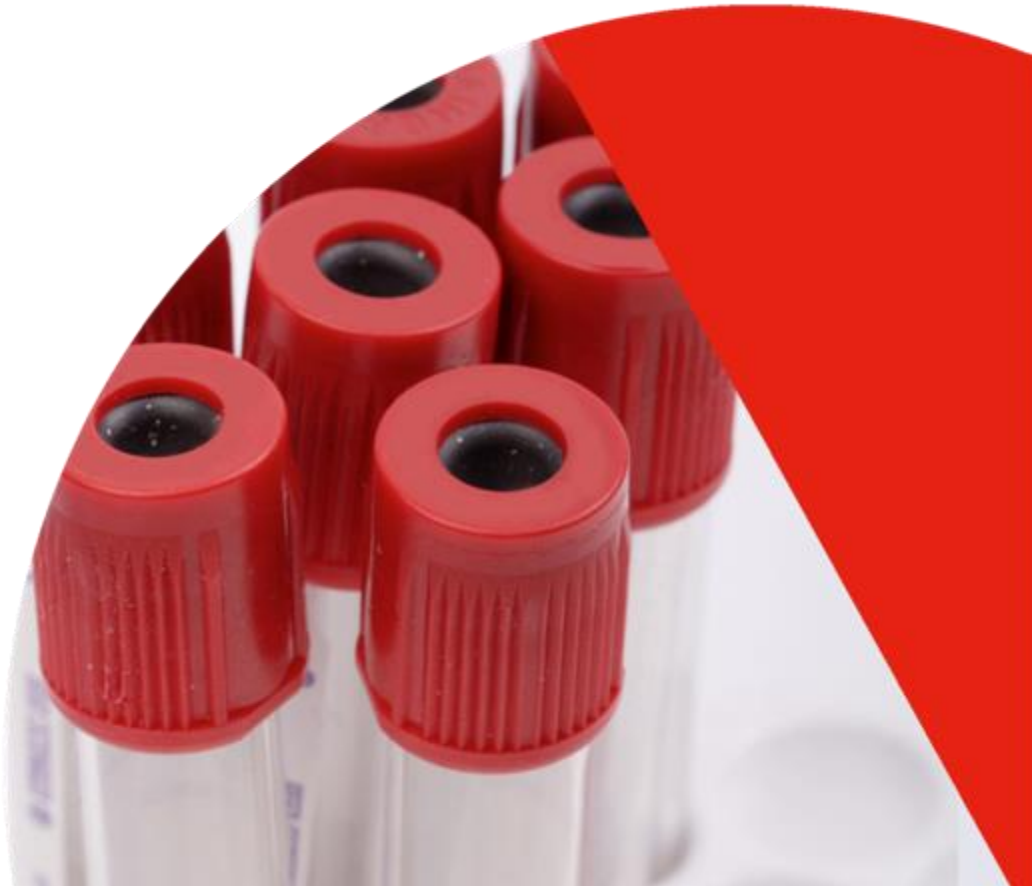
Update on the IVDR



AMDM Focus Meeting

October 11, 2018

Stefan Burde

Timeline

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)

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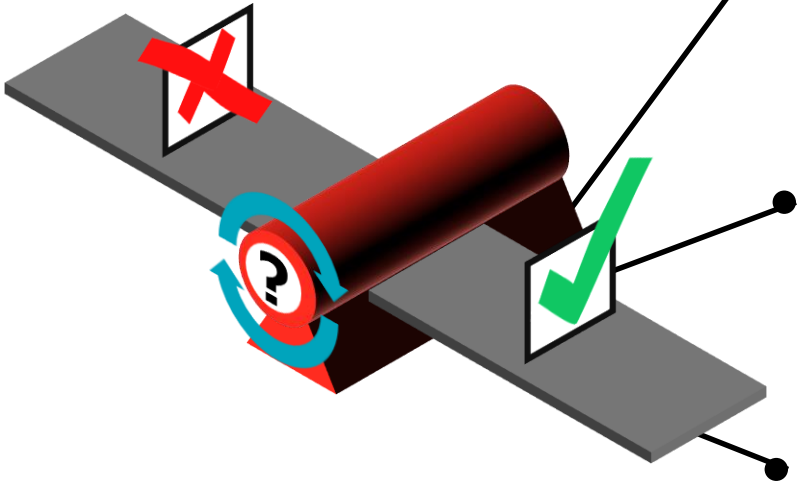
Advantages to the changes

Why is it happening?



New risk-based classification scheme captures the majority of devices, and is applicable to new devices that may come to market in the future

The level of regulatory scrutiny is commensurate with the relative risk of the device

Current directive focuses on a limited number of devices of particular concern at the time of issue

Structure of IVDR

Chapters	**10**
Articles	**113**
Annexes	**15**

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	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

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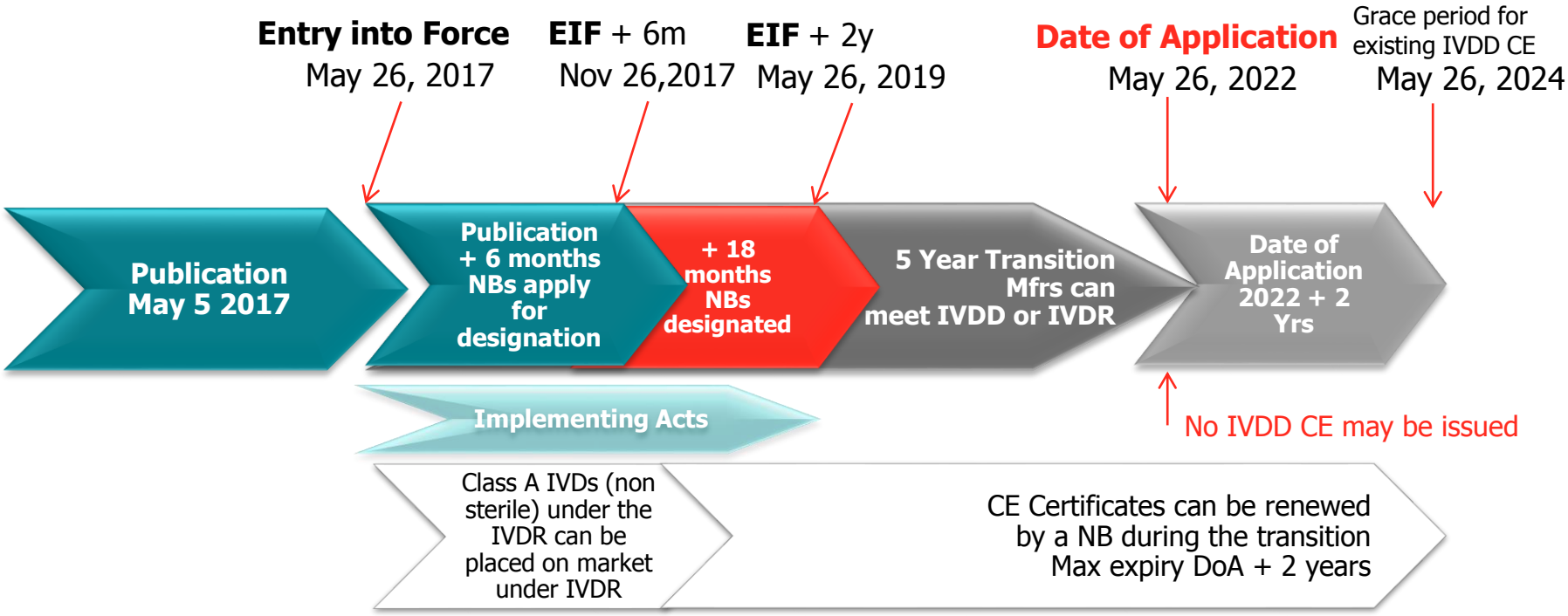
Transitional arrangements for IVDR



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 [illegible] as d[illegible] [Re[illegible] me[illegible]

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 [illegible] as d[illegible] [Re[illegible] me[illegible]

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.

Classification

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.

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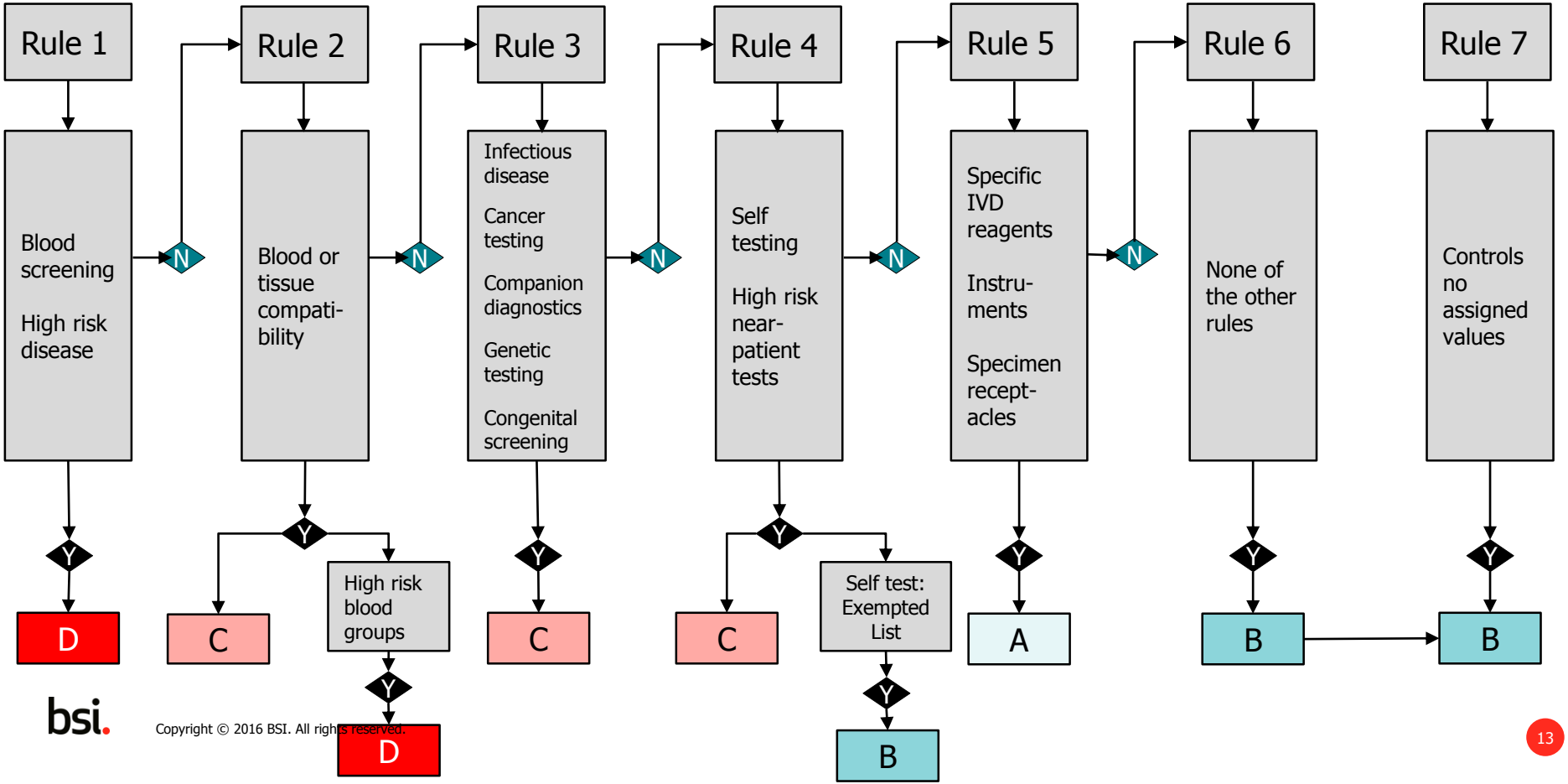
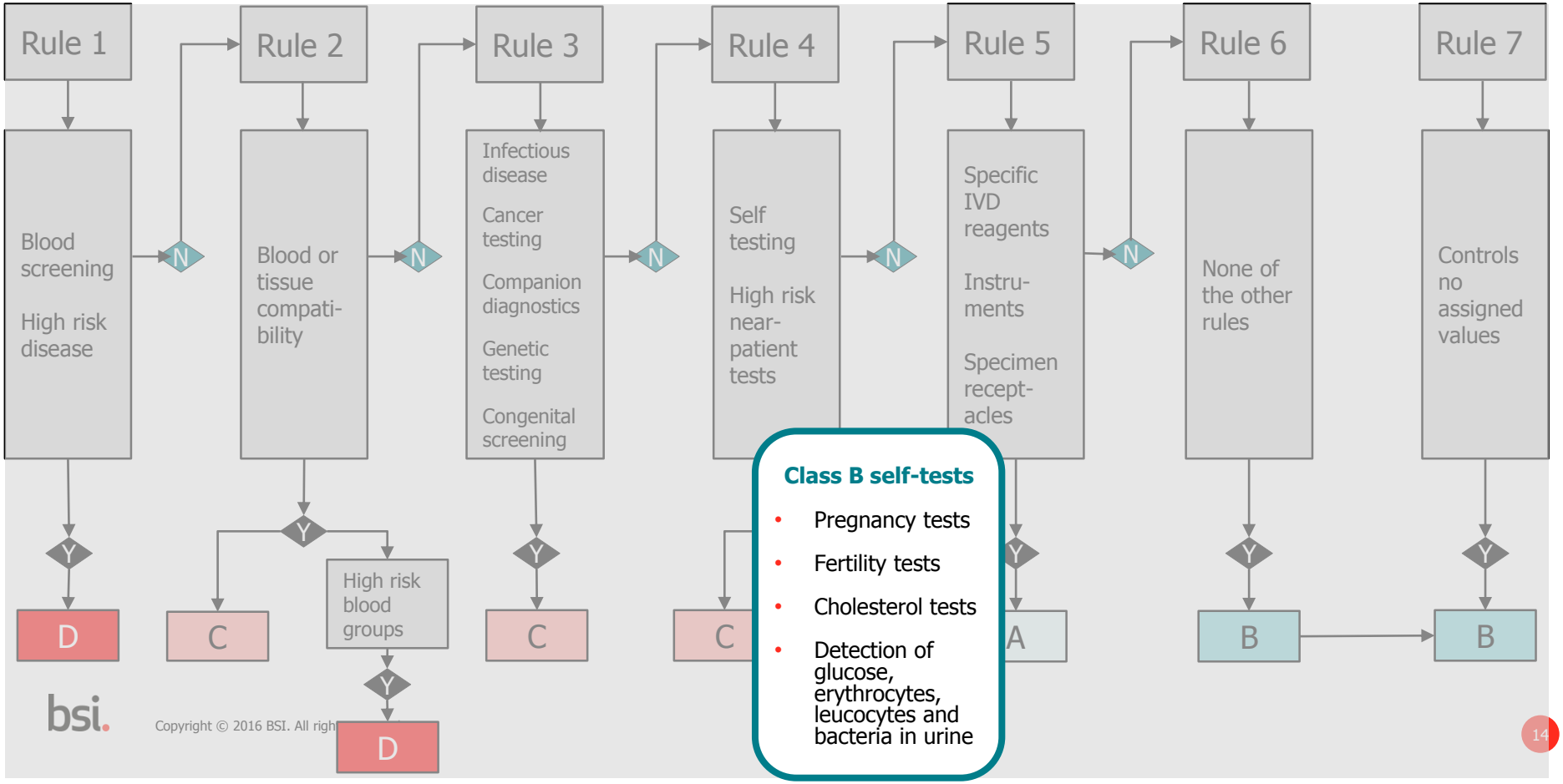
Classification



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

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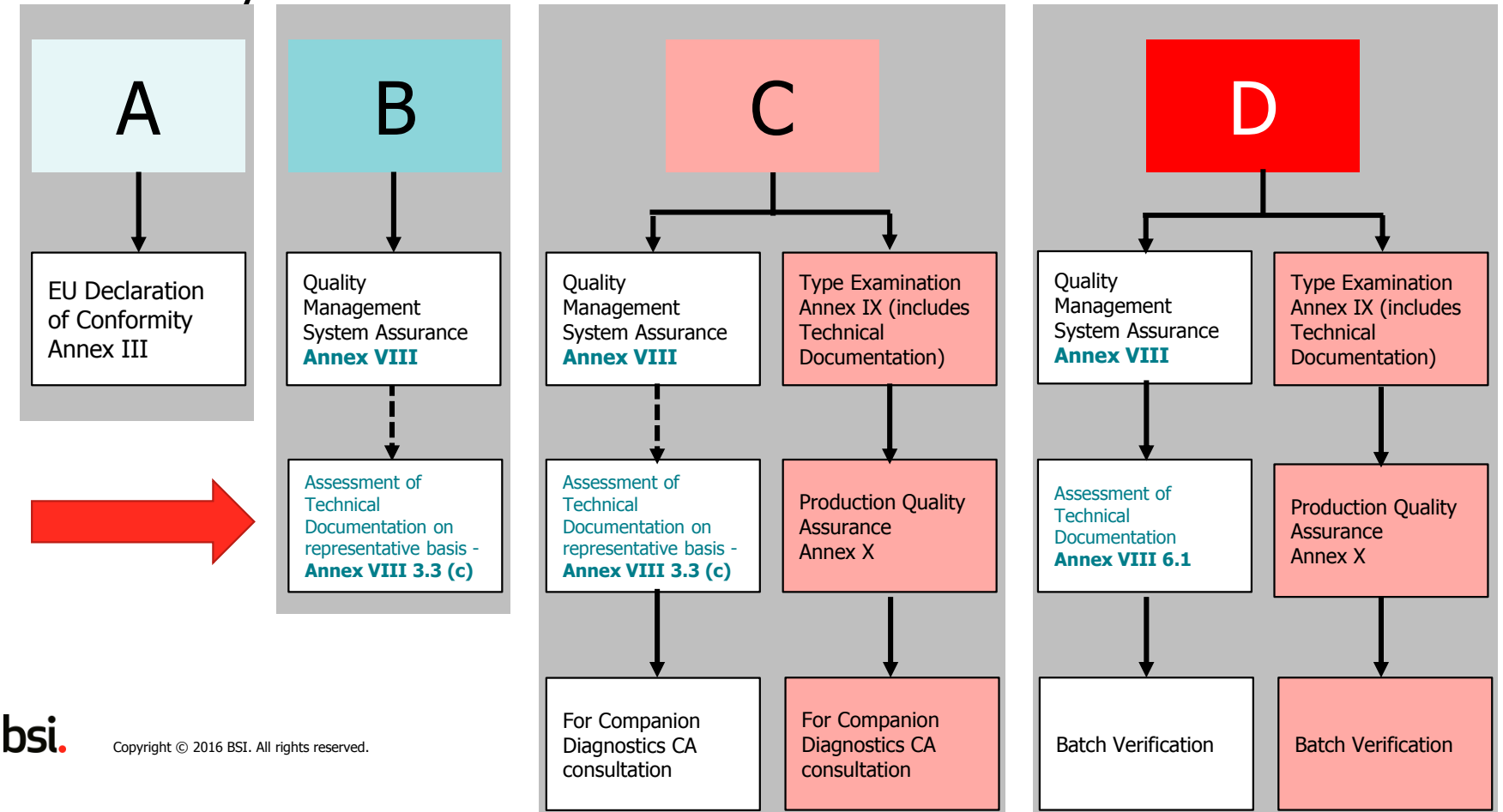
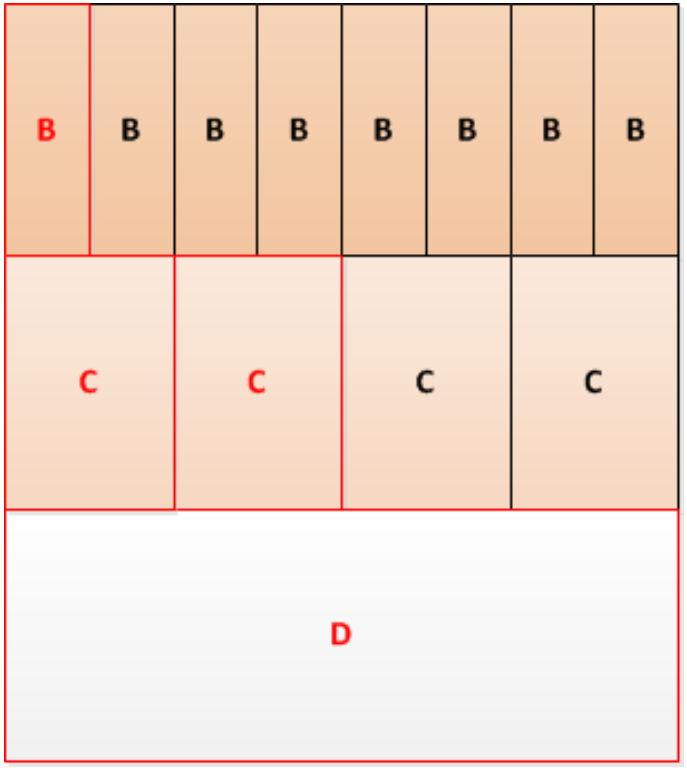
Conformity Assessment

Conformity Assessment

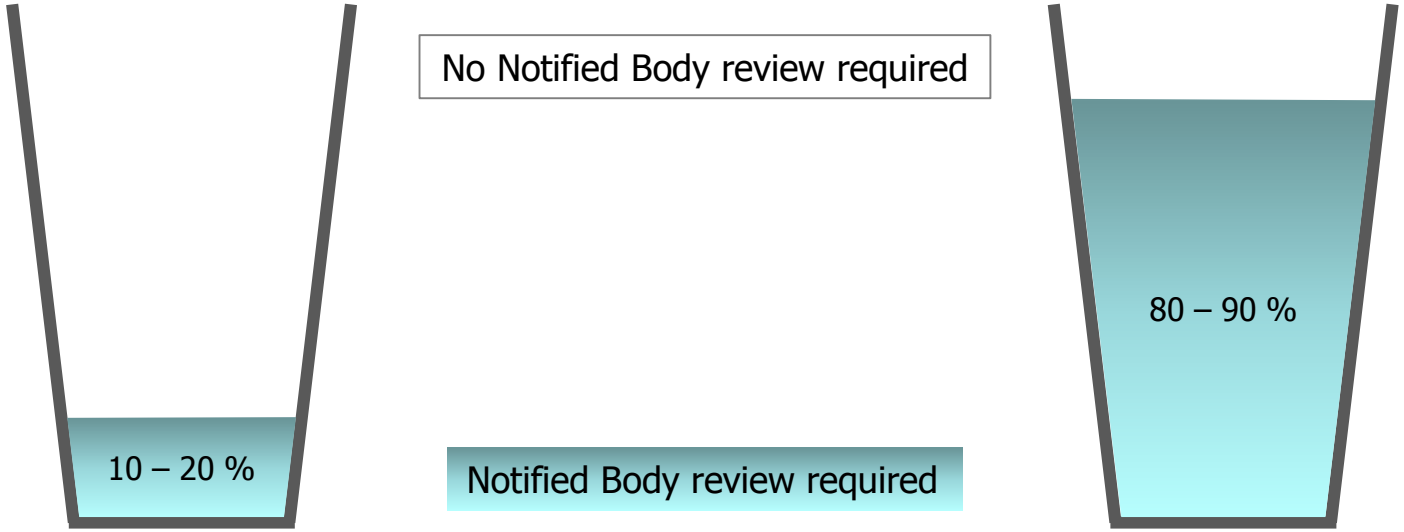


Sampling Plans

- 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



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General Safety and Performance Requirements

IVDR General Safety and Performance Requirements

I. General requirements

8 Requirements listed here.

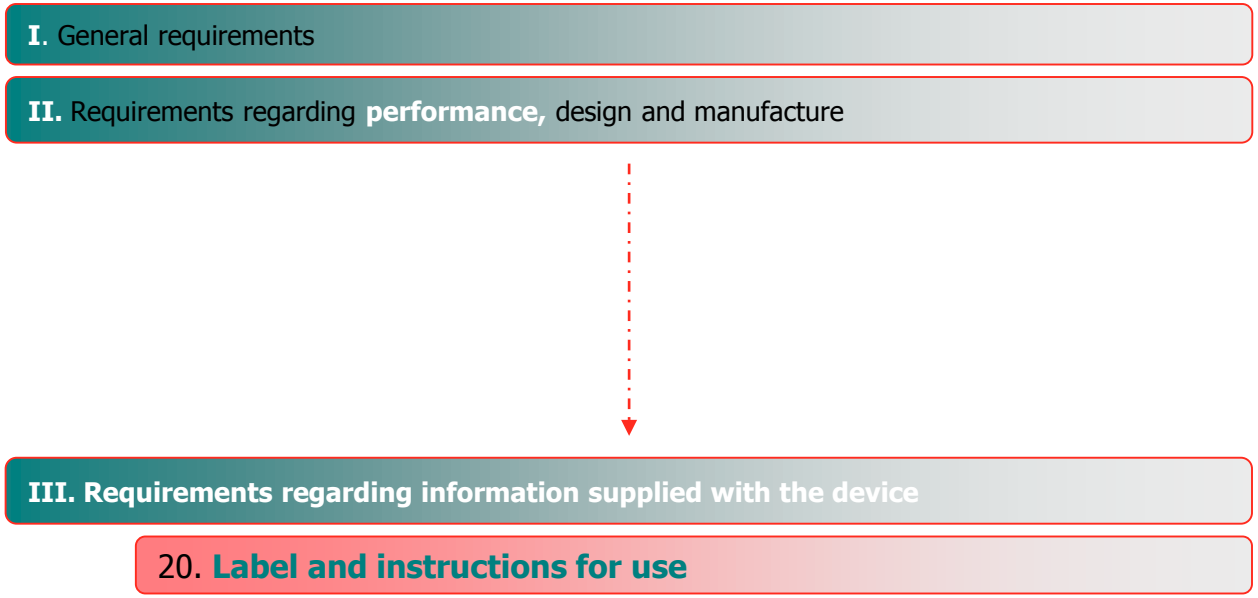
IVDR General Safety and Performance Requirements

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



IVDR General Safety and Performance Requirements

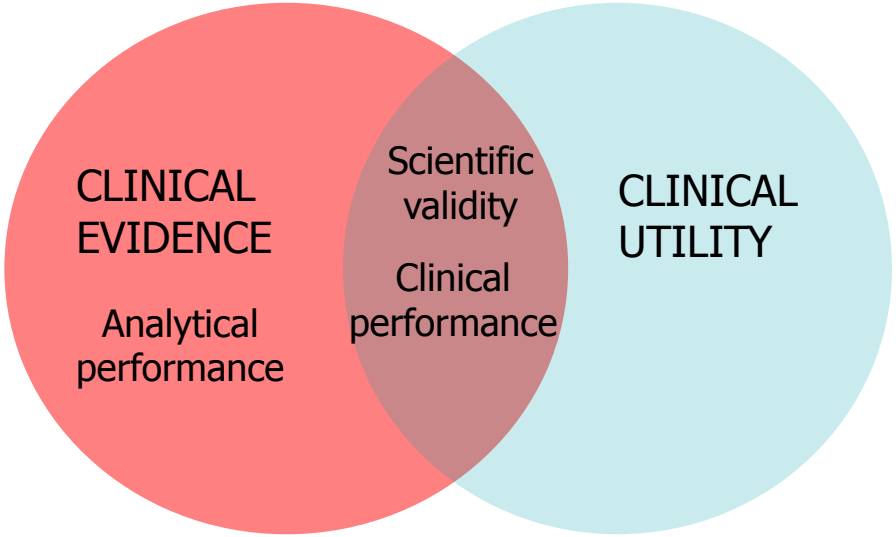
- The IVDR has additional requirement to the IVDD
  - These include more detailed requirements on
    - Analytical performance
    - Clinical performance
    - Risk management
    - etc.
- The essential requirements of the IVDD are similar to the IVDR but they are now called GENERAL SAFETY AND PERFORMANCE 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

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

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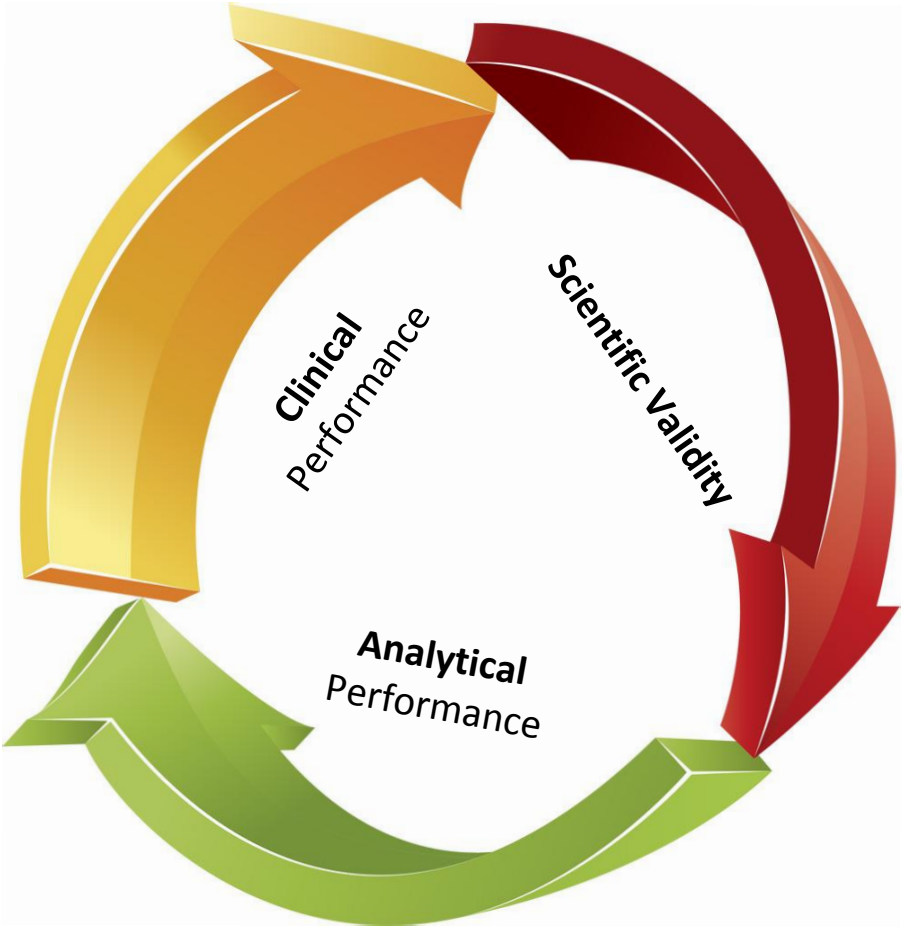
Performance Evaluation

- 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



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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)**

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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

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

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.

Technical Documentation

Some practical pointers

Technical Documentation

Key Annexes

Annex II: Technical Documentation

Annex III: Technical Documentation on Post-market Surveillance

Annex XIII: Performance Evaluation, Performance Studies and Post-market Performance Follow-up

Required documentation.	
Labelling (Annex II Sec. 2)	
IFU (Annex II Sec. 2)	
Documentation of compliance to SPR – e.g. Checklist (Annex II Sec. 4)	
Post-market Surveillance (PMS) Plan (Annex III Sec. 1)	
PMS Report (Annex III Sec. 2)	
PSUR (Annex III Sec. 2)	**N/A** for Class A sterile and B
Summary of Safety and Performance (SSP) (Art 29.1)	**N/A** for Class A sterile and B
Declaration of Conformity (Annex IV)	
Performance Evaluation Plan (Annex XIII Sec. 1.1)	
Scientific Validity Report (Annex XIII Sec. 1.2.1)	
Analytical Performance Report (Annex XIII Sec. 1.2.2)	
Clinical Performance Report (Annex XIII Sec. 1.2.3)	

Required documentation.	
Performance Evaluation Report (Annex XIII Sec. 1.3.2)	
Clinical Performance Study Plan (Annex XIII Sec. 2.3.2)	
Clinical Performance Study Report (Annex XIII Sec. 2.3.3)	
Post-market Performance Follow-up (PMPF) Plan (Annex XIII Sec. 5)	
PMPF Evaluation Report (Annex XIII Sec. 6)	**N/A** for new application
Risk Management Plan, report and FMEAs. (Annex I sec 4, EN ISO 14971-2012)	
Compliance with Common Specification	If a CS exists for the device
Stability (Annex II 6.3)	
Manufacturer's details, EU rep and person responsible for regulatory compliance. (Article 10,11,15)	
Device description, UDI, classification and rationale. (Annex II 1.1, Annex VI C, Annex VIII)	

Requirements for Document Content.
Technical documentation must be:
Clear
Readily searchable (optical recognition, unprotected and bookmarked)
Unambiguous (paginated)
The **SPR checklist** (or equivalent) must include the **precise identity of the controlled documents** offering evidence of … conformity with the SPR
Cross-reference to the location of the evidence within the Technical Documentation must be included

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.

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Questions?

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