

Identify desired route to conformity

Determine the order of submission to the Notified Body

Budget for cost of notified body assessments

Consider product lifecycle / obsolescence



General Safety and Performance Requirements

Reminder - IVDD Essential Requirements

A. General requirements

B. Design and manufacturing requirements

1. Chemical and physical properties

2. Infection and microbial contamination

3. Manufacturing and environmental properties

4. Devices which are instruments or apparatus with a measuring function

5. Protection against radiation

6. Requirements for medical devices connected to or equipped with an energy source

7. Requirements for devices for self-testing

8. Information supplied by the manufacturer

IVDR General Safety and Performance Requirements

I. General requirements

8 Requirements listed here.

IVDR General Safety and Performance Requirements

I. General requirements

II. Requirements regarding **performance**, design and manufacture

9. Performance characteristics

10. Chemical, physical **and biological** properties

11. Infection and microbial contamination

12. Devices incorporating materials of biological origin

13. Construction of devices and interaction with their environment

14. Devices ~~which are instruments or apparatus~~ with a measuring function

15. Protection against radiation

16. Electronic programmable systems – devices that incorporate programmable systems and software that are devices in themselves

17. Devices connected to or equipped with an energy source

18. Protection against mechanical and thermal risks

19. **Protection against the risks posed by** devices **intended** for self-testing **or near-patient testing**

IVDR General Safety and Performance Requirements

I. General requirements

II. Requirements regarding **performance**, design and manufacture



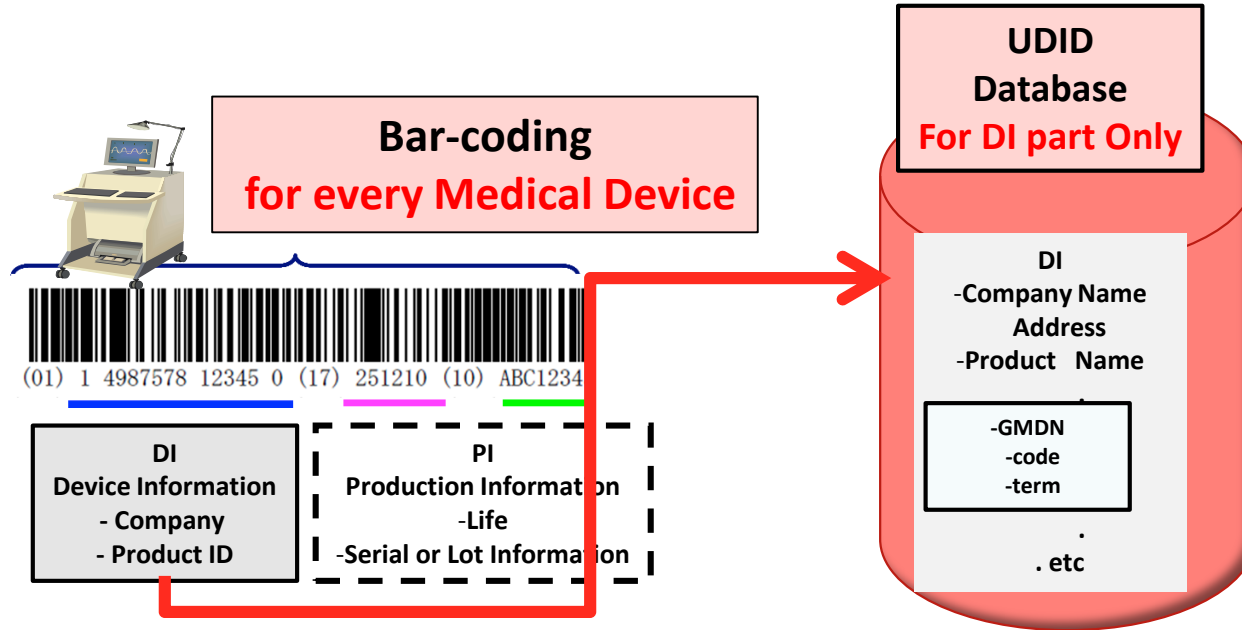
III. Requirements regarding information supplied with the device

20. **Label and instructions for use**

IVDR General Safety and Performance Requirements

- The IVDR has additional requirement to the IVDD
 - These include more detailed requirements on
 - Analytical performance
 - Clinical performance
 - Risk management
 - etc.
- The essential requirements of the IVDD are similar to the IVDR but they are now called GENERAL SAFETY AND PERFORMANCE REQUIREMENTS
- Even if you have all the data to meet the IVDR you will need to reformat all technical files to prove compliance to the IVDR

Unique Device Identifier





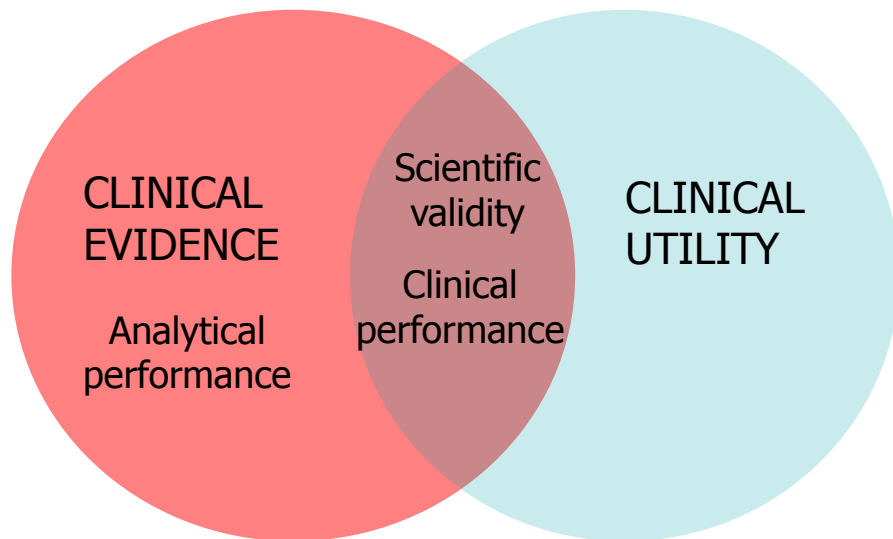
Clinical Evidence

'Clinical benefit' consideration



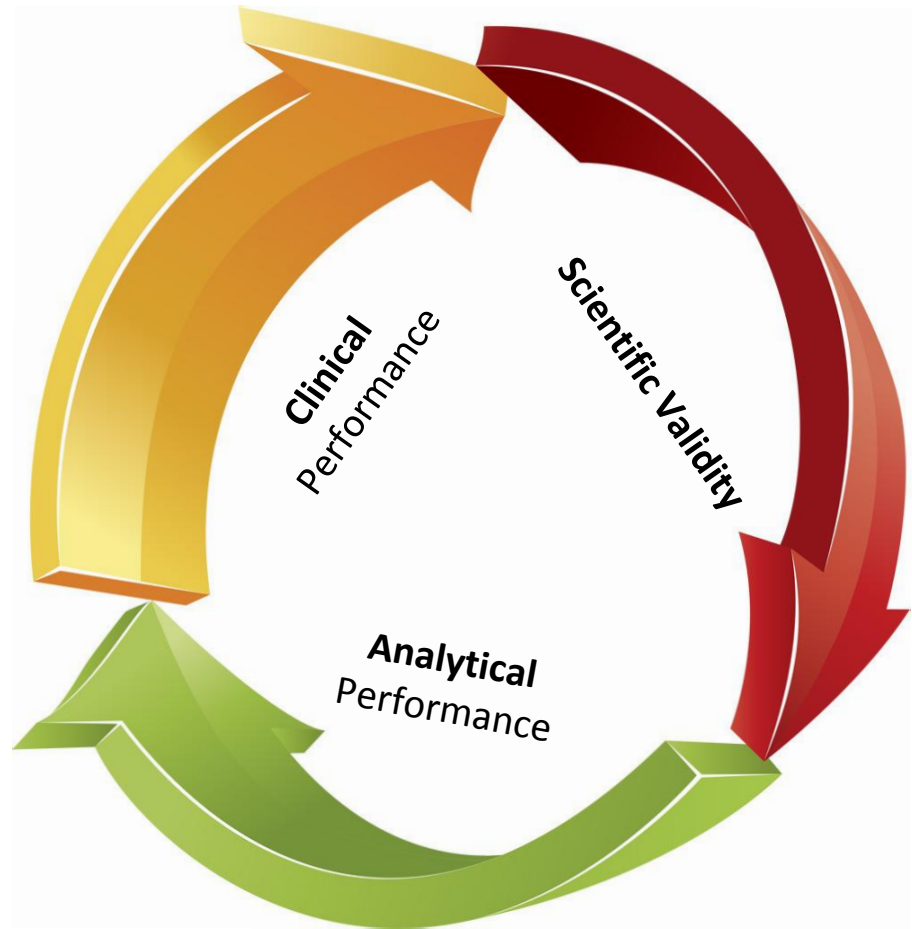
Clinical Evidence

- New requirement for Clinical Evidence
- ***Clinical evidence*** = clinical data and performance evaluation results, pertaining to a device of sufficient amount and quality to allow a qualified assessment of whether the device achieves the intended clinical benefit and safety, when used as intended by the manufacturer
- Based on harmonised guidance
- **GHTF documents** (IMDRF archive):
 - Clinical Performance Studies for In Vitro Diagnostic Medical Devices
 - Clinical Evidence for IVD Medical Devices – Key Definitions and Concepts
 - Clinical Evidence for IVD Medical Devices – Scientific Validity Determination and Performance Evaluation



Performance Evaluation

- Sum total = **Clinical Evidence**
- ***Process*** of Performance Evaluation
- Done according to a **Performance Evaluation Plan**
- Collated as a **Performance Evaluation Report**
- Continuous during life-time of the device



Expectations for Performance

Performance Evaluation Plan, as well as a file of **Clinical Evidence** will form part of the Technical Documentation, as a **Performance Evaluation Report**

- **Clinical Performance studies** may be required, unless justified

Interventional performance studies – new requirements

- In line with clinical trial expectations for clinical trials of medicinal products

Clinical Evidence will need to be updated

- Consolidated text states if there has been a 'trigger', then the PE Report will need updating

Post-market Surveillance and **Post-market Performance Follow-up (PMPF)**

Summary of safety and performance

Refer to Article 24(1) EU 2017/746

Applicable to class C and D
devices (not devices for
performance evaluation)



Post market surveillance



Post market surveillance

For **each device** manufacturers shall plan, establish, document, implement, maintain and update **a post-market surveillance system** in a manner that is proportionate to the risk class and appropriate for the type of device.

Suited to actively and systematically gathering, recording and analysing relevant data on a device **throughout its entire lifetime** ...

Data gathered by the manufacturer's post-market surveillance system shall in particular be used:

- (a) to **update** the benefit-risk determination and to improve the risk management
- (b) to **update** the design and manufacturing information, the instructions for use and the labelling
- (c) to **update** the performance evaluation
- (d) to **update** the summary of safety and performance referred to in Article 29
- (e) for the identification of needs for **preventive, corrective or field safety corrective action**
- (f) for the identification of options to improve the usability, performance and safety of the device
- (g) when relevant, to contribute to the post-market surveillance of other devices; and
- (h) to detect and report trends in accordance with Article 83. The technical documentation shall be updated accordingly.

Outputs of post market activities

Post market surveillance plan

Prepare a documented plan and follow it

Post market surveillance report

Class A & B devices – prepare a report and update as needed

Periodic safety update report

Class C & D devices – prepare a summary at least annually

- Results of post market surveillance and post market performance follow up
- Risk Management
- Sales numbers

For Class D – submit electronically to the EUDAMED database

Vigilance

Requirements are similar to the IVDD:

Report to the relevant competent authorities the following:

- any serious incident involving devices made available on the Union market
- any field safety corrective action in respect of devices made available on the Union market, including any field safety corrective action undertaken in a third country in relation to a device which is also legally made available on the Union market

Reporting timelines:

- **Serious incident:** immediately on establishing a causal relationship, **no more than 15 days**
- **Serious public health threat:** immediately upon awareness, **no more than 2 days**
- **Death or serious deterioration in state of health:** immediately on establishing a causal relationship, **no more than 10 days**

Post market performance follow up



Post market performance follow up

PMPF is a **continuous process** to update the performance evaluation, and shall be addressed in the post-market surveillance plan.

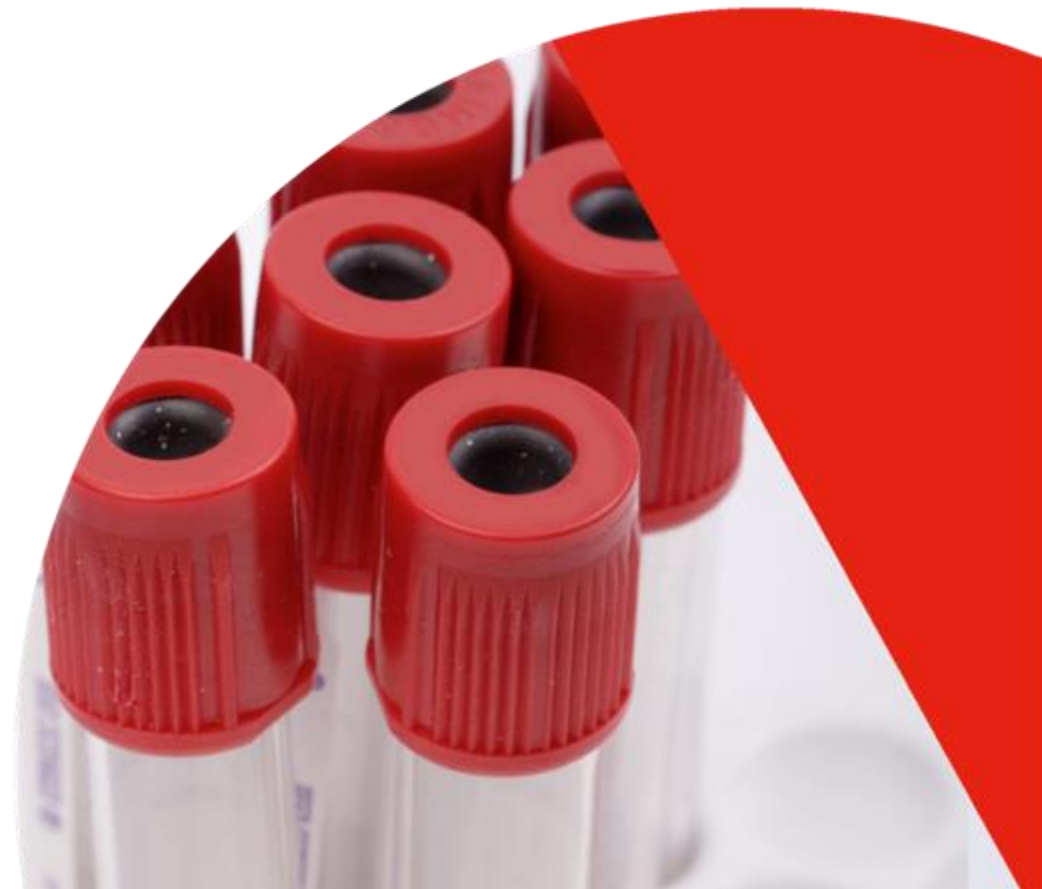
PMPF shall be performed pursuant to a **documented method laid down in a PMPF plan**. This includes:

- (a) confirming the safety and performance of the device throughout its expected lifetime,
- (b) identifying previously unknown risks or limits to performance and contra-indications,
- (c) identifying and analysing emergent risks on the basis of factual evidence,
- (d) ensuring the continued acceptability of the clinical evidence and of the benefit-risk ratio referred to in Sections 1 and 8 of Chapter I of Annex I, and
- (e) identifying possible systematic misuse.

Results are captured in a **report** that forms part of the technical documentation and **updates the performance evaluation report**.

What does it mean?

Considering the impacts



Impact

Technical Documentation

Every technical file needs to be touched to be updated – Additional reports will be needed

Additional studies may be required – analytical, clinical

Risk Management may need to be revised

Greater requirements for updating technical documentation going forward

All products will need to be relabeled for UDI & other labeling requirements

Resources

Personnel – documentation & technical

Clinical studies – sites, investigators, informed consent...

Cost of the above

Time to get additional data – before submission of documentation for notified body review.

Summary



IVDR Impacts

- Sweeping changes are necessary
- Significant increased resource and organizational requirements
- Do not wait until the end of the transition period
- Prepare a transition plan
- Engage with notified body, subcontractors, authorized reps, etc.

Questions?

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