

Instrument/Method Validation

Lebah Lugalia

Lab QA/QC
Coordinator

UNC Project

Lilongwe, Malawi

Instrument/Method Validation



QUESTION AND ANSWER PRESENTATION

Instrument Validation

- What is instrument validation?

Instrument Validation

- Definition:

It is a series of processes through which you test your system to verify or validate the performance specifications published by the manufacturer of the instrument.

Instrument Validation

- Why is it important to validate the instrument?

Why Validate your instrument/method?

- It is required by the CLIA regulation (CLIA 42 CFR part 493.1253). International sites participate in DAIDS/NIH funded studies, we must be in compliance with the U.S. regulations.
- You want to validate the manufacturer's claims for their method performance characteristics, under your current environmental conditions, e.g. temp, humidity, water, electricity, operator skills etc.

Why validate your instrument?

- You want to ensure that the amount of error present in the system won't affect the interpretation of the test result and compromise patient care.
- Ensure that effects of shipment and storage did not affect your instrument performance.

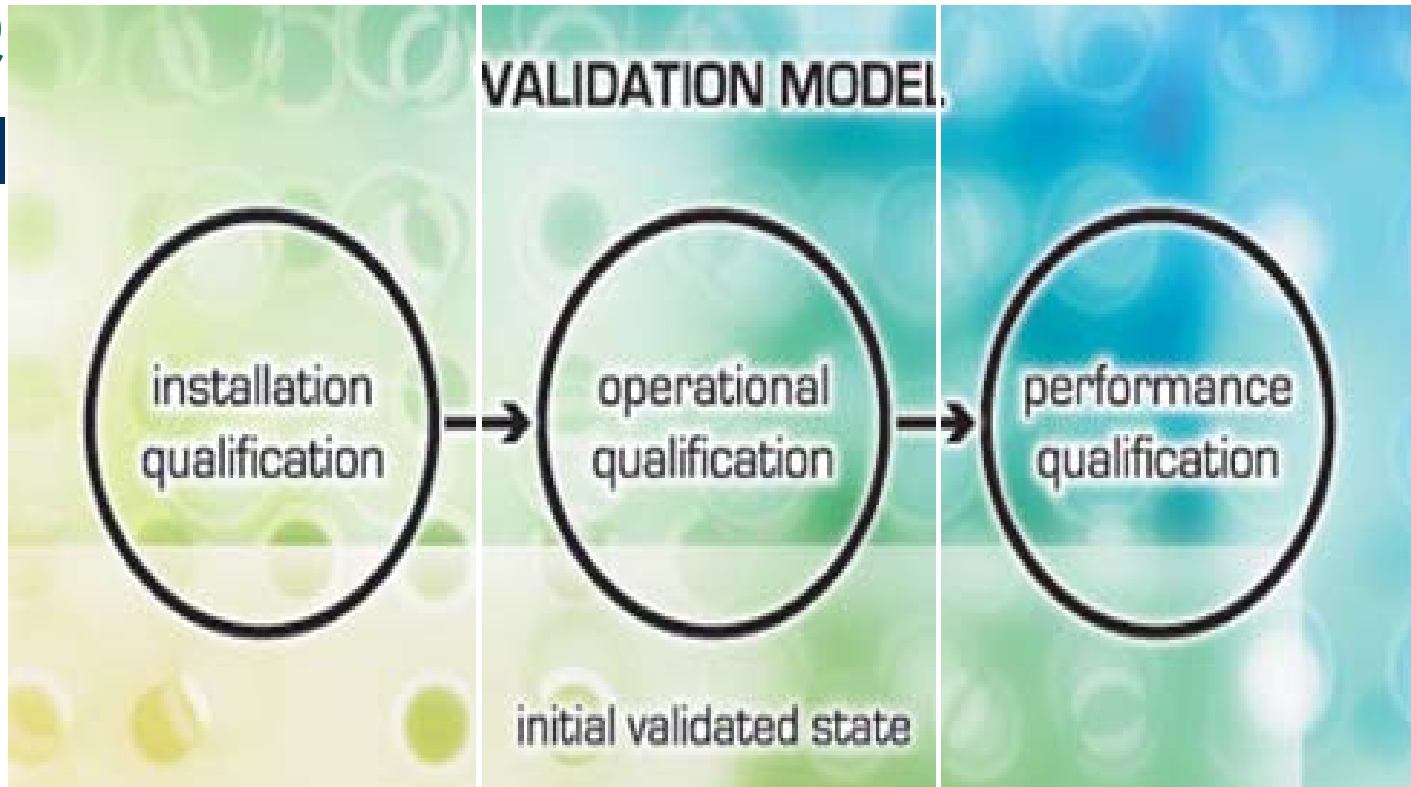
Instrument Validation

- When do you validate your instrument?

When to validate instrument

- Initial installment of the instrument.
- When a new method or test is implemented.
- When a major part is changed e.g. photometer of a chemistry instrument.
- When an instrument is borrowed.
- When you MOVE your instrument from one location to another.
- Annually (if time allows).

Three validation principles – IQ, OQ, PQ



IQ- Installation Qualification

- Installation qualification verifies that the equipment and its subsystems have been installed in accordance to manufacturer's specifications.
- Usually performed by the company's field representative.
- Examples:
 - Verification that all components parts are functional
 - Verification that local supply voltages conform to instrument
 - Verify that the ambient conditions exist for optimal instrument performance.
 - Verify correct versions of software were issued with the instrument.
 - Setting up of instrument parameters (date, time, language, test protoc.

OQ- Operation Qualification

- This validation provides evidence that the instrument operates as expected and confirms that installation was successful.
- Done by the field representative and lab technicians.

Training of instrument operation.

Testing of controls, calibrators and a few patient samples.

Instrument Validation - PQ

- What experiments are performed in Performance Qualification (Method Validation)?

Instrument Validation - Experiments

- Precision (Replication)
- Linearity (to verify reportable range)
- Accuracy (correlation or comparison)
- Reference Intervals (Normal values)
- Analytical Sensitivity
- Analytical Specificity

Instrument Validation

- What are CLIA guidelines for validation?

CLIA Regulations

- CLIA regulations are based on the complexity of the test method.
- 3 categories:
 - 1. Waived tests – does not require validation.
 - 2. Non-waived unmodified tests – moderate and high complexity tests – needs validation.
 - 3. Non-waived, modified (or in-house developed) tests – validation is required.
- Information about classification of specific tests is available at : <http://www.cms.gov/clia/>

Instrument Validation - Linearity

- Definition of Linearity?

Instrument Validation- Linearity

- Linearity or AMR(analytical measurement range) is an assessment of the lowest and highest levels at which an analyte can be accurately measured without any type of dilution or concentration.
- It is important to validate the manufacturer's claims for reportable range of their system/method.

Instrument Validation- Precision

- Definition of Precision?

Instrument Validation- Precision

Definition

- Precision is the degree of reproducibility among several independent measurements of the same sample for the same analyte.

Instrument Validation- Precision

- Precision experiment is performed to estimate the imprecision or random error of the analytical method.
- Precision is measured in terms of coefficient of variation (CV) and standard deviation (SD). The smaller the CV and SD, the better the precision.

Instrument Validation - Accuracy

- Define Accuracy?

Instrument Validation - Accuracy

- Definition:

A measurement of the exactness of an analytical method, or the closeness of agreement between the measured value and the true value.

Instrument Validation - Accuracy

- Performed to estimate inaccuracy or systematic error of the new method.
- Experiment is performed by analyzing forty or more patient samples by the new method (test method) and a comparative method, then estimate the systematic errors on the basis of the differences observed between the two methods.

Accuracy/Correlation Experiment

- Westgard has a set of statistical tools on the internet to help calculate the statistics:
 - www.westgard.com/mvtools.html

Reference Range Intervals or NRR

- Definition of a Reference Range Intervals?

Reference Range Intervals or NRR

- Definition:

Reference ranges are a measured set of values determined to occur in a healthy non-diseased population.

Reference Range Intervals or NRR

- Why should you validate the manufacturer's reference intervals or establish your own NRR?

Reference Range Intervals or NRR

- Differences in demographics of your population due to environmental or genetic factors.
- Differences in test methods and instruments.

HPTN 035 and MTN 015 protocol required tests

- What validation exercises are required for:
 1. ALP, ALT, AST, T.Bil and Creatinine?
 2. CBC/DIFF?
 3. CD4?
 4. APTT, PT, INR?
 5. RPR/TPHA?
 6. HIV ELISA?
 7. Western Blot?

HPTN 035 and MTN 015 protocol required tests

- 8. RNA PCR?
- 9. Probe-Tec CT/GC?
- 10. HIV Rapid Tests?
- 11. HSV-2?

Validation Summary

Need to write up a validation summary and file together with results data in a binder.

- Report should be signed by performing technician and lab Manager/Director or designee.
- Submit validation data and summary to Network Lab for approval.

Reasons why we don't validate our instruments/methods?

- Discussion

NEW METHOD – BC CX-5 PRO





REFERENCES

- Method Validation by Westgard
- HPTN Lab Manual by Network Lab