Performance Evaluation

PART 2

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By Royal Charter

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Performance Evaluation – Part 2

PART 1 Performance Evaluation

- Introduction to Performance Evaluation
- Performance Evaluation Plan
- Scientific Validity
- Link to PE Report & conclusion

Performance Evaluation under the In Vitro Diagnostic Regulation (IVDR) – Part 1

Download the presentation >

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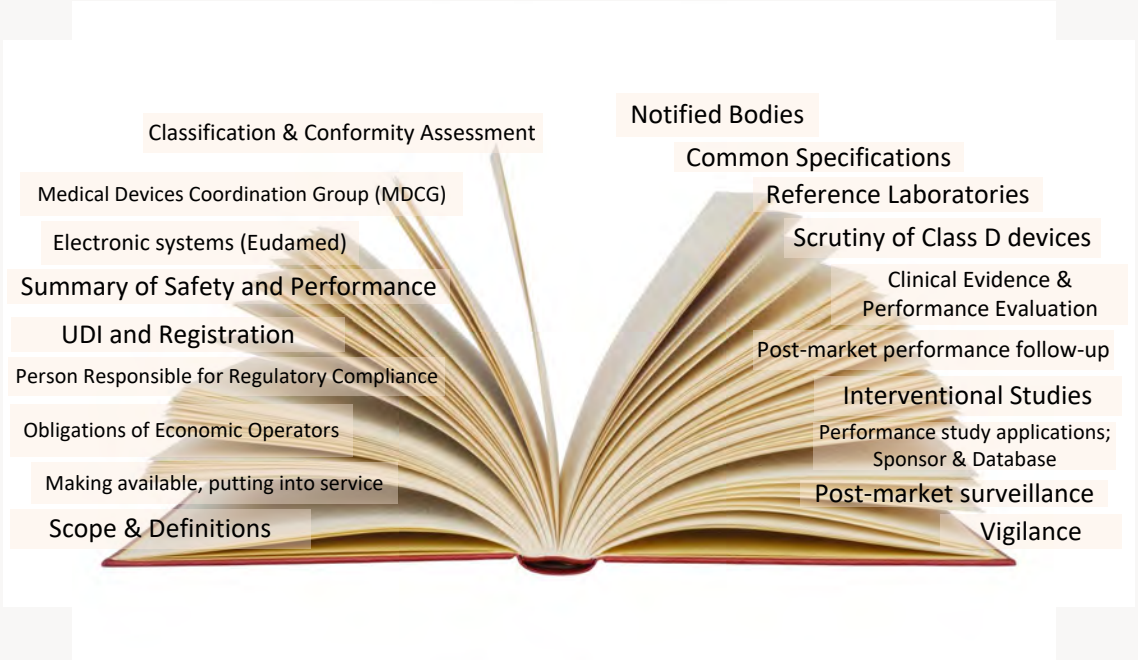
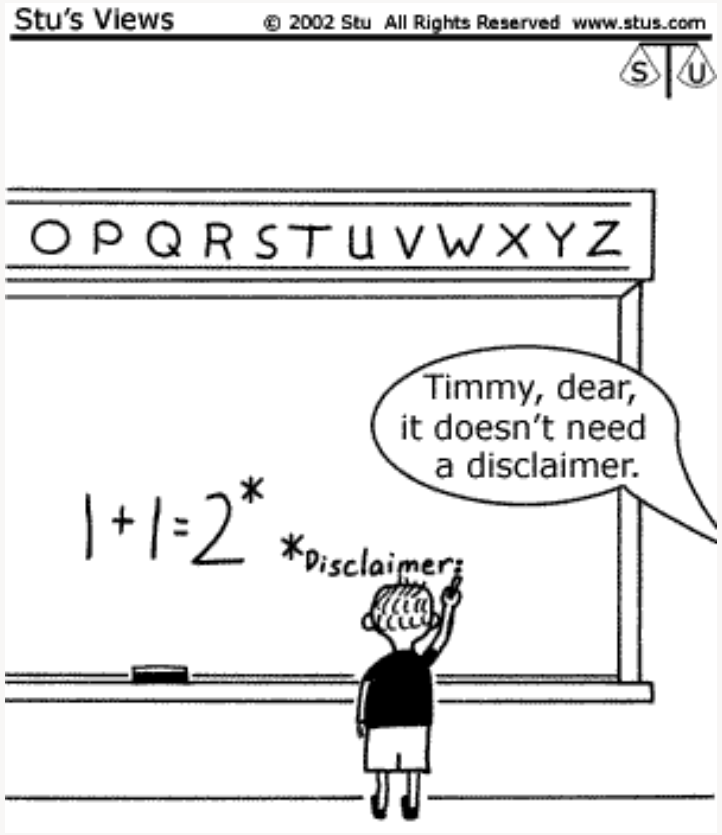
www.bsigroup.com/IVDR

Performance Evaluation – Part 2 Agenda

- Introduction to Performance Evaluation (brief)
- Clinical Performance
- As part of the Performance Evaluation Report (PER)
- Link to Post-Market Performance Follow-up (PMPF)



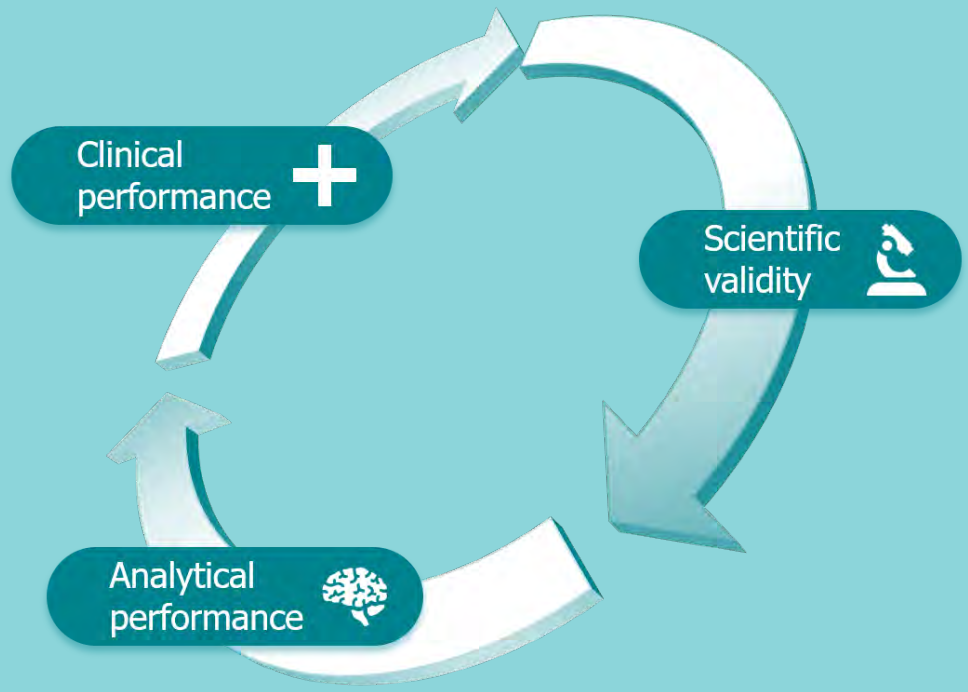
Disclaimer



- Information presented within this webinar is based on our current understanding of the IVDR
- Subject to change

Introduction

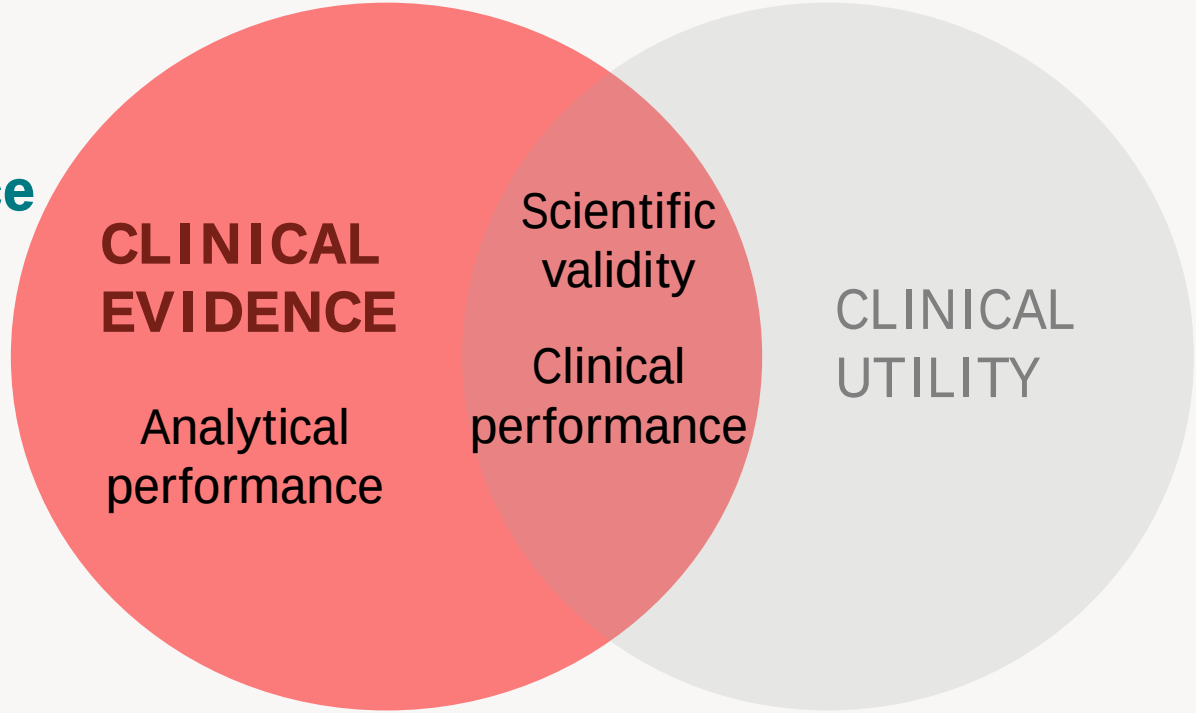
- Performance Evaluation under the IVDR



Clinical Evidence

= Scientific Validity + Analytical Performance + Clinical Performance

= 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



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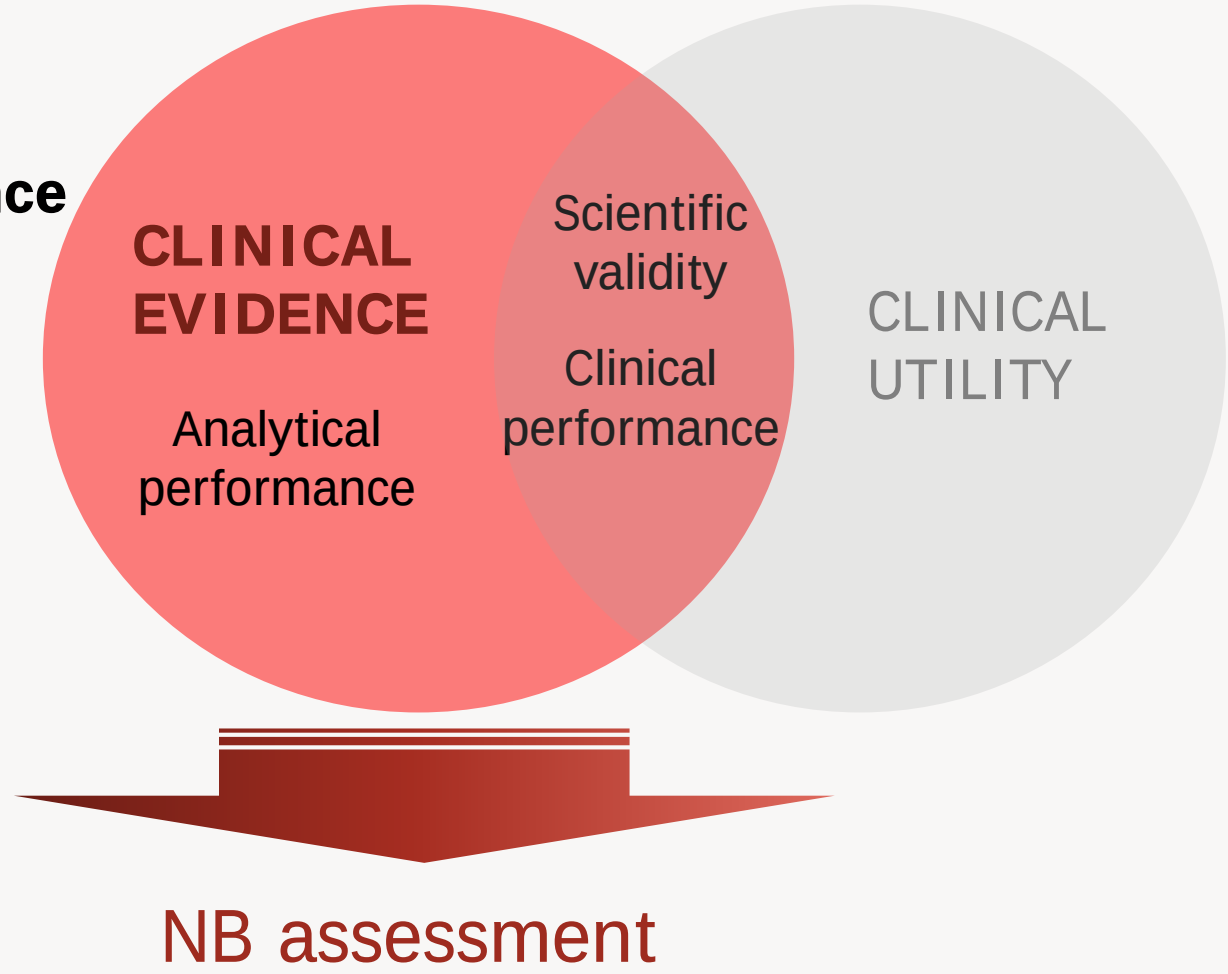

‘Clinical benefit’ consideration

Reference: IVDR Preamble (64)

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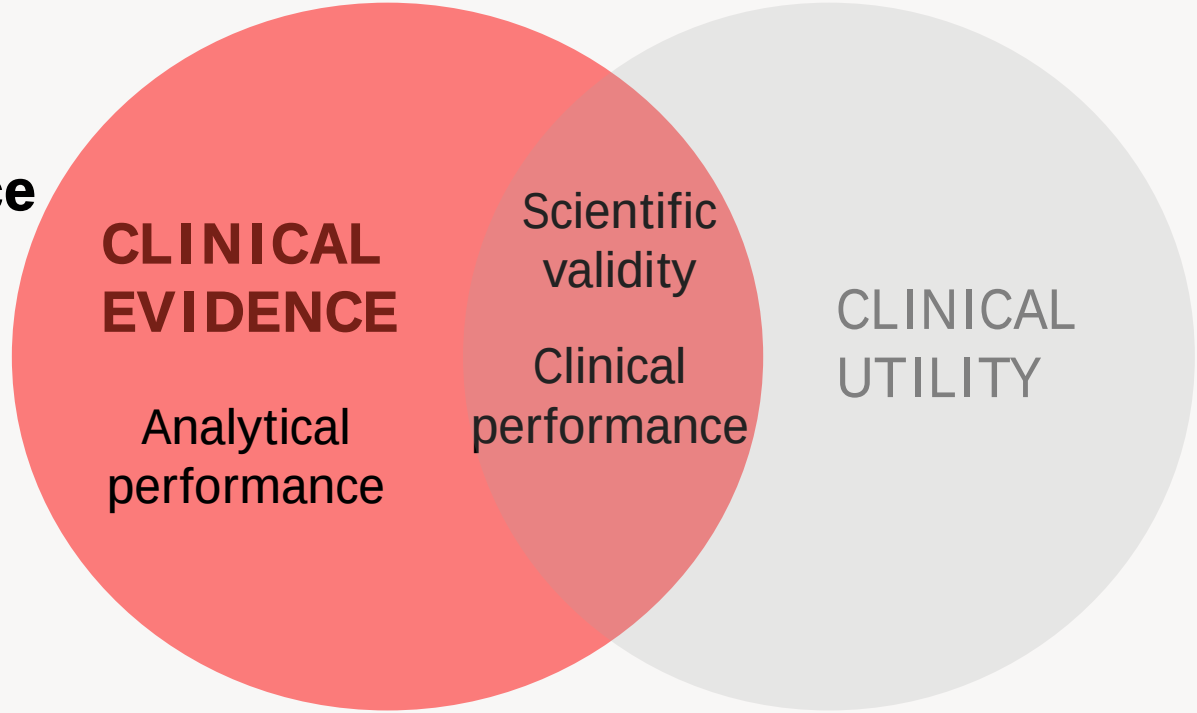

Clinical benefit of an IVD = **Accurate medical information** ≠ **Final clinical outcome**

ie NOT Clinical Utility

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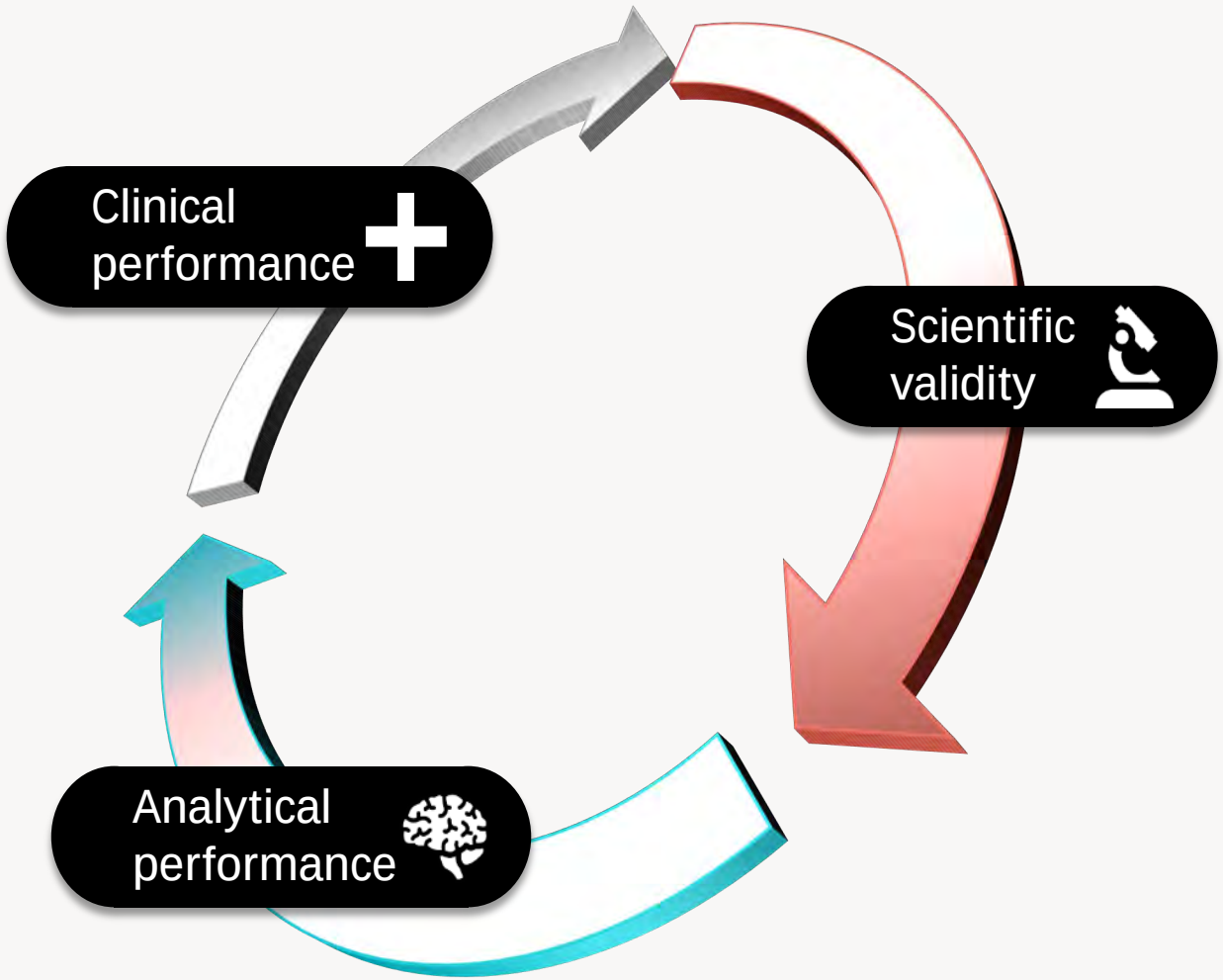
Performance Evaluation

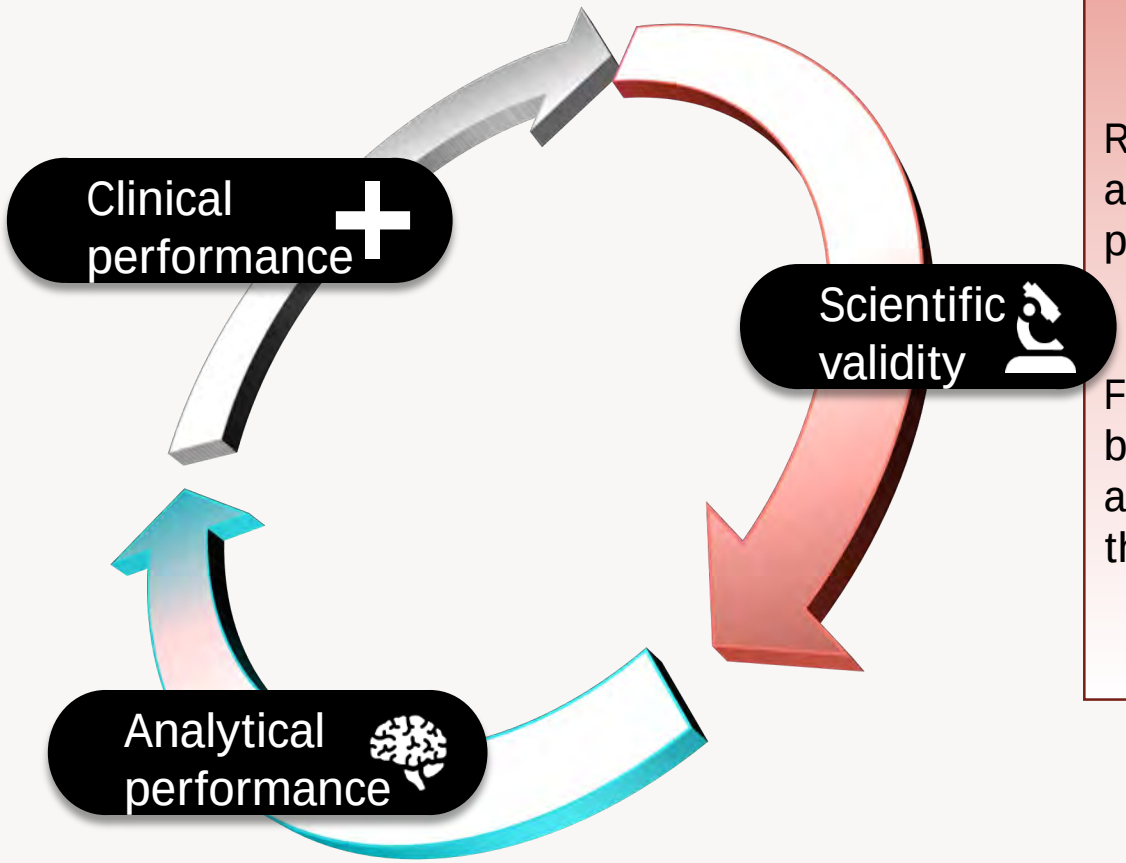
- *Process* of Performance Evaluation
- Ref Annex II & **Annex XIII**

- Done according to a **Performance Evaluation Plan**

- Collated as a **Performance Evaluation Report**

- *Continuous during life-time of the device*

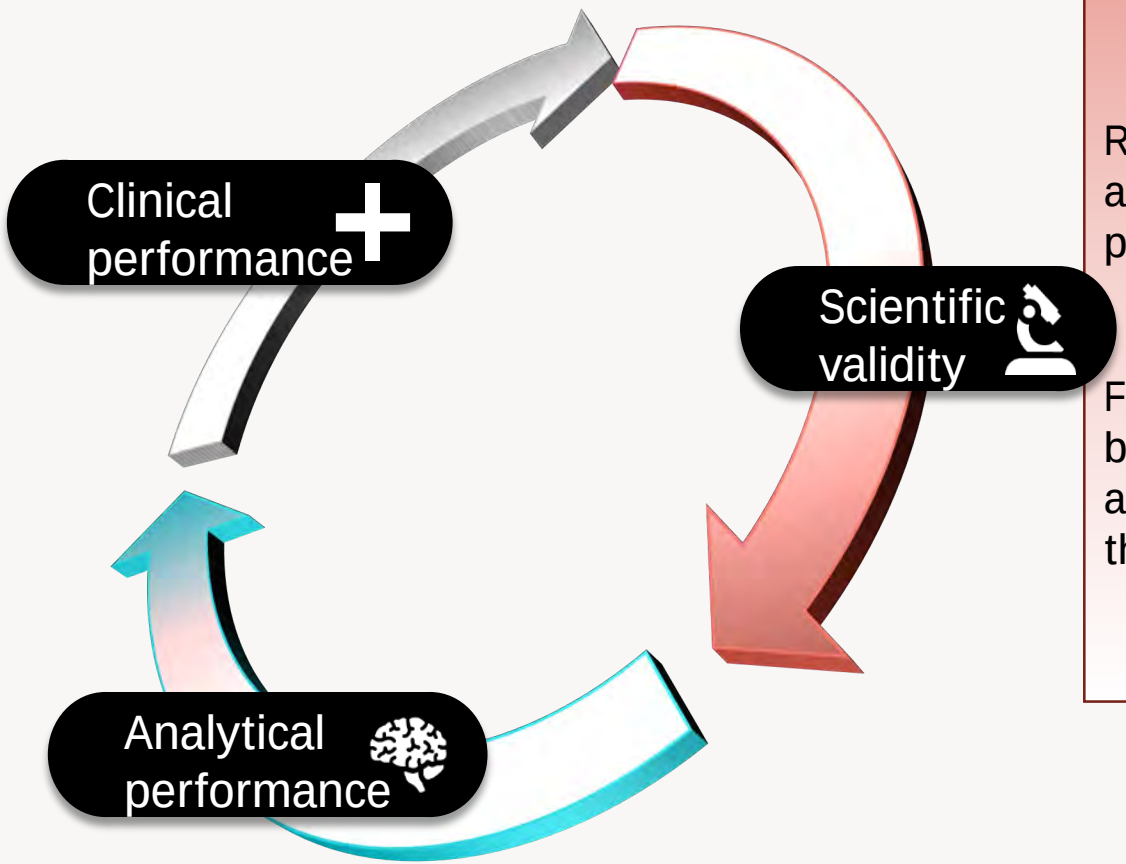




Scientific Validity

Refers to the association of an analyte to a clinical condition or physiological state

For established analytes, this may be from literature; but for novel analytes or companion diagnostics this would need to be established



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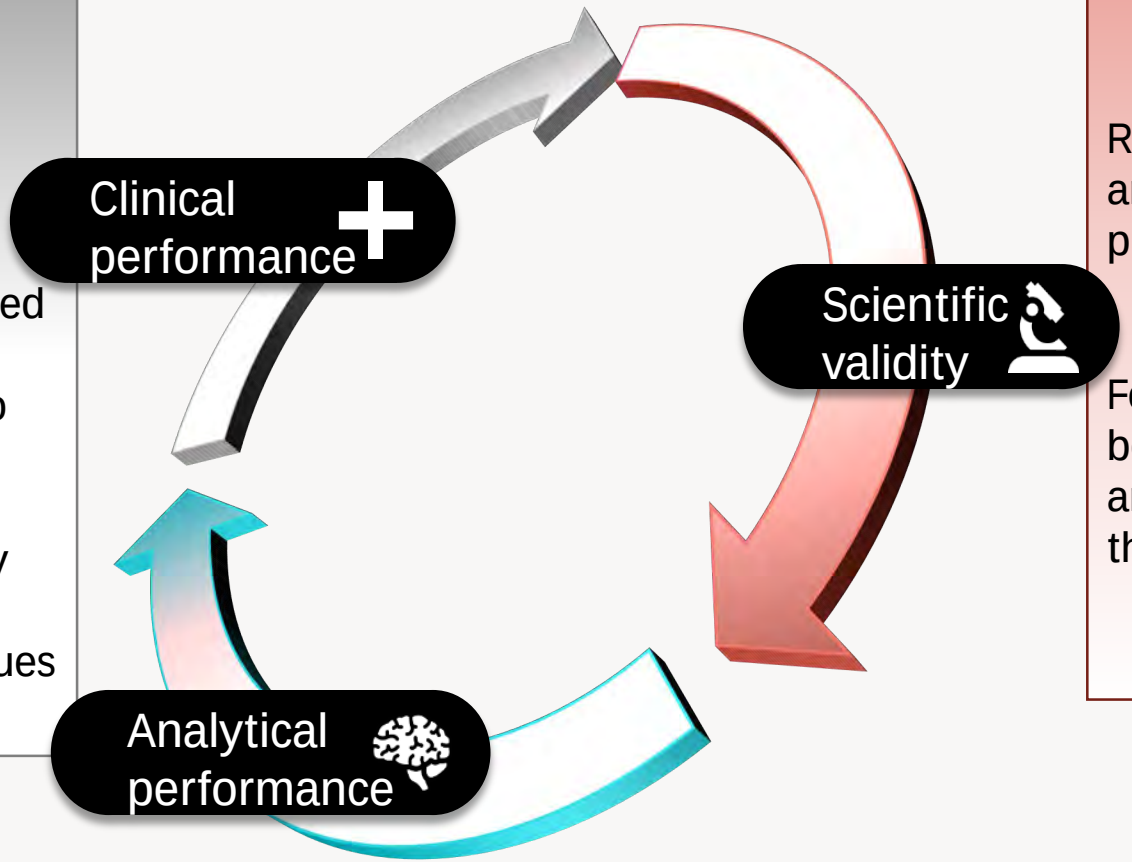
Analytical Performance

Refers to the ability of an IVD medical device to correctly detect and measure a particular analyte
Performance requirements similar to IVD Directive essential requirements

Clinical Performance

Ability to yield results that relate to a particular clinical condition or physiological state for the intended use and in accordance with target population, and where applicable to the intended user

Data to support diagnostic accuracy compared to reference test; information related to expected values



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Performance Evaluation

- Critical part of the Technical Documentation for a device

PE Webinar: Part 1!

❖ **Performance Evaluation Plan**

❖ **Performance Evaluation Report**

- ❖ - Scientific Validity Report
- ❖ - Analytical Performance Report
- ❖ - Clinical Performance Report
- ❖ - *& Conclusion (see An XIII, 1.3.2)*

Important Aspects of Annex XIII

- Performance evaluation – thorough and objective, considering both favourable and unfavourable data.
- Depth and extent **shall be proportionate** and appropriate to the characteristics of the device including the risks, risk class, performance and its intended purpose.

➢ Output will lead to **Plan** for **Post-market Performance Follow-up (PMPF)**

✓ *Justify if PMPF studies are NOT required!*

Clinical Performance

- Reference: **IVDR Annex XIII**

Clinical Performance – Requirements – Annex I

- GSPR 1 and 8 – indirectly reference it via *intended performance*
- GSPR 9.1
  - Devices **shall** achieve the performances as stated by the manufacturer...:
    - (a) the analytical performance...
    - (b) the clinical performance, such as diagnostic sensitivity, diagnostic specificity, PPV, NPV, likelihood ratio, expected values in normal and affected populations
- GSPR 9.4
  - The characteristics and performances of the device **shall** be specifically checked under normal use conditions for self-testing and near-patient testing devices
- Annex II (Technical documentation) refers out to Annex XIII
  - Section 6 – Product Verification and Validation

Clinical Performance – Requirements – **Annex XIII**

- Section 1.2.3
  - The manufacturer **shall** demonstrate the clinical performance of the device in relation to all the parameters described in point (b) of Section 9.1 of Annex I, unless any omission can be justified as not applicable.
  - Demonstration of the clinical performance of a device **shall** be based on one or a combination of the following sources:
    - Clinical performance studies
    - Scientific peer-reviewed literature
    - Published experience gained by routine diagnostic testing
  - Clinical performance studies shall be performed unless due justification is provided for relying on other sources of clinical performance data.

➢Clinical performance **shall** be demonstrated and documented in the *clinical performance report*

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Clinical Performance Elements

1. **Clinical performance studies**
2. **Scientific peer-reviewed literature**
3. **Published experience gained by routine diagnostic testing**

➢ **and Other sources of clinical data**

1. Clinical Performance Studies

- Annex XIII Part 2
  - 2.1 Purpose of clinical performance studies
  - 2.2 Ethical considerations
  - 2.3 Methods
    - Study design
    - Clinical Performance Study Plan
    - Clinical Performance Study Report
  - Other performance studies

Reference – ISO 20916: 2019*

Clinical performance studies **shall** be performed unless due justification is provided for relying on other sources of clinical performance data.

* ISO 20916:2019 - In vitro diagnostic medical devices. Clinical performance studies using specimens from human subjects. Good study practice

1. Clinical Performance Studies

- Weight of wording seems to suggest that ‘clinical performance studies’ are the preference

➢ *BUT what about clinical studies that were performed before the publication of the IVDR?*

- ➢ *Can these be termed ‘Clinical Performance Studies’?*
  - ➢ *These would need to satisfy requirements under Annex XIII 2.3*
- ➢ *Or are these ‘**other sources of clinical data**’?*

Clinical performance studies **shall** be performed unless due justification is provided for relying on other sources of clinical performance data.

2. Scientific peer-reviewed literature

- Difficult to anticipate which devices can rely solely on this method of demonstrating compliance
  - Most likely to be used in conjunction with other methods

- Performance Evaluation Report requirements (Annex XIII 1.3.2) link to this.
- This report **shall** include:
  - the justification for the approach taken to gather the clinical evidence;
  - the literature search methodology and the literature search protocol and literature search report of a literature review; ...

- MEDDEV 2.7/1 revision 4 contains literature review methodology tips for MDD / AIMD

3. Published experience gained by routine diagnostic testing

- Not defined in the IVDR !
- Broad interpretation of “published”:
  - Generally means made available to the public and with an identifiable source
- “Routine diagnostic testing”:
  - The device being used according to its routine intended purpose on the EU population
    - *Manufacturer should be able to justify*

➢Possible examples *(that do not fall under element 2.)*

✓Government, WHO or health institution evaluations

✓Data from proficiency testing or external quality assurance (EQA) schemes

A word on ‘Legacy’ devices

- *Not defined under the Regulations*
- There is no ‘grand-fathering’
- All parts of the IVDR apply!

- PMS data can be used for Clinical Performance but only if it is presented as or to supplement data meeting the definition of Annex XIII 1.2.3:
  - Clinical performance studies
  - Scientific peer-reviewed literature
  - Published experience gained by routine diagnostic testing

➢ or, other sources of clinical data

Performance Evaluation Report

- Reference Annex II & XIII

Performance Evaluation Report

- Reference Annex II sec 6.2

- The Performance Evaluation Report is a *critical* part of the technical documentation

…we will review against all specified requirements

❖**Performance Evaluation Plan**

❖**Performance Evaluation Report**

- ❖- Scientific Validity Report
- ❖- Analytical Performance Report
- ❖- Clinical Performance Report
- ❖- & *Conclusion (see An XIII, 1.3.2)*

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Performance Evaluation Report

- Reference Annex II sec 6.2

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✓ **We will not start our review without it!**

Performance Evaluation Report

- bringing the review together... Performance evaluation report – Annex XIII 1.3.2
- This report shall include the scientific validity report, the analytical performance report, the clinical performance report and an assessment of those reports allowing demonstration of the clinical evidence.
  - the justification for the approach taken to gather the clinical evidence;
  - the literature search methodology and the literature search protocol and literature search report of a literature review;
  - the technology on which the device is based, the intended purpose of the device and any claims made about the device's performance or safety;
  - the nature and extent of the scientific validity and the analytical and clinical performance data that has been evaluated;
  - the clinical evidence as the acceptable performances against the state of the art in medicine;
  - *any* new conclusions derived from PMPF report

Performance Evaluation Report

- Reference Annex II sec 6.2

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❖**Performance Evaluation Plan**

❖**Performance Evaluation Report**

… linked to:

➢**Post Market Performance Follow-up Plan**

- ❖- Annex XIII part B
- ❖- **Linked to conclusion of PER**
- ❖- PMPF evaluation report shall update the PER
- ❖- If deemed not appropriate, then justification to be given in the PER (An XIII, 8.)

➢**Summary of Safety and Performance**

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Link to Post-Market Performance Follow-up

- Annex XIII Part B. sec 4
  - '...with the aim of confirming the safety, performance and scientific validity throughout the expected lifetime of the device, of ensuring the continued acceptability of the benefit-risk ratio and of detecting emerging risks on the basis of factual evidence.'

➢As PMPF is used to confirm the safety and validity of the device on the market - **if it is already confirmed** during Performance Evaluation and Risk Management that the device is safe, then PMPF studies are not required to *further confirm,* unless issues are flagged by Post-Market Surveillance

✓**PMPF is about confirming benefit-risk ratio when you have outstanding residual risks**

✓Ref: Annex XIII Part B sec 8. – **if PMPF is not deemed appropriate, then justification shall be provided in the PE Report**

Notified Bodies

- *Expectations on Notified Bodies for evaluation of the Performance Evaluation Report*

✓ **Requirements for NBs are also driven through legal text under Annex VII**

Annex VII Requirements to be met by Notified Bodies

- Section 4.5.4 – Performance evaluation assessment

The notified body's assessment of performance evaluations as referred to in Annex XIII **shall cover**:

- *the intended use specified by the manufacturer and claims for the device defined by it,*
- *the planning of the performance evaluation,*
- *the methodology for the literature search,*
- *relevant documentation from the literature search,*
- *the performance studies,*
- *post-market surveillance and post-market performance follow up,*
- *validity of equivalence claimed in relation to other devices, the demonstration of equivalence, the suitability and conclusions data from equivalent and similar devices,*
- *the performance evaluation report,*
- *justifications in relation to non-performance of performance studies or PMPF*.

- Additional (similar) requirements in Annex IX Chapter II

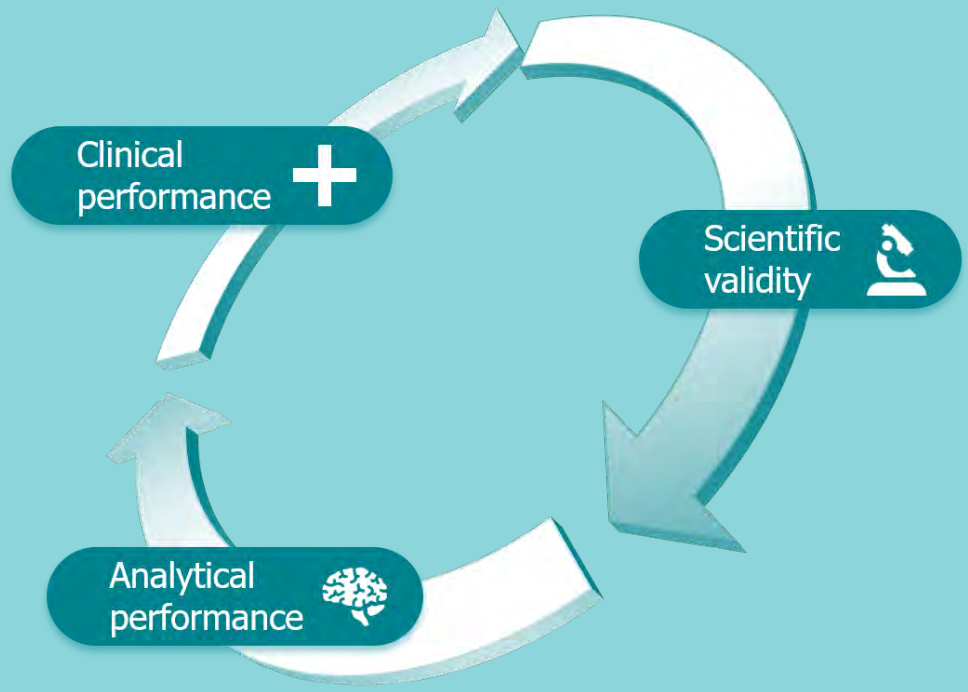
Guidance

- It is expected that Guidance on Performance Evaluation in Q4 2020 from the MDCG on IVD Performance Evaluation

- *Therefore, until this is issued, all requirements are still open to interpretation!*

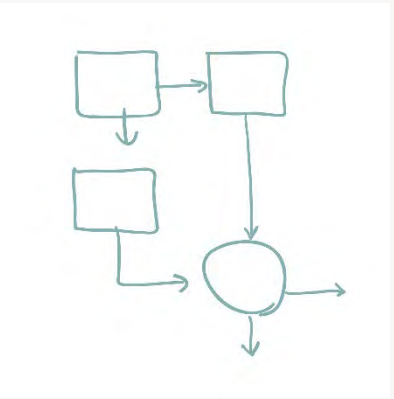
Summary

- Peformance Evaluation – PART 2



Learning Points... **Part 1** reminder!

- Performance evaluation is a **continual** process



- Driven by a Performance Evaluation **Plan**
  - See Annex XIII!

- The stated Intended use/purpose is critical for setting the clinical evidence required
  - **Scientific Validity** should link to the clear claim/s being made

Learning Points... **Part 2**

- Clinical Performance may be from multiple sources
  - ➢ Must be from at least one of 3 elements listed in Annex XIII

- ‘Clinical Performance Studies’ need to meet requirements of Annex XIII 2.3
  - ➢ **Data from ‘legacy’ studies will not meet these requirements – therefore would be ‘other sources of clinical data’**

- Link to the plan for Post-Market Performance Follow-up
  - Further studies may be needed if there are residual risks not addressed by the clinical evidence provided

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IVDR resources

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