Performance Evaluation

PART 1

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Technical Team Manager - IVD

26 Aug 2020

By Royal Charter

bsi.

Agenda

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

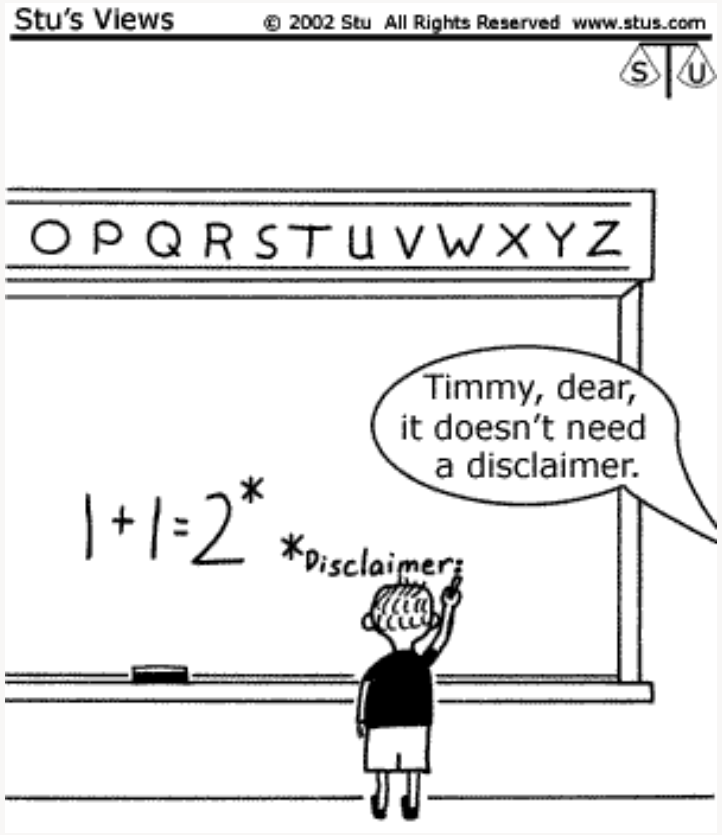
We would like to hear your thoughts…

Poll Question 1

We would like to hear your thoughts…

Poll Question 2

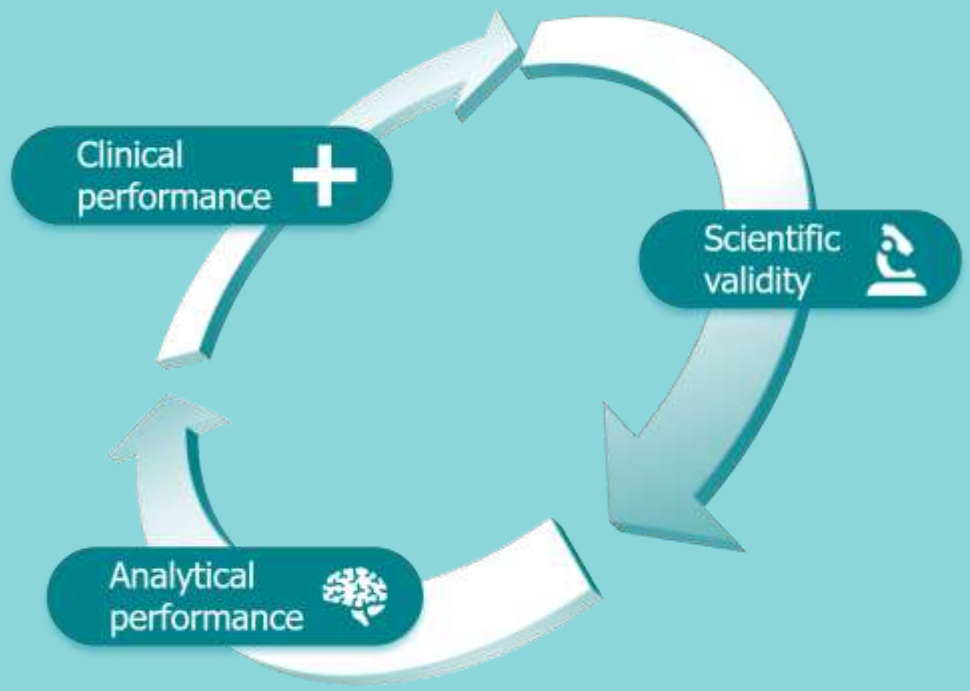
Disclaimer



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

Introduction

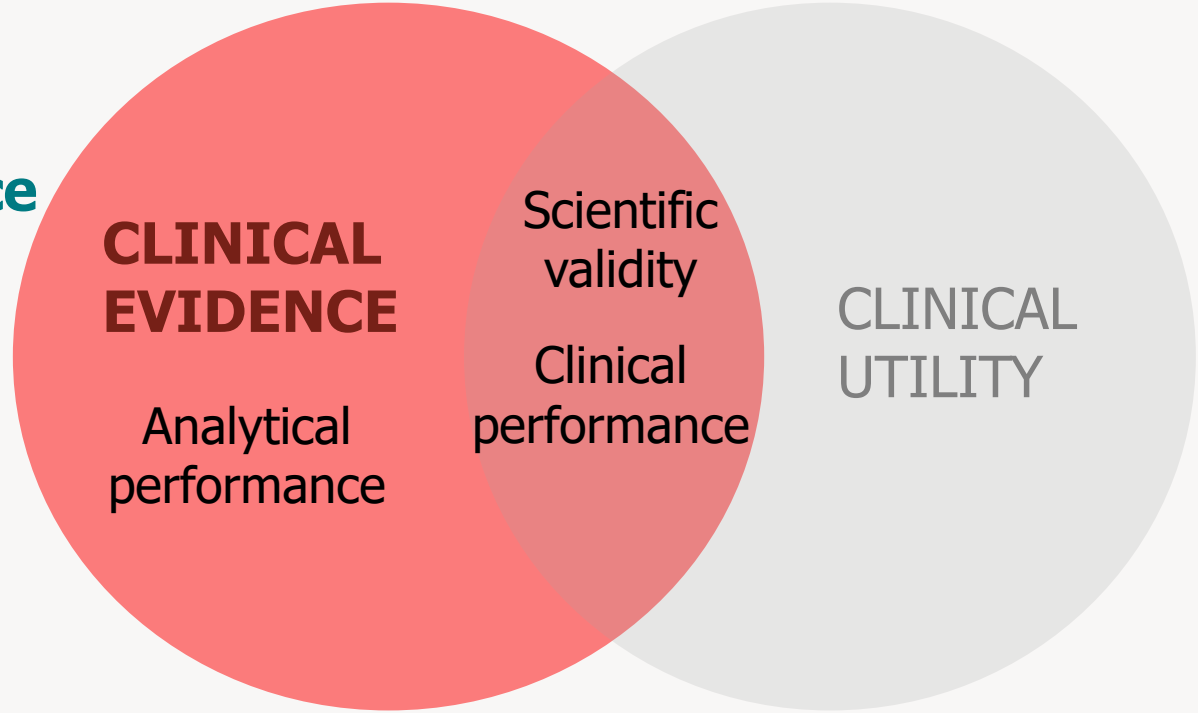
- Performance Evaluation under the IVDR



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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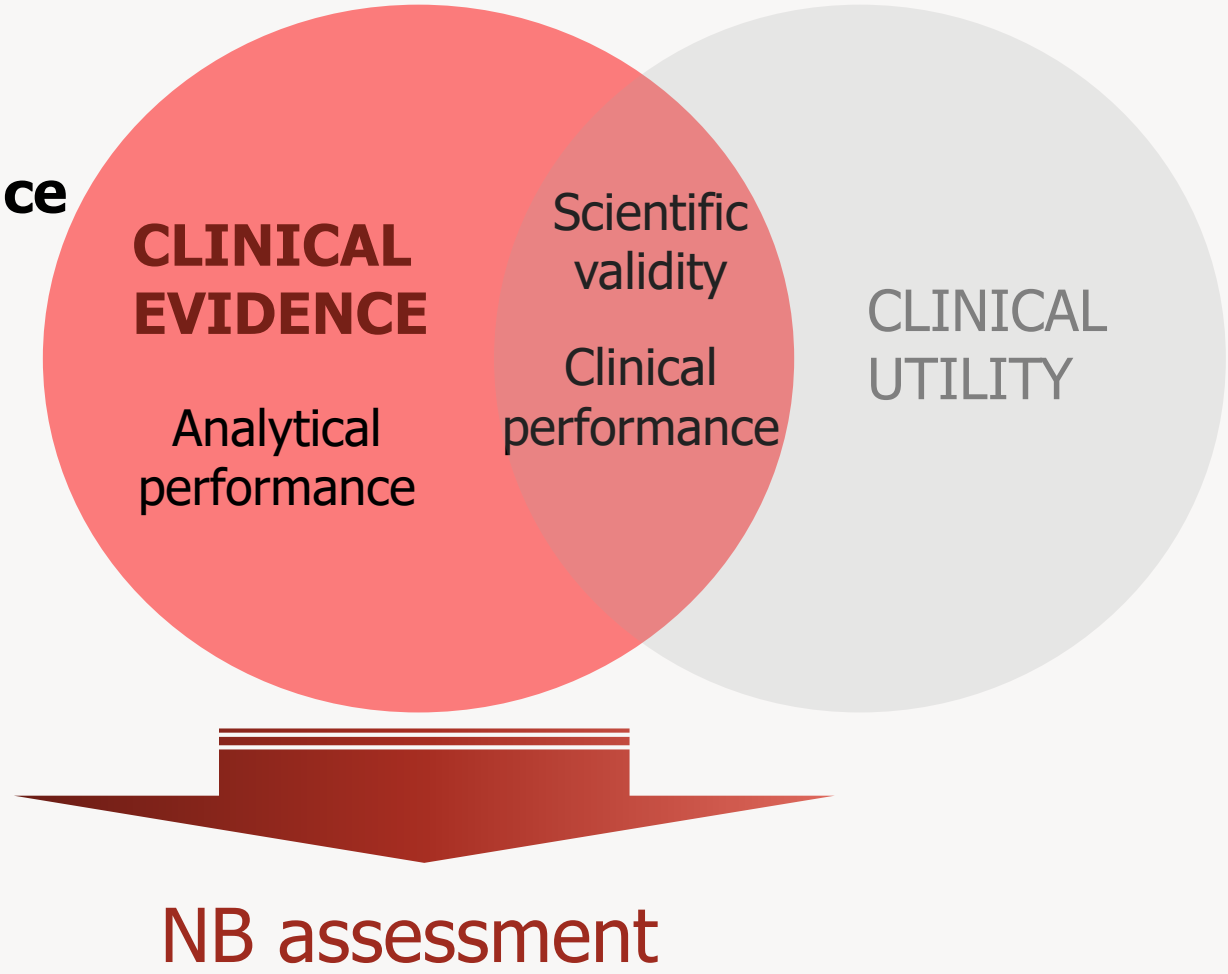

‘Clinical benefit’ consideration

Reference: IVDR Preamble (64)

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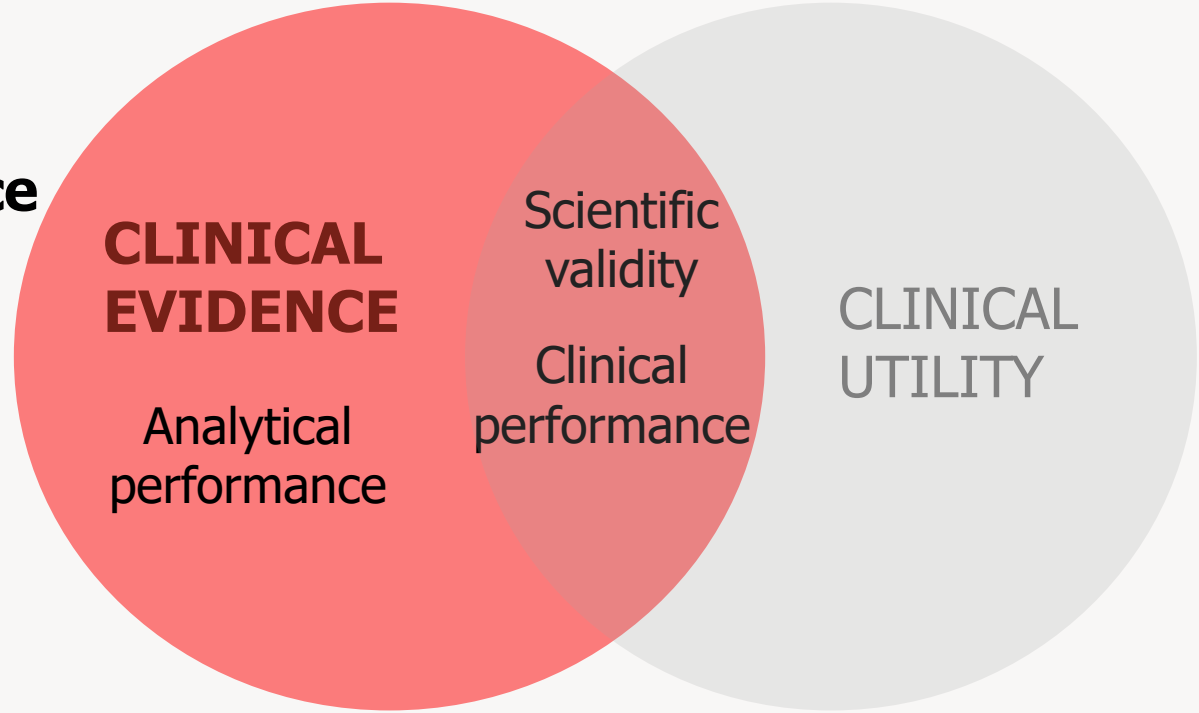


Clinical benefit of an IVD = **Accurate medical information** ≠ **Final clinical outcome**

ie NOT Clinical Utility

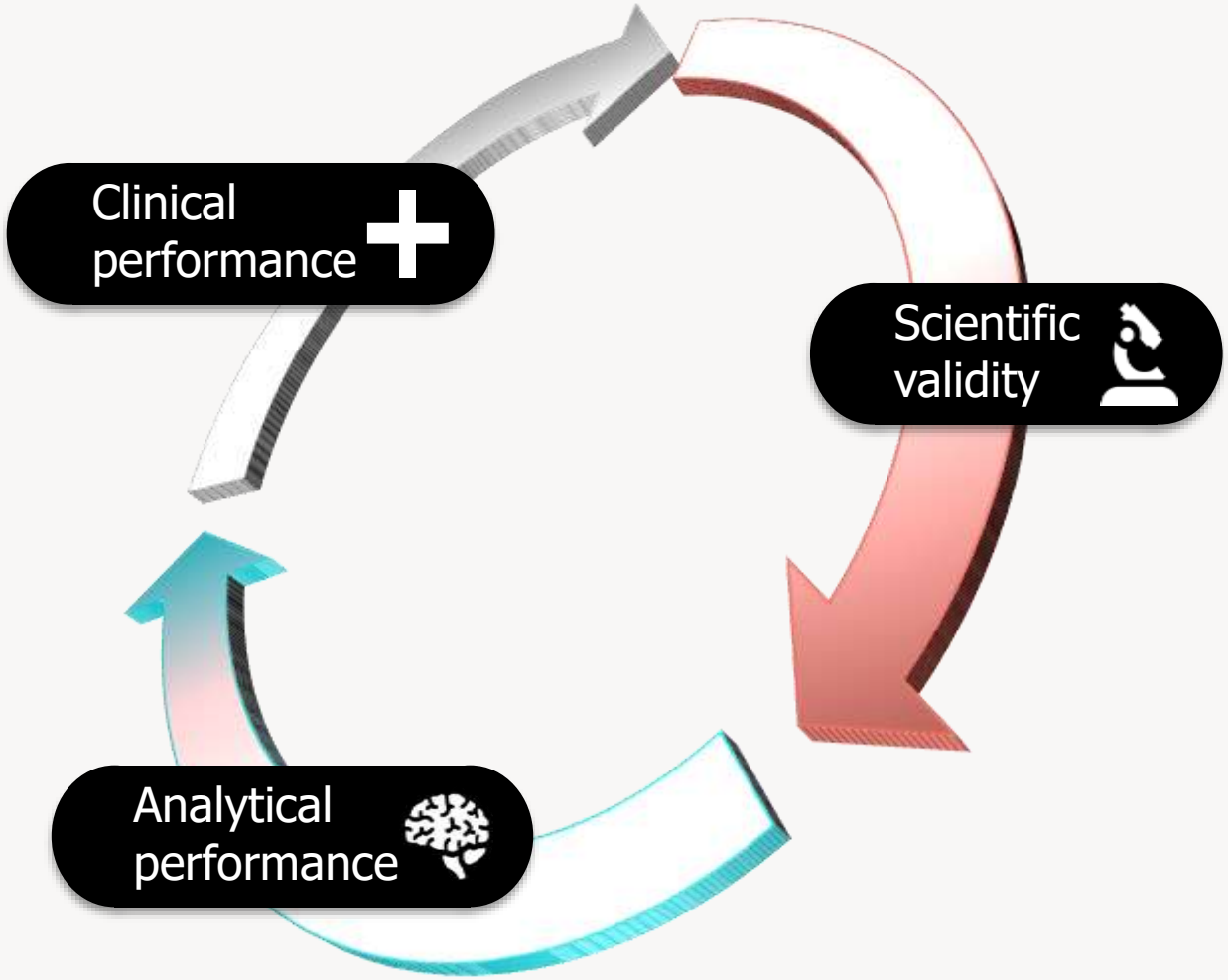
Performance Evaluation

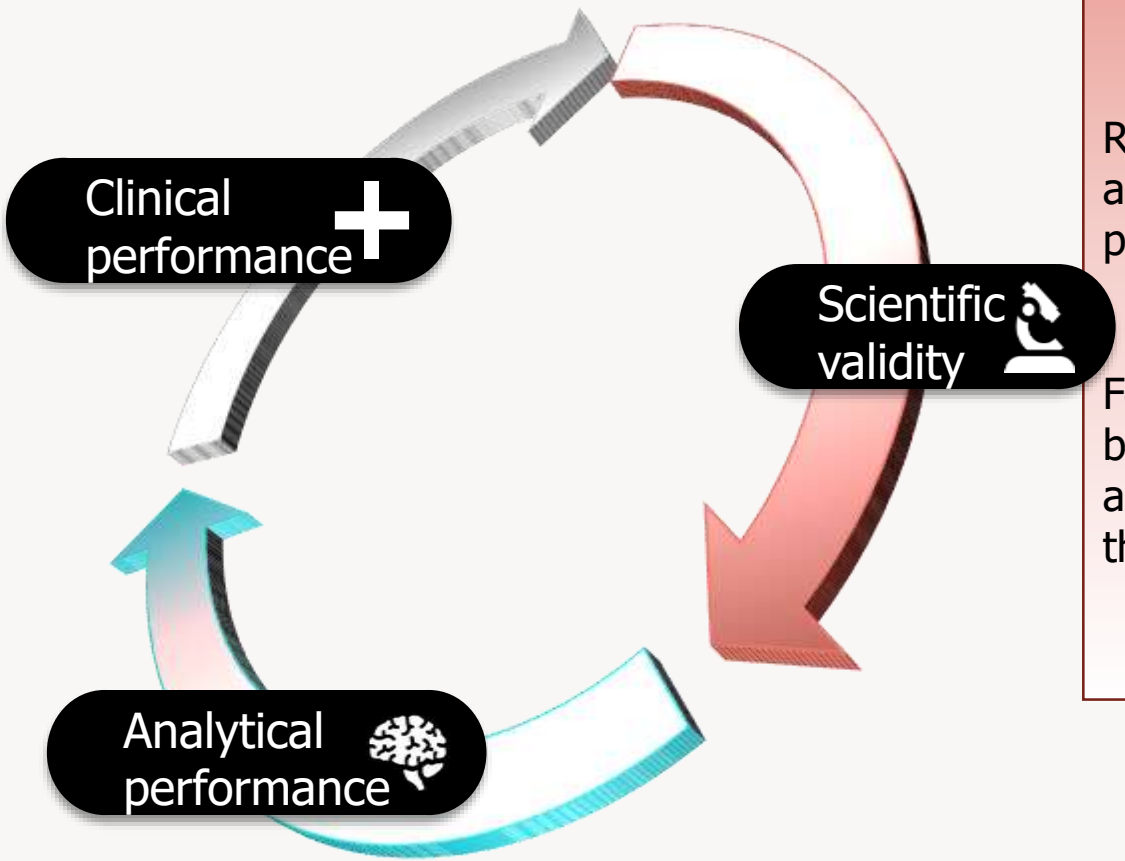
- ***Process*** of Performance Evaluation
- Ref Annex II & **Annex XIII**

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

- Collated as a **Performance Evaluation Report**

- *Continuous during life-time of the device*

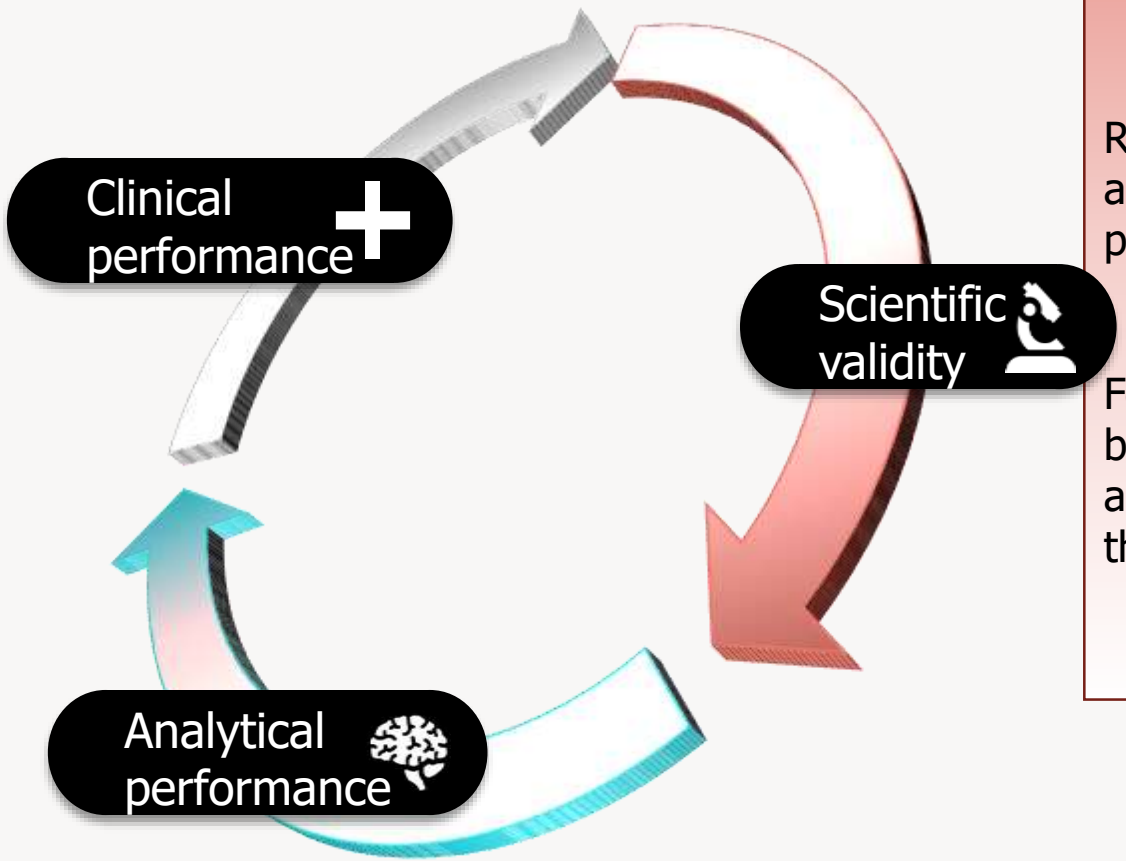




Scientific Validity

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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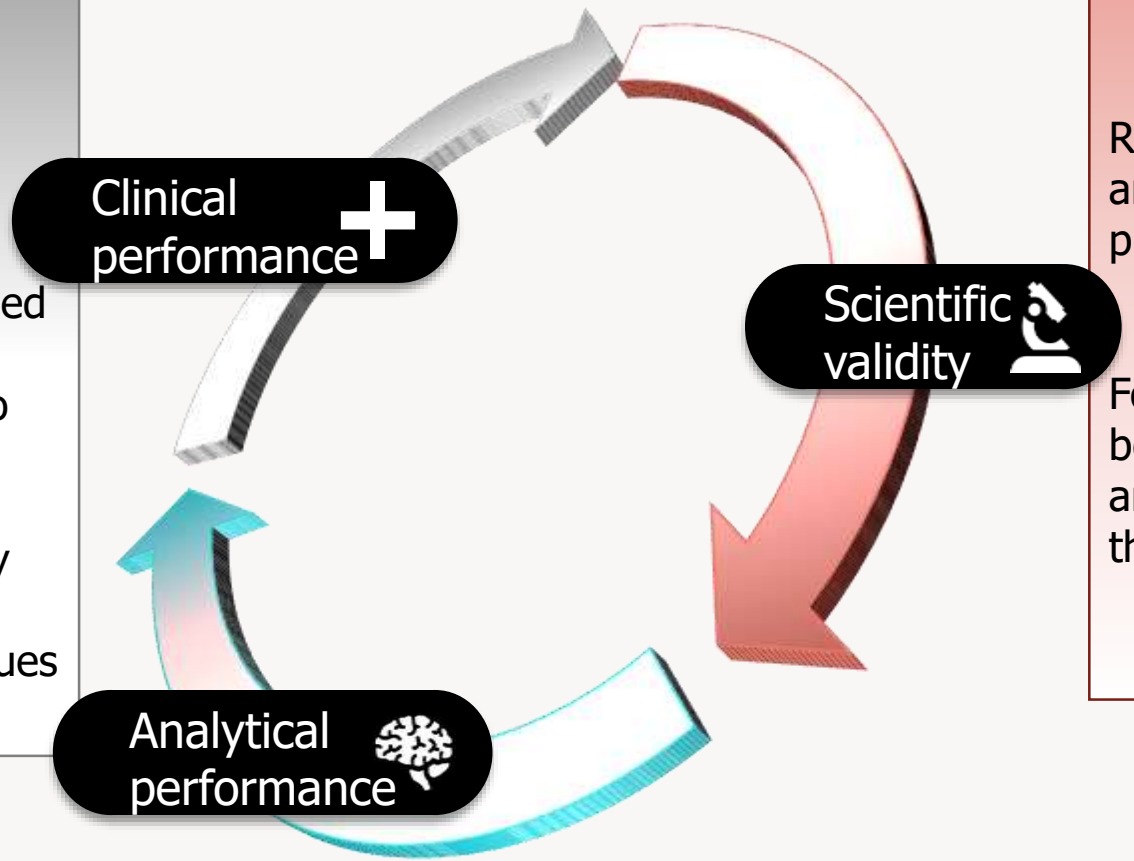
Analytical Performance

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

❖**Performance Evaluation Plan**

❖**Performance Evaluation Report**

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

PE Webinar: Part 2!

Important Aspects of Annex XIII

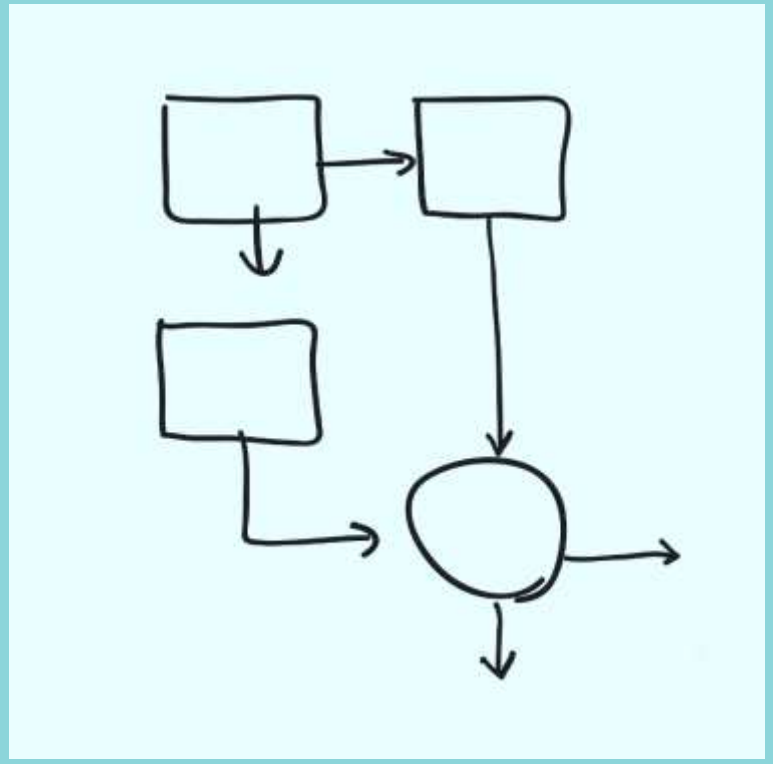
- Performance evaluation – thorough and objective, considering both favourable and unfavourable data.
- Depth and extent **shall be proportionate** and appropriate to the characteristics of the device including the risks, risk class, performance and its intended purpose.

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

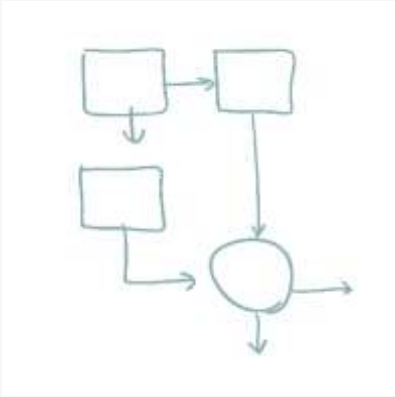
✓ *Justify if PMPF studies are NOT required!*

Performance Evaluation **Plan**

- Reference: **IVDR Annex XIII**



Performance Evaluation Plan

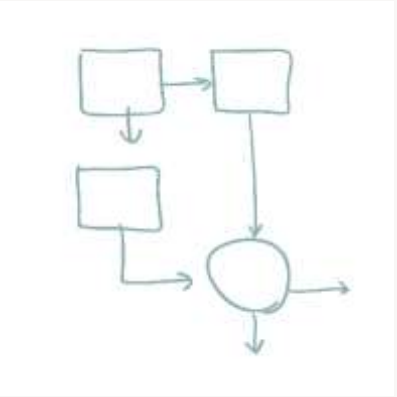


- *Reference Annex XIII*

1. '…To plan, continuously conduct and document a performance evaluation, the manufacturer shall establish and update a performance evaluation plan. The performance evaluation plan shall specify the characteristics and the performance of the device and the process and criteria applied to generate the necessary clinical evidence.'

- Defined Contents under Annex XIII sec 1.1

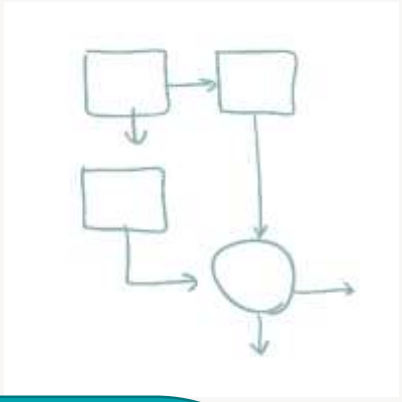
Performance Evaluation Plan



- PE Plan *shall include at least*…

✓ — a specification of the **intended purpose** of the device;
✓ — a specification of the **characteristics of the device** as described in Section 9 of Chapter II of Annex I and in point (c) of Section 20.4.1. of Chapter III of Annex I;
✓ — a specification of the **analyte or marker to be determined** by the device;
✓ — a specification of the **intended use** of the device;
✓ — identification of **certified reference materials or reference measurement** procedures to allow for metrological traceability;
✓ — a clear identification of **specified target patient groups** with clear indications, limitations and contra- indications;
✓ — an identification of the **general safety and performance requirements** as laid down in Sections 1 to 9 of Annex I that require support from relevant scientific validity and analytical and clinical performance data;

Performance Evaluation Plan



- PE Plan *shall include at least*…

✓ — a specification of **methods, including the appropriate statistical tools, used for the examination** of the analytical and clinical performance of the device and of the limitations of the device and information provided by it;

✓ — a description of **the state of the art**, including an identification of existing relevant standards, CS, guidance or best practices documents;

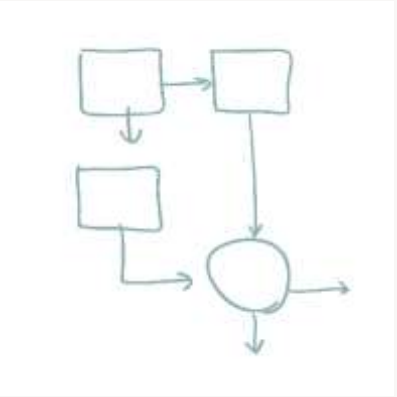
✓ — an indication and specification of parameters to be used to determine, based on the state of the art in medicine, the **acceptability of the benefit-risk ratio for the intended purpose or purposes** and for the analytical and clinical performance of the device;

✓ — for **software** qualified as a device, an identification and specification of reference databases and other sources of data used as the basis for its decision making;

✓ — **an outline of the different development phases** including the sequence and means of determination of the scientific validity, the analytical and clinical performance, including an indication of milestones and a description of potential acceptance criteria;

✓ — the **PMPF planning** as referred to in Part B of this Annex.

Performance Evaluation Plan



- PE Plan *shall include at least*…

✓Where any of the above mentioned elements are *not deemed appropriate* in the Performance Evaluation Plan due to the specific device characteristics a justification shall be provided in the plan.

Should all devices have a PE Plan?

- **YES!**

- All devices *shall* have a PE Plan (ref Annex XIII sec 1)
  - ‘*shall* plan, conduct and document’
- See also Article 10.3; Article 56.1
- *Shall* specify and justify the level of clinical evidence

➢Annex VII defines requirements for NBs

Requirements of the NB under Annex VII

Annex VII, section 4.5.1 - Conformity assessment activities, General requirements

- …— *to review the manufacturer's procedures and documentation relating to performance evaluation,*
- *— to address the interface between the manufacturer's risk management process and its appraisal and analysis of the performance evaluation and to evaluate their relevance for the demonstration of conformity with the relevant requirements in Annex I…*

Annex VII, section 4.5.4. - Performance evaluation assessment

- *…//…The notified body shall examine, validate and verify that the manufacturer's procedures and documentation adequately address:*
- *(a) the planning, conduct, assessment, reporting and updating of the performance evaluation as referred to in Annex XIII…*

Requirements of the NB under Annex VII

4.5.4. Performance evaluation assessment continues

- *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.*

Our IVDR review experience so far…

- *Is it OK to have a Performance Evaluation Plan to cover multiple devices?*

➢ Think about your assessor of the technical documentation
  - ✓ they need to be able make a conclusion of conformity for the device being reviewed
    - ✓ this may be for a product specific certificate;
    - ✓ or be a device sampled as part of a group of devices to be certified

➢ Does the plan make sense for a specific device?

…it is possible, but remember what the NB has to do!

Where a device is 'legacy', *what is the "Plan"?*

- The PE Plan is how you are approaching evaluation of performance today
  - It is not an old study protocol!

- What is the intended use today? (ie what claims are you making?)
- What is 'state of the art' today?
- How are you going to draw upon all performance information available to you today?
  - See reference to methodology Annex XIII sec 1.2
  - See under Clinical Performance Annex XIII sec 1.2.3

Scientific Validity

- Reference: **IVDR Annex XIII sec. 1.2**

Scientific Validity

Annex XIII 1.2.1. Demonstration of the scientific validity

The manufacturer shall demonstrate the scientific validity based on one or a combination of the following sources:

— relevant information on the scientific validity of devices measuring the same analyte or marker;

— scientific (peer-reviewed) literature;

— consensus expert opinions/positions from relevant professional associations;

— results from proof of concept studies;

— results from clinical performance studies.

The scientific validity of the analyte or marker shall be demonstrated and documented in the scientific validity report.

Scientific validity - consider

- Separation of performance claims from the scientific validity 'claims'
  - Link to Intended Use in the IFU
  - Claims being made in Marketing materials

- Reference: IVDR Article 7
  - Claims includes 'labelling, instructions for use, making available, putting into service and advertising of devices…'
    - (d) suggesting uses for the device other than those stated to form part of the the intended purpose for which the conformity assessment was carried out.

- Should consider 'state of the art' *(links to description in the PE Plan!)*

Scientific validity - consider

- Annex VII states that the NB shall review the methodology for Literature searching
- How do we know that a literature review is ‘systematic’ literature review?

- Note that literature searching for *clinical performance* claims should be robust, unless it is a novel analyte

Use of Literature

- GHTF guidance available: GHTF/SG5/N7:2012
- No IVDR Performance Evaluation guidance *yet*

- Reference to articles
  - Your NB needs a summary/rationale of why the articles are relevant / appropriate
  - – link to the intended purpose
    - Pg references in the articles would be useful
    - We may need to request copies of the articles

Performance Evaluation Report

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**

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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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Performance Evaluation Report

- Reference Annex II sec 6.2

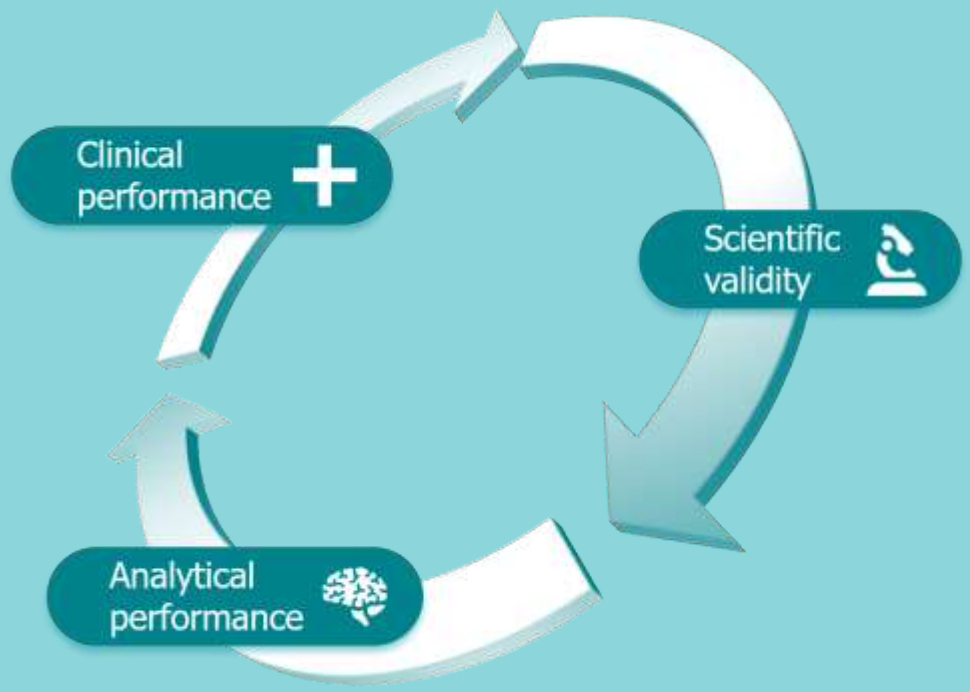
- The Performance Evaluation Report is a *critical* part of the technical documentation

…we will review against all specified requirements

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

Summary

- Peformance Evaluation – PART 1



Learning Points

- 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

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