NEW YORK STATE OF OPPORTUNITY. Department of Health | Wadsworth Center

Complying with New York State Clinical Laboratory Standard QA S3

Thursday, January 18, 2018

The webinar will begin at 2:00PM EST

March 14, 2018

Topic: Complying with NYS Standard QAS3
Presenter: Derek Symula, Ph.D.
Director, Clinical Proficiency Testing Program

Date: Thursday, January 18, 2018
Time: 2:00 pm, Eastern Standard Time (New York, GMT-04:00)

This training session will include:

- When does *Quality Assessment Sustaining Standard of Practice 3 (QA S3): Ongoing Verification of Examination Accuracy* apply?
- Using PT to verify performance
- How to design an internal verification program
- Issues to consider when implementing an alternative approach

**This training may be used as 1 hour of continuing education to fulfill Human Resources Sustaining Standard of Practice 10 (HR S10): Continuing Education. Laboratories must prepare a roster of all attendees for the webinar, attach this webinar announcement email, have the laboratory director sign the roster and maintain all this documentation for review by one of our Clinical Laboratory Consultants. CLEP will not provide a continuing education certificate.

A question and answer period will follow the presentation.

- Please save your questions until then.
- Use the Webex Q/A feature to submit questions in writing.
- We may not be able to answer all questions in the allotted time.

All participants' phones will be muted for the duration of the webinar.

Today's Webinar Team

Beverly Rauch – Deputy Director, CLEP

Stephanie Shulman – Director, CLEP

Derek Symula – Director, Clinical Proficiency Testing

Quality Assessment Sustaining Standard of Practice 3 (QA S3): Ongoing Verification of Examination Accuracy

For all tests performed by the laboratory that are not included in Subpart I, (42 CFR 493 Subpart I) the laboratory:

a) shall have a system for verifying the reliability and accuracy of test results;

b) shall perform this verification process at least semiannually;

c) shall evaluate all accuracy verification challenges:

i. to ensure that results are consistent with the laboratory's specified performance criteria when an event is not graded by the external quality assurance program;

ii. to identify shifts and trends regardless of the score received; and

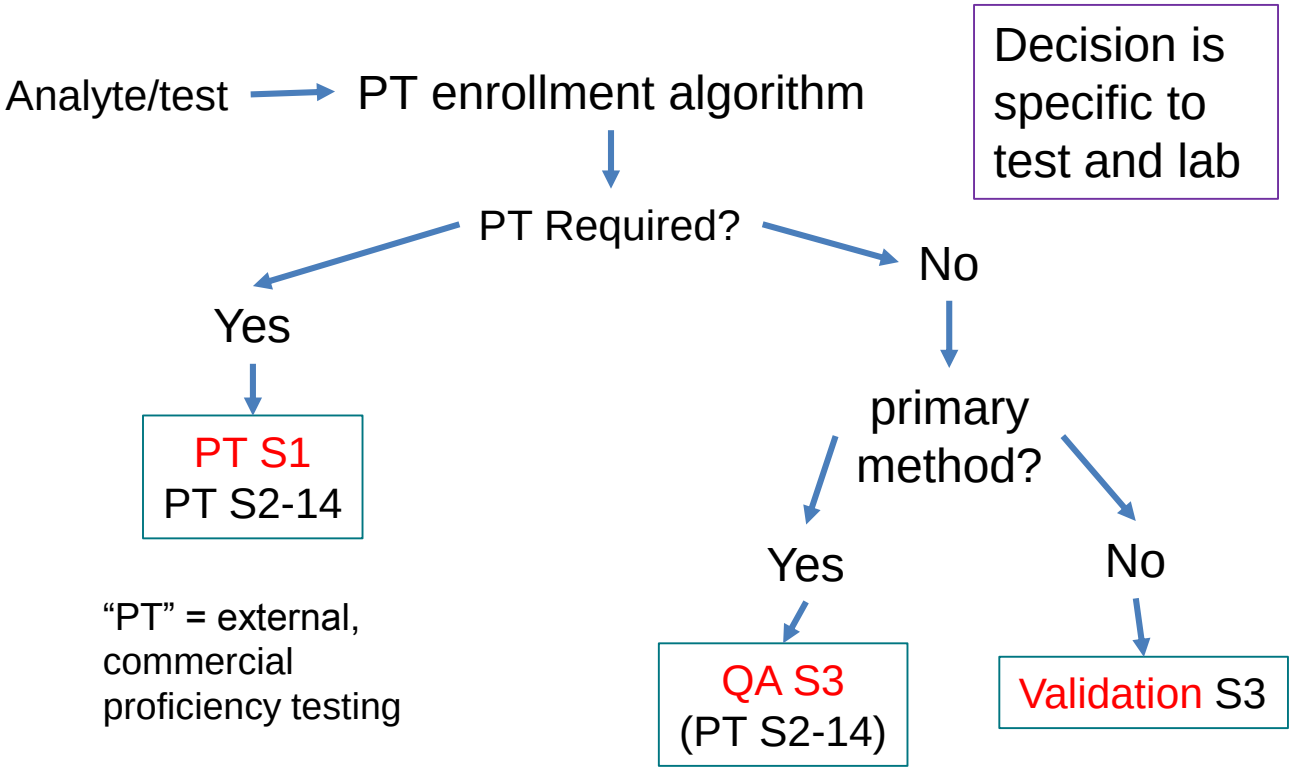
d) shall initiate and document a review of verification results within two weeks and subsequently perform and document corrective action when:

i. the score received in an external proficiency testing program is less than 100 percent, the result(s) are unacceptable or indicate review is required;

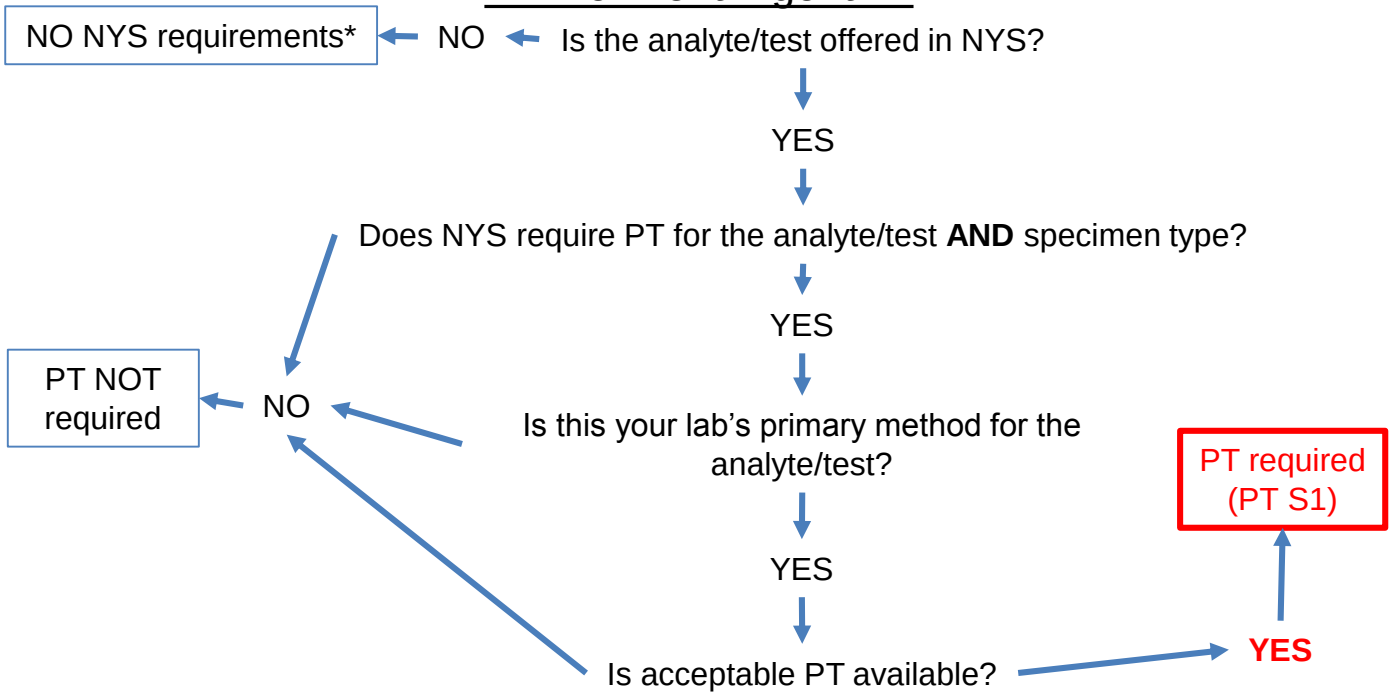
ii. results do not meet the laboratory's specified performance criteria; or

iii. shifts and trends are identified.

When does QA S3 apply?



Does NYS Require Proficiency Testing for this Test? – Enrollment Algorithm



When does QA S3 apply?

NYS does NOT require PT for the analyte/test AND specimen type

Primary method for analyte not listed in CLIA subpart I

- Hemoglobin A1c
- Parasite antigen detection

Primary method for analyte listed in CLIA subpart I, but PT not required for the specimen type(s) your laboratory tests

- Urine glucose
- Body fluid – RBC, WBC

When does QA S3 apply?

PT is required, but not available

- PT is required, but no acceptable external PT available
- PT is required and available for the analyte, but your method doesn't work with any of the surveys. More likely for a laboratory developed test.

When does QA S3 apply?

QA S3 potentially applies to any test used for patient results that is performed in your comprehensive clinical lab, including:

- Laboratory Developed Tests (LDTs)
- Research Use Only (RUO)
- FDA approved or cleared
- Waived tests
- High, medium, low complexity

How to Comply with QA S3

"…have a system for verifying the reliability and accuracy of test results…at least semi-annually…"

Option 1: External PT

Option 2: Non-PT process

semi-annual means two times per year:

- first event in the first six months of a year
- second event in the last six months of a year
- at least four months and not more than eight months between events

How to Comply with QA S3 – Using PT

PT is not required, but you can voluntarily enroll in PT to comply with QA S3.

Requirements:

- Enroll in PT
- Participate in PT
- Evaluate your performance

How to Comply with QA S3 – Using PT

PT is not required, but you can voluntarily enroll in PT to comply with QA S3.

Enroll in PT - What kind of PT can I use?

- Program/survey does not need NYS approval
- Two events/year minimum, approximately six months apart
- Event doesn't need to be formally graded (can be educational)

Can use the PT to meet multiple requirements, if applicable

How to Comply with QA S3 – Using PT

PT is not required, but you can voluntarily enroll in PT to comply with QA S3.

Participate in PT

- If you miss an event – still has to be “semi-annual”
- **ALL NYS PT STANDARDS APPLY**
  - Treat samples as patient samples
  - Performance - CMS-approved providers send scores to NYS
  - “PT cheating”
  - Regulatory consequences
    - Potential loss of permit/CLIA# for PT issues

How to Comply with QA S3 – Using PT

Evaluate your performance

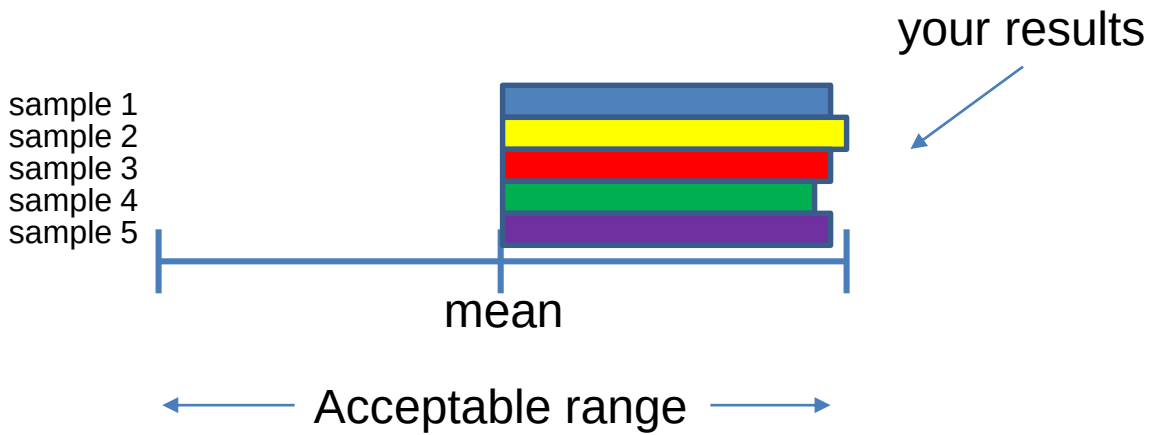
Review the results within two weeks

- <100% or unacceptable, if graded
  - Investigate
  - Take corrective action, document
- Shifts, trends, deviations from performance specifications
  - Bias, repeats, marginal QC, etc
  - Investigate
  - Take corrective action, document

Potential to impact patient results?

How to Comply with QA S3 – Using PT

Evaluating when score = 100%
- shifts and trends -



Calibration?
QC?
Normal result → Abnormal result?

How to Comply with QA S3 – Using PT

Advantages of using PT to comply with QA S3

- Test accuracy
- Validated samples
- Compare to peers
- Simplifies evaluation – score is objective
- Convenience – samples, acceptability criteria, etc

How to Comply with QA S3 – Using PT

Disadvantages of using PT to comply with QA S3

- Generally does not evaluate entire test process (e.g. pre-examination)
- Can be difficult to treat some PT samples as patient specimens
- Potential matrix effects
- Potential regulatory consequences

  One sample per event?
  One incorrect result = 0%

How to comply with QA S3 – Using non-PT processes

"…have a system for verifying the reliability and accuracy of test results…at least semi-annually…"

If you choose not to participate in external PT, you can use a variety of alternative QA processes, including:

- Split sample – two labs and/or two methods
- Repeat testing
- Reference material – Calibrator, standard, etc
- External "peer group"

Treat like PT as much as possible

How to comply with QA S3 – Using non-PT processes

General Guidance

- SOP - Overall process and details
  - Samples
  - Comparisons
  - Acceptability criteria
  - Results evaluation
  - Investigation process / root cause analysis
  - Documentation
  - Frequency – at least semi-annual

Must comply with PT S4 – inter-laboratory communication – and PT S5 – PT sample referral

How to comply with QA S3 – Split samples

Samples

- Cover the reportable range over the year
  - Challenge limit of detection
- Primary specimen?
- How many positive, negative, high, low…?
- How many do you need to detect discordance?
- Replicates?
- Blinding
- Patient samples
  - How to de-identify/anonymize?
  - What if there is discordance?

How to comply with QA S3 – Split samples

Comparison

- If two labs, same method at both labs best
- If two different methods
  - Validate correction factor
  - Other differences?
    - Sensitivity
    - Specificity
    - Interference
- Repeat review of results
  - Not appropriate for most tests
  - Appropriate for e.g. manual diff, KOH prep

How to comply with QA S3 – Split samples

Comparison

- What will be compared?
  - Quantitative
    - Compare values
    - Compare positive/negative
    - Expected method variance?
  - Qualitative
    - Consistent criteria
    - Expected method variance?
- What difference would change clinical interpretation?

How to comply with QA S3 – Split samples

Sample acceptability criteria

- Qualitative – consistent lab/method scoring criteria
- Quantitative – how similar do the numbers have to be?
  - e.g. Routine QC criteria
  - e.g. Allowed difference (CLSI GP29-A2) based on:
    - Method variance for Lab A
    - Method variance for Lab B
    - Inter-laboratory variance
    - Number of replicates

Concordance

|Lab A result - Lab B result| < allowed difference

How to comply with QA S3 – Split samples

Acceptability criteria - event

- How many results must be concordant?
  - Target concordance = 80%, Kappa > 0.8, etc
  - Kappa statistic = (observed – chance)/(1-chance)

  chance = (proportion negative results, lab A) x (proportion negative result, lab B) + (proportion positive results, lab A) x (proportion positive result, lab B)

Target concordance assumes that you investigate anything <100% and take corrective action.

How to comply with QA S3 – Split samples

Evaluation

9 of 10 samples concordant for a quantitative test

- 90% concordance
- Is this good enough?
- What was different about the discordant sample?
- Which lab or method is wrong for the discordant sample?

How to comply with QA S3 – Split samples

Investigation, root cause analysis, and corrective action

- Technical
- SOP
- Personnel
- Corrected reports?
- “Cease testing”? – 50% concordance? kappa = 0.4?

How to comply with QA S3 – Split samples

Documentation

- Document all steps – including corrective action
- Retain documentation for two years, five years for Immunohematology (PT S7)

How to comply with QA S3 – Split samples

Advantages

- Evaluates ~all of the test steps
- Potential for accuracy vs a gold standard method

Disadvantages

- May be challenging to find samples across reportable range and/or for specimen type
- Potential for different interferences in different methods
- Requires good understanding of test performance

How to comply with QA S3 – Split samples

Inter-laboratory comparison

Example – NYS Toxicology expectations

Samples

- ≥4 samples (5 or more preferred)
- Should have a positive for every analyte at least once every two years
- ~35% of analytes should be positive each event

Comparison

- Coordinate and agree on TAT/dates
- Set appropriate positive/negative cutoff for each analyte

Acceptability criteria

- Recommend 25% tolerance

How to comply with QA S3 – Repeat testing

Perform same test over time on same samples

samples 1-5	samples 1-5	samples 1-5	samples 1-5
February	August	February	August

Test each sample twice

samples 1-5	samples 1-5 samples 6-10	samples 6-10 samples 11-15	samples 11-15 samples 16-20
February	August	February	August

How to comply with QA S3 – Repeat testing

Samples

- Similar to split samples
- How common is a positive?
- Blinding + who will manage it

Comparison

- Similar to split samples
- Time A vs time B
- Same method, lot-to-lot variation

Evaluation

- Similar to split samples
- Resolving discordance

How to comply with QA S3 – Repeat testing

Advantages

- You already have the samples
- Single method

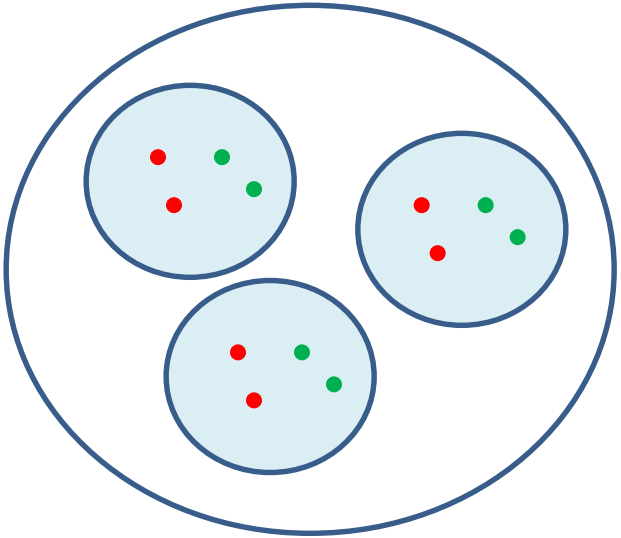
Disadvantages

- Potential issues with sample availability or stability
- Variance introduced by different lots of reagents, calibrators, software updates, etc
- *Demonstrates reproducibility, not necessarily accuracy*
  - Do you have additional information about accuracy?

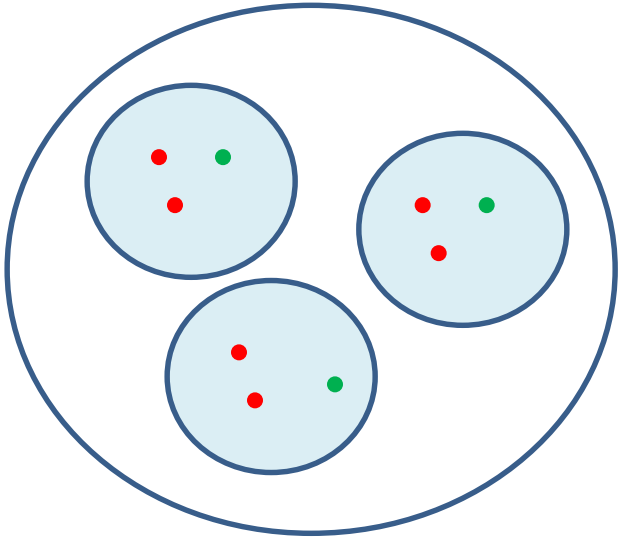
How to comply with QA S3 – Repeat testing

Cytogenetics – Fluorescence In Situ Hybridization

Normal signal pattern



Abnormal signal pattern



How to comply with QA S3 – Repeat testing

Cytogenetics – Fluorescence In Situ Hybridization

Samples

- Fixed cells stable for a long time

Comparison

- Quantitative
  - # of cells with specific signal pattern
  - Compare to previous and to normal range
- May have both previous result and reference diagnosis (karyotype)

How to comply with QA S3 – Reference material

Use manufacturer's standard, calibrator, QC material, etc or similar external reference material

Samples
- Reference material
- Use different lot from current QC, calibrator, etc

Comparison
- Compare results to known (true) value
- May be peer groups through manufacturer

Evaluation
- Similar to other approaches

How to comply with QA S3 – Reference material

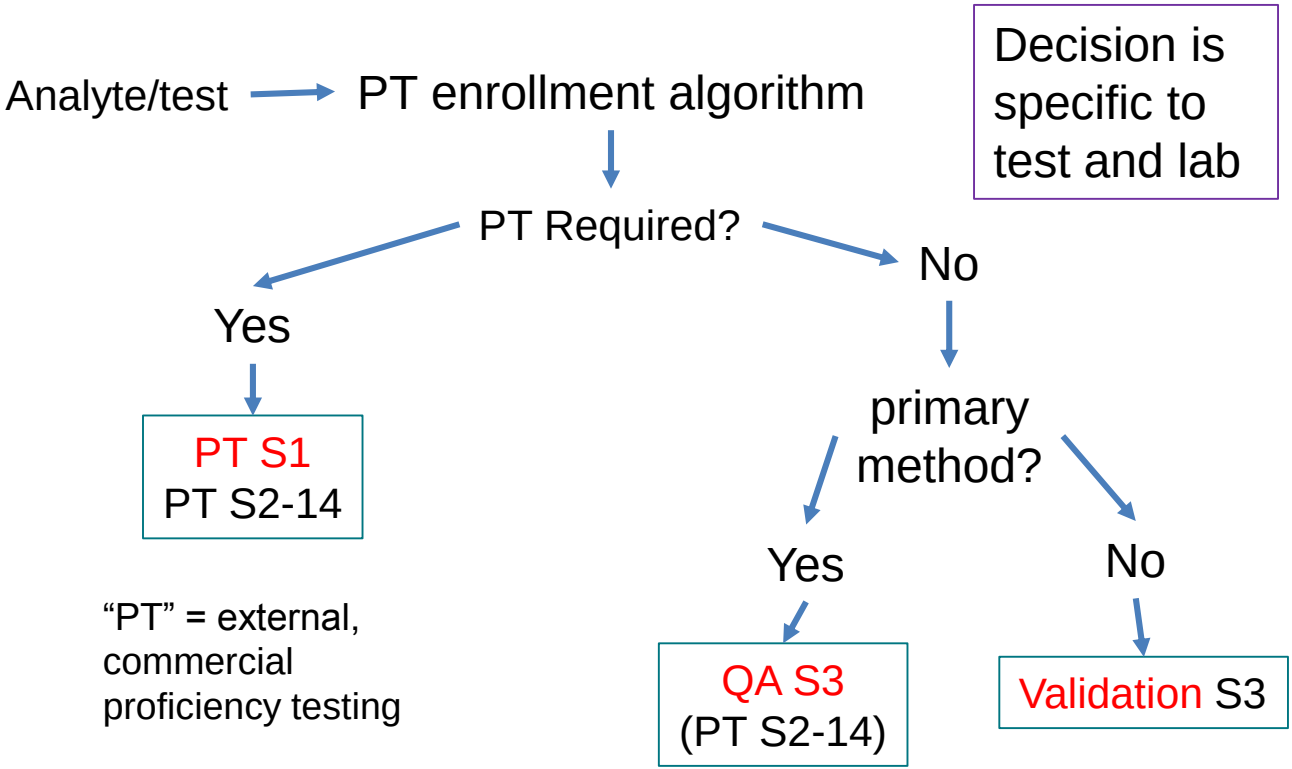
Advantages

- Good measure of test accuracy
- Don’t need to procure specimens

Disadvantages

- Not a specimen – not looking at entire test process
- Many tests don’t have reference material

When does QA S3 apply?

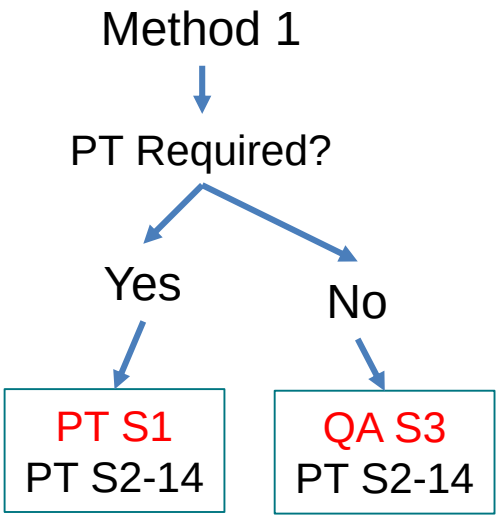


Validation S3

Validation Sustaining Standard of Practice 3 (Validation S3): Multisystems Agreement

A laboratory that performs the same test using different methods or instruments, or performs the same test at multiple test sites, shall have a system in place that evaluates and defines the relationship between test results every six months.

When does Validation S3 apply?



Method 2 for same analyte:

- PT NOT required
- QA S3 NOT required
- Validation S3 required

Method 1 or 2 backup instrument:

- PT NOT required
- QA S3 NOT required
- Validation S3 required

How to comply with Validation S3

General Guidance

- SOP - Overall process and details
  - Samples
  - Comparisons
  - Acceptability criteria
  - Results evaluation
  - Investigation process / root cause analysis
  - Documentation
  - Frequency – at least semi-annual

How to comply with Validation S3 and other requirements at the same time

Using proficiency testing

Before the PT deadline	**After** the PT deadline
Testing to satisfy QA S3	Testing secondary method and/or backup instrument to satisfy Validation S3

How to comply with Validation S3 and other requirements at the same time

Using proficiency testing

Before the PT deadline	**After** the PT deadline
Testing to satisfy PT S1	Testing secondary method and/or backup instrument to satisfy Validation S3

How to comply with Validation S3 and other requirements at the same time

Using split samples

Before the deadline	After the deadline
Testing to satisfy PT QA S3	Testing secondary method and/or backup instrument to satisfy Validation S3

Questions?

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