



Global Harmonization Working Party

Towards Medical Device Harmonization

Acceptance of Clinical Oversea Data for Clinical Evidence versus Local Testing for IVD Medical Devices

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BUILDING BRILLIANCE TOGETHER

Agenda

In Country Lab Testing Landscape

Challenges and Impact

How does the manufacturer demonstrate safety and effectiveness of an IVD Medical Device?

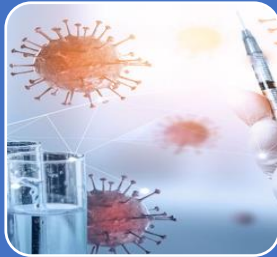
Recommendation

Different Levels of In-Country Lab Testing and Governmental Controls



PRE- MARKET

Testing of samples by the regulatory body (Reference Labs) for approval



POST – MARKET

Lot testing for re-registration or for batch release



PRE and POST- MARKET

Stability testing and verification of the shelf-life claims

In-Country Lab Testing Landscape



No local clinical testing required Pre-market and Post-market

- United States, Australia, Canada, Singapore, Malaysia, Saudi Arabia, Laos, Cambodia, etc

Local clinical testing **only for high-risk products** required, premarket or Post-market

- Japan, Korea, EU Brazil, China Indonesia, Thailand, India Philippines

Local clinical testing required for all products

- Russia

CHALLENGE



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People, knowledge and infrastructure

- Wide range of IVD portfolios - difficult to find qualified personnel
- WORKLOAD AND CAPACITY FOR TESTING AND REVIEW
- Unfamiliarity with testing procedures
- ADEQUATE USE OF TECHNOLOGY AT THE TESTING SITES

Sample Availability

- Extremely difficult for institutions, hospitals and laboratories to get suitable human tissue samples

Challenges with samples

- Non-random selection of samples
- Integrity, stability, and control issues of the samples
- Insufficient volume of samples and inappropriate storage of products and samples
- Process of sample handling not always under control
- Dilute panels from processed samples
- Insufficiently characterised samples and failure to understand/explain discrepancies or product deficiencies



Placing Instruments

- Reference laboratories might require placement of instruments
- Reference laboratories do not allow the placement of the instrument purely for evaluation purposes, unless it can be used for routine testing as well.

Time and resources

- Substantial resources and investment from manufacturers to get required kits and equipment into the testing sites.

Lot Availability

- 3 lot available at the time (considering Global Manufacturing Bottlenecks/Scale Up requirements)



- 1. Restricted or delayed access to innovative IVD medical devices**
- 2. Financial burden to the patients and healthcare system**
- 3. Delay of innovative, cutting edge products in the country**
- 4. Affect confidence of foreign investors looking to develop the local economy.**

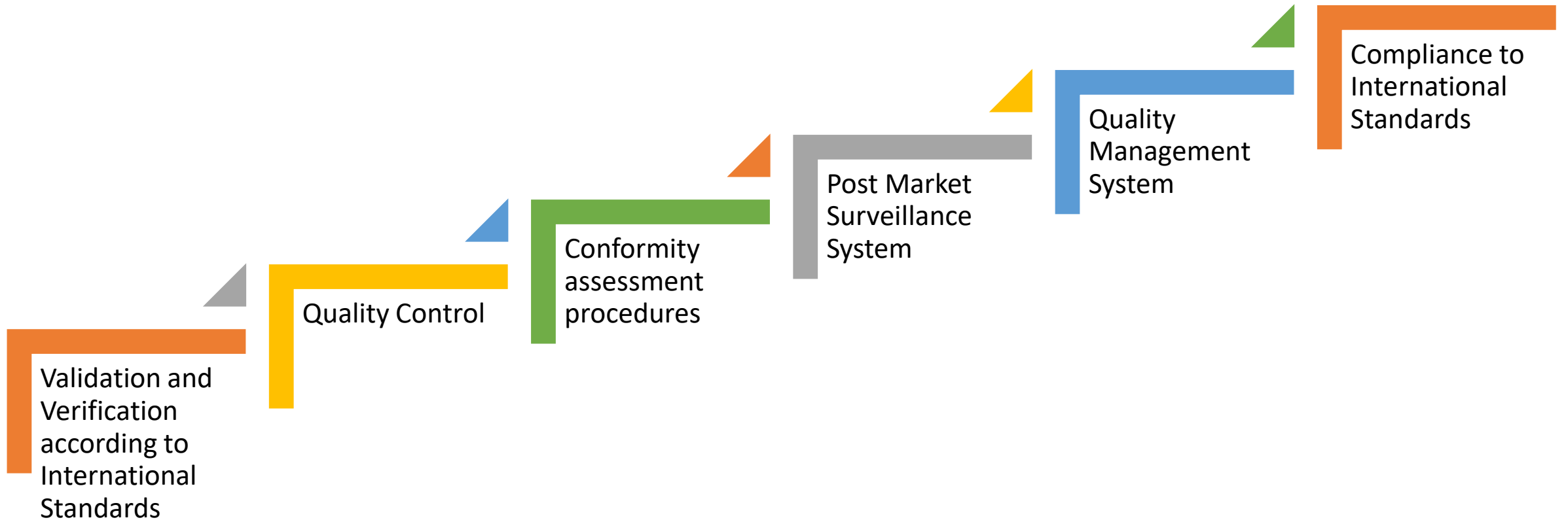
How does the manufacturer demonstrate safety and effectiveness of an IVD Medical Device?

Manufacturer's Responsibility and Liability



- The manufacturer carries the **liability for the product.**
- The manufacturer **is responsible to test and control** the product to the **highest standard** and to keep the **product state-of-the art.**
- Any discrepant testing results must be documented and evaluated (**Post-Market-Surveillance and Vigilance Requirements**).

Manufacturers' Measures to Ensure High Quality, Safety, and Effectiveness –Key Elements



Validation and Verification - Clinical Evidence

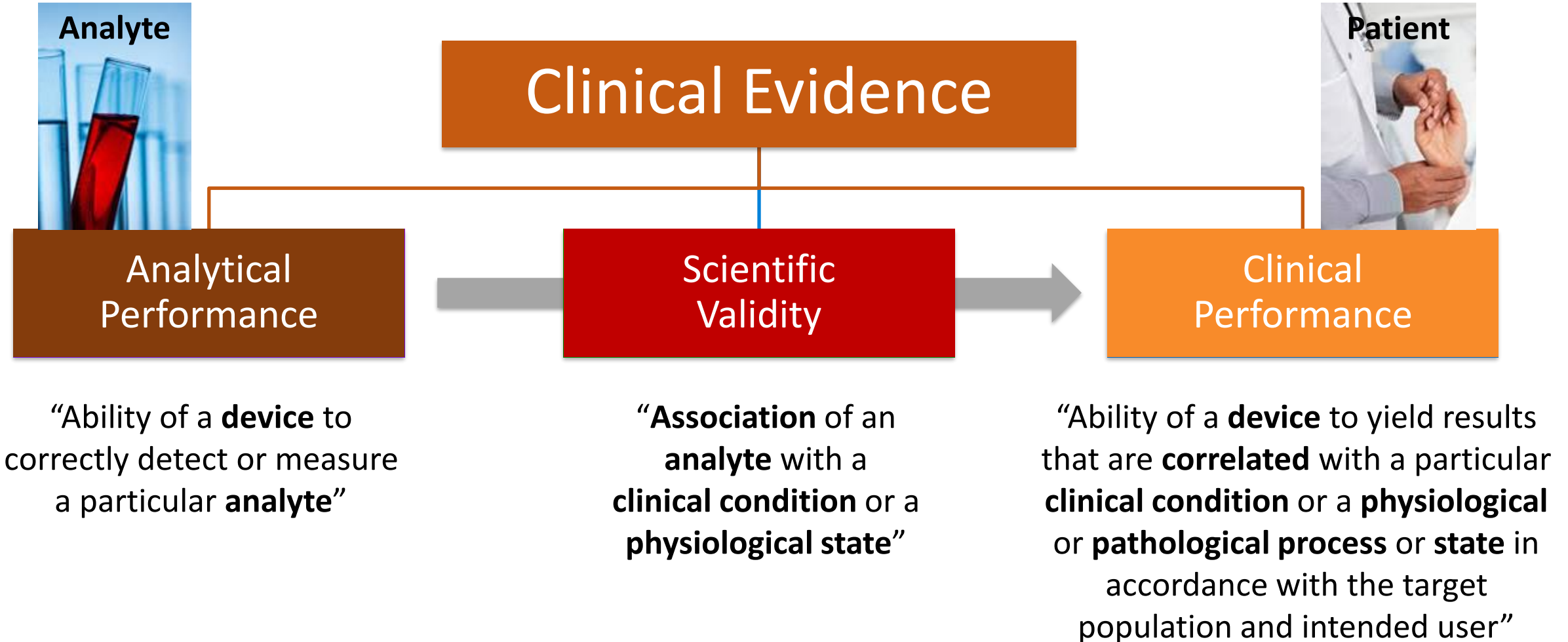
The **clinical evidence** shall be such as to scientifically demonstrate, by reference to the **state of the art in medicine**, that the **intended clinical benefit(s)** will be achieved and that the device is **safe**.

“[...] The manufacturer shall specify and justify the **level of the clinical evidence** necessary to demonstrate conformity with the relevant general safety and performance requirements.

That level of clinical evidence shall be appropriate in view of the **characteristics** of the device and its **intended purpose**. [...]”



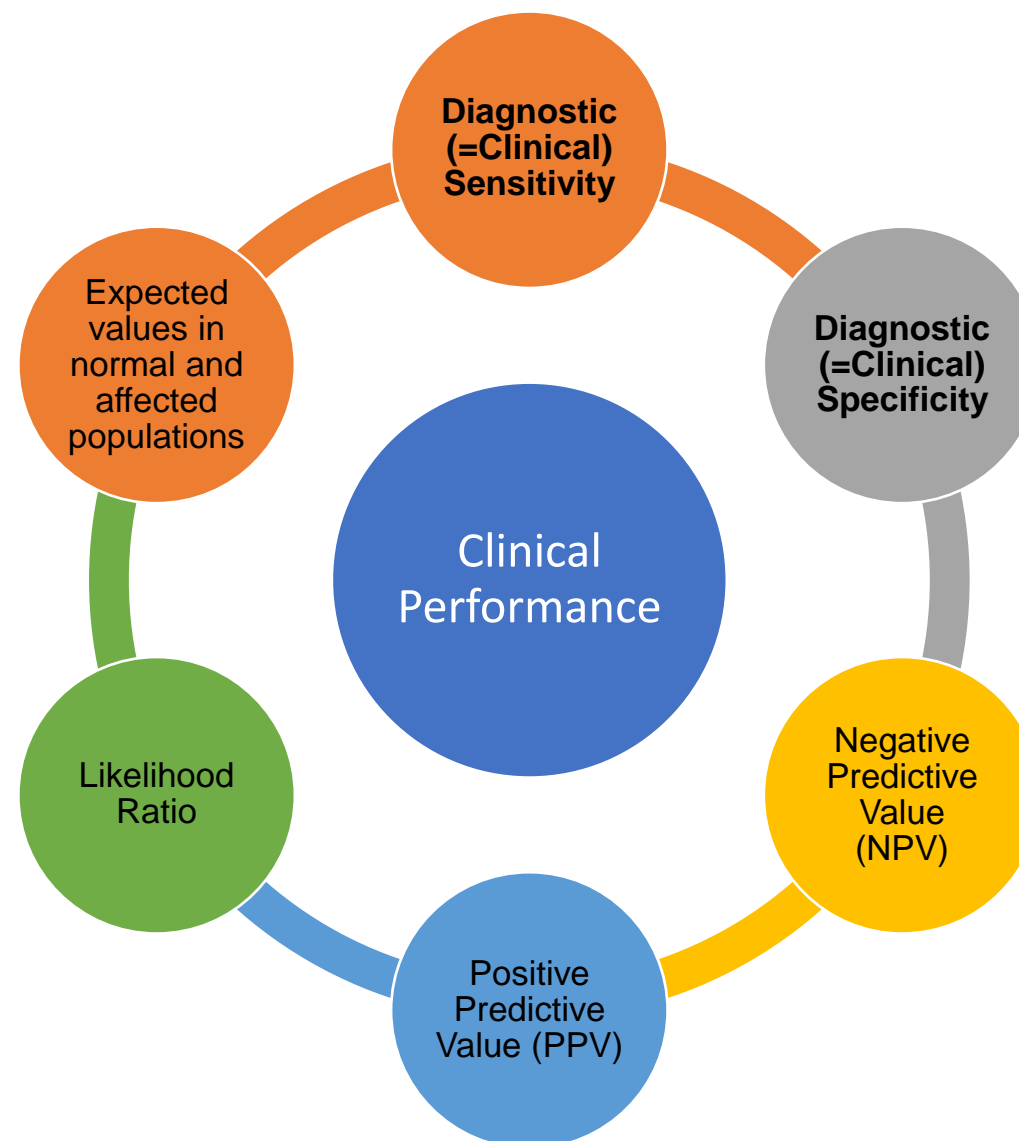
Validation and Verification - Clinical Evidence - Components



- **Analytical Performance Evaluations** are conducted according to robust and recognised international standards.
- All custom platforms are **validated and verified**.
- **Analytical Performance Evaluations** explores all aspects of the assay performance



- Demonstrated by correlation of the use of an IVD with a specific clinical condition, **in accordance with the target population and intended user**
- Measure of the IVD Medical Device's ability to correctly **identify patient's status** as either having or not having a disease or condition
- **Statistically relevant**
- **Driver- Intended use**





Manufacturers carry out extensive quality control testing

Product inspection and testing during manufacturing and use to uncover defects



Procedures used in each assay to assure a test run is valid and results are reliable



- Kit Controls provided with the kit; used to validate the test run
- Quality Control Samples – low positive externally produced samples
- Validated test methods

Validation and Verification – Stability Studies



Real Time
Stability

Accelerated
Stability

Shelf life

Transport

In use stability
On/board
Reconstitution
Open vial/bottle

Post Market Surveillance



- Ongoing monitoring alongside data collection on product performances
- Proactive detection and investigation of any potential quality or safety issues
- Corrective and preventive actions
- Change control procedures

Recommendation



Do not mandate in-country lab testing, unless scientifically justified.

Local studies should only be required in rare cases for high- risk products, when there is **insufficient scientific evidence** available (based on the nature of the IVD medical device).

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Recommendation

Instead.....

- **Review of global clinical evidence report** instead of asking for local performance/clinical studies
- Ask for **CoA** by manufacturer, Conformity Assessment Body and/or reference labs in the country of origin
- **Accept and recognize oversea clinical evidence** to ensure safety and effectiveness of the medical device/IVD
- **Implement an effective Post-Market-Surveillance and Vigilance Reporting System including Change Management**
- Ask questions and challenge the manufacturer on their results, if needed



- Better access to IVD medical devices for patients, especially for new diagnosis of diseases, and improved assays for existing conditions;
- Reduced costs for patients and for the healthcare system;
- Increased efficiency for government agencies and regulators;
- More regulatory resources on post-market surveillance;
- Attractive local market and robust economy



Reference

Position Paper- Acceptance of Overseas Clinical Evidence for IVD Medical Devices

