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MINISTRY OF HEALTH, GOVERNMENT OF INDIA

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# 22nd Asian Harmonization Working Party Annual Meeting

MAKE IN INDIA

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## 4-8 December, 2017 I New Delhi

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# Objectives and Limitations:
# In-Country Testing- Industry Perspective

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# Testing and Validation of IVD Medical Devices by the Manufacturer

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- Quality Control
- Stability of Products
- Validation and Verification
- Performance Evaluation

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## Quality Control:

- 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 – the negative and positive control provided with the kit; used to validate the test run
  - ✓ Quality Control Samples – low positive externally produced samples
  - ✓ Should be treated in the exact same manner as test samples

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# Types of Quality Control:

- "On-Board" or analyzer QC: built-in device controls or system checks
- Internal QC: sample controls
- External QC: e.g. blind proficiency survey, precision controls
- Other types of QC: control processes to ensure result reliability

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# Potential sources of laboratory error during testing of an IVD Medical Device

**Operator:** Improper specimen preparation or handling
Incorrect test interpretation
Failure to follow test system instructions

**Specimen:** Bubbles
Clots
Incorrect tube additive

**Analysis:** Calibration factor incorrect
Mechanical failure

**Environmental:** Temperature
Humidity
Light intensity
Altitude

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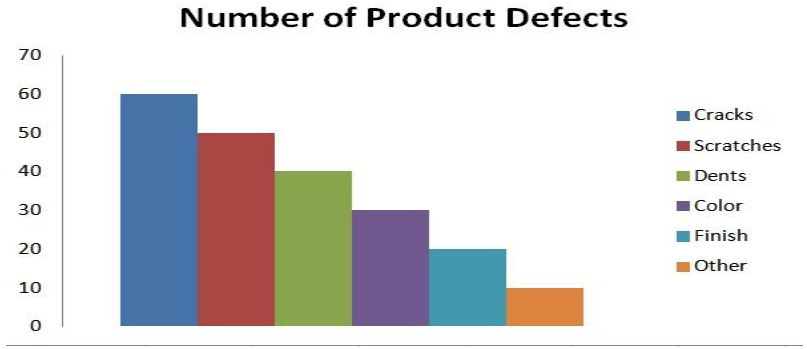
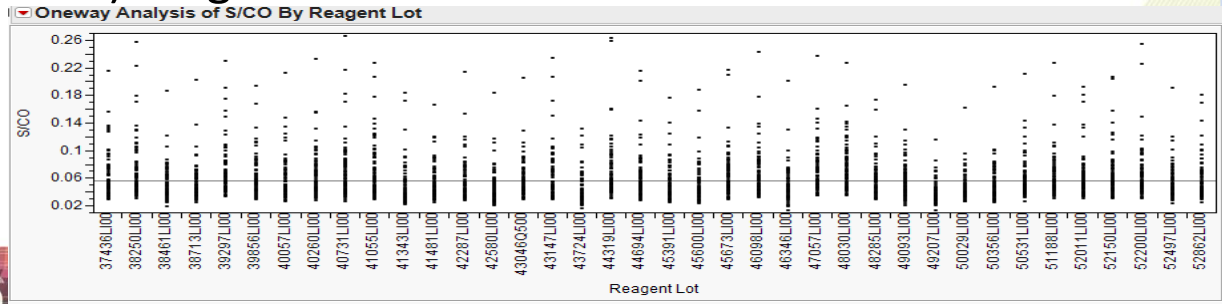
## Examples of Quality Control Tools:

- Intra-laboratory QC
- Inter-laboratory QC
- Calibration checks
- Electronic system checks
- Repeat testing of patient samples
- Control charts (see examples)
- Cause and Effect (fish bone) Diagram



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# Quality Control during Use of the IVD Medical Device

- Test runs require validation in the applicable test setting (lab, operator, environmental factors etc.)
- Control should be run as per manufacturer's instructions for use
- Control value out of specified range:
  might be indication of deterioration of reagents
  or errors in technique

**Extensive Stability Testing**

- Testing product at predefined time intervals using a predefined protocol. Results are analyzed according to predefined acceptance criteria. Data may be summarized as a Levy-Jennings plot.
- The study is to be completed to the end of the target shelf life but may be continued until significant degradation in performance can be seen
- Minimize lot changes during the stability study. Otherwise: crossover testing

**Other Stability Testing:**

- Accelerated testing, heat stress; the Arrhenius Equation may then be used to predict the shelf life of the product.
- Open vial/ on-board stability testing
- Reconstituted stability testing
- Inverted stability testing
- Stability testing during transportation temperatures
- On-market stability controls

**Verification and Validation of IVD Medical Devices:**

- Demonstrates that the IVD medical device achieves its intended performance during normal conditions of use by the intended user in the intended environment (e.g. laboratories, physician's offices, healthcare centers, home environments) and in the intended use population
- Address whether devices produced in accordance with the design actually satisfy user needs and intended uses

**Analytical performance:**

Ability of an IVD medical device to detect or measure a particular analyte

Product design should address, such as:

- Sensitivity
- Specificity
- Accuracy (Precision and Trueness)
- Linearity
- Control of known relevant interference
- Limits of detection (LOD), limit of blank (LOB), limit of quantitation (LOQ)

Where performance depends on use of calibrators and/or control materials: traceability of assigned values through available reference measurement procedures and/or available reference materials of a higher order

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## Clinical Performance

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

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# Why do I tell you all of this?

## Manufacturer‘s Responsibility and Liability

- It is the responsibility of the manufacturer 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)
- The manufacturer carries the liability for the product

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# Testing of IVD Medical Devices in- country or by Governmental Bodies

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## Different Levels of In-Country Lab Testing and Governmental Controls

- Local testing up to 3 lots with limited samples (positive/negatives) performed by the local affiliate/ distributor
- Testing by the regulatory body with limited samples (positives/ negatives) and prepared panels (interferences) or seroconversion panels (low positives)
- Lot testing for re-registration or for release of every batch
- Stability testing and verification of the shelf-life claims

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## Issues

- Selection of samples (random)
- Integrity, stability and control of the samples
- Volume of samples
- Process of sample handling is not always controlled
- Panels are sometimes from processed samples (e.g. Diluted)
- Samples are not always well characterized to understand/ explain discrepancies or product deficiencies
- Untrained lab personnel or not enough personnel
- Not appropriate storage of products and samples

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**Recommendation**

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

**Instead.....**

- Review of the analytical performance data, clinical evaluation data and the final analysis and report give a good understanding of reliable results or a good study management
- Ask questions and challenge the manufacturer on their results, if needed
- Ensure an effective Post-Market-Surveillance and Vigilance Reporting System
- Implement an External Quality Control Schemes (EQAS) in your country (supports to increase the lab quality)

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**Benefits**

- Patients have early access to new diagnosis of diseases or conditions
- Patients have early access to improved assays
- No extra resources for refridgirators or lab personnel
- You can use your personnel wisely and spent more time on on-market potential issues
- Consider audits of the manufacturing sites
- Increase the quality of your laboratories in your country

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**A Final Note:**

The biggest issue in laboratories is not the quality of the IVD Medical Devices, but:

- Sample mix-up
- Sample integrity
- Untrained personnel

Think globally- Infectious diseases travel fast and do not know borders!

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# Thank you