AABB Annual Meeting Education Program 2014

October 25-28, 2014 | Pennsylvania Convention Center | Philadelphia, PA

Presentation Handouts

# (9129-QE) Validation 101

October 25, 2014 ✧ 4:00 PM - 5:30 PM

Advancing Transfusion and Cellular Therapies Worldwide

# Event Faculty List

**Event Title:** **(9129-QE)** Validation 101
**Event Date**: October 25, 2014
**Event Time**: 4:00 PM - 5:30 PM

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# VALIDATION 101

A blood bank supervisors experience

Cindy Sidebottom, MT (ASCP)
Gateway Medical Center
Clarksville, TN

## Background

- Medical technologist generalist since 2001
- Blood bank section leader since 2006
- Maintain generalist competency
- Gateway Medical Center
  - 270 bed facility
  - Transfuse ~5000 blood products annually

## Coming Soon

You're getting a new instrument!

- Excitement
  - Something new
  - Improves quality
  - Standardizes testing
- Anticipation
- Realization
  - Regulatory requirements
  - Validation requirements
  - Complicated process
- Panic
- Plan, Train, Execute, Approve, Implement

## Where do you begin?

Figuring it out

- What is required?
  - Created skeletal outline of requirements from FDA, AABB, and CLSI.
- What is acceptable?
  - What are other hospitals doing?
  - What is the vendor doing?
  - What should we do?
    - Tests to be validated
    - Sample numbers
    - Execution
    - Acceptance criteria
    - Type of samples to be tested

## The Plan

Purpose
Clinical Significance
Intended Use
Supplies
Responsibilities
PQ
Corrective Action
Acceptance Criteria
Revalidation
Approval

- Writing the validation plan
  - Creating a plan for an unknown process
    - TP, TN, FP, FN
    - Reaction grades or qualitative?
    - Not everything will correlate 100%, just breathe. You will survive
  - Incorporating guidelines that were initially designed for chemistry/coag/heme
    - Sensitivity
    - Specificity
    - Concordance
  - Finalize
  - Approval

The validation plan becomes the reference document for your entire validation process.

## Train

Train the trainer

- Select super users
- Train super users
- Super users train end users
  - Tech buy-in
- Documentation, documentation, documentation

## Execute

Testing the samples

- For me, this was the easiest part.
- You have a plan, now follow through.
- Incorporated super users and end users in validation.
  - Competency
  - Confidence
  - Stubborn techs
- Not a quick process

## Approval

Summary & Approval

- Summarize plan
- Summarize results
- Address non-concordant results head on
  - TP vs FP: who's the real deal?
  - Why did it happen
  - Is it clinically significant
- Outline causes for revalidation
- Approval

## Implementation

Implementation

- D-Day
- Tech issues
  - Confidence
  - Competence
  - Stubborn techs
- Issues will arise

# QUESTIONS?

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# VALIDATION 101

AABB Annual Meeting 2014
Rosemary Steuber BS MT SBB (ASCP)CM MHA
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## Validation 101 Objectives

- Describe the basic purpose of validation and its implications as it applies to blood bank automation
- Review regulatory guidelines
- Explain process (including IQ, OQ, PQ) and execution of validation
- Describe possible pitfalls that should be avoided during validation

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## Purpose of Validation

- To establish documented evidence that a specific process will consistently produce an outcome meeting its predetermined specifications and quality attributes
- Basically, *is it going to function as expected with a high degree of assurance and reliability?*

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## Purpose of Validation

- Manufacturer's role
  - responsible for FDA clearance
- Facility's role
  - responsible for acceptable performance on site, i.e., patient population, geography and operating conditions

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## Regulatory and Accrediting Agencies' Requirements

- U.S.
  - FDA
- Other countries
- State & Local government
- Other agencies
  - AABB
  - CAP
  - COLA
  - Joint Commission

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## FDA Validation Regulations

- Blood Suppliers & Transfusion Services
  - Comply with Code of Federal Regulations (CFR)

-Blood and components viewed as a 'drug' and regulated as such

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## FDA Validation Regulations

- Code of Federal Regulations
- Title 21 – Food and Drugs
- Chapter 1 – cGMPs
  - Current Good Manufacturing Practices
- Subchapters:
  - "F" – Biologics (600 Series)
  - "C" – Drugs (200 Series)
  - "H" – Medical Devices (800 Series)


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## AABB Standards Requirements

- BBTS 3.2 Qualification of Equipment
  - All equipment shall be qualified for its intended use, including FDA-cleared or approved devices
    - 3.2.1 Installation Qualification (IQ)
    - 3.2.2 Operational Qualification (OQ)
    - 3.2.3 Performance Qualification (PQ)
      - 3.2.3.1 Performance specifications established by the manufacturer shall be met


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## College of American Pathologists (CAP) Requirements

### ALL COMMON CHECKLIST:

- COM.40000
  There is a summary statement, signed by the laboratory director (or designee who meets CAP director qualifications), documenting review of validation studies and approval of each test for clinical use
- COM.40300
  Analytic Accuracy/Precision
- COM.40400
  Analytic Sensitivity
- COM.40500
  Analytic Interferences

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## The **Validation** Process

The basic process should include:

- Writing a plan
- Approving the plan
- Executing the plan
- Final review/acceptance
- Implementation

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## The **Validation** Process

- It is basically a 'roadmap to success' for a new method or process to incorporate into patient testing.
- Directions are needed to get where you want to go…
- The 'driver' needs to approve them before setting off on the journey…
- Who will be along for the journey…
- How many miles will it take to get there…
- What are some of the 'speedbumps' along the way…
- Who is authorized to give the approval and 'go ahead' for the validation trip…

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## Writing the Plan

- Define the validation process
- Understand and document the manufacturer's
  - Specifications
  - Limitations
    - Ex: Package insert claim is 98% sensitivity, don't write the plan to expect 100%
- Package inserts
- Operator Manual

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## Writing the Plan

Specification limitations- examples:

- Does it detect IgM antibodies?
- What tests have received FDA clearance by the manufacturer?
- What can be reported as test of record (FDA cleared assay)?
- What methodologies has a reagent been approved for?

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## Writing the Plan

Include in the plan:

- How the validation will be performed
- How validation will be assessed

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## Writing the Plan: Guidelines and SOPs

- Standard format
  - Some regulatory agencies may offer sample plans, formats for validation plans
- Guidelines for validation and approval process
  - Who will review and/or approve
  - Process for approval
  - Required result analysis
- Other requirements
- Discuss deviations from requirements before writing the plan

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## Writing the Plan

- A well-written validation plan will answer the questions:
  - Who will be involved?
  - What is being validated?
  - When will it be validated?
  - Where will it be validated (facility/site, etc)?
  - How is it being validated?

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## *Who* will be involved?

- Facility's own SOP's
- Facility and Vendor Information
  - Names, addresses, phone/fax numbers, contact persons
- Responsibilities
  - Who will:
    - Develop the plan
    - Review/Accept the plan
    - Execute the plan
      - »Vendor
      - »Employees
    - Perform final review/sign-off
- Who and what will be affected by the new process

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## *What* is being Validated?

- Title of plan
- Description of what is being validated
- Purpose
  - State the reason for performance of the validation
    - Provide proof that the system will consistently produce results that meet the facility's requirements
    - What are you hoping to accomplish
- Where will the validation take place
  - Department
  - Facility
  - System

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## *How* is it being Validated?

- Number and type of specimens to test
- Any unique testing protocols for the system being validated
  - Frozen samples
  - Age of specimens
  - Specimen spin times
  - Adult vs. Pediatric samples
  - Patient samples vs. Unit samples
  - Use of Proficiency or QC material be used for validation

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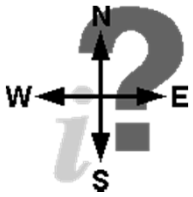
## *How* is it being Validated?

- What tests will be validated
- Process for test go-live
- SOP validation

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## *How* is it being Validated?

- Process of validation
  - Installation Qualification (IQ)
  - Operational Qualification (OQ)
  - Performance Qualification (PQ)
  - and sometimes Design Qualification (DQ)

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## *How* is it being Validated?

- Acceptability requirements
  - Define failures & exceptions
    - Who
    - Process
- Apply appropriate calculations to determine acceptability
- Calculations should be well documented and traceable

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## *How* is it being Validated?

- **Installation Qualification (IQ)**
  - Confirmation that equipment complies with technical specifications, standards, codes and regulations
  - Equipment functions performed and documented with expected results
  - Usually performed by the vendor
    - Plan should address who will perform this

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## *How* is it being Validated?

- **Operational Qualification** (**OQ**)
  - Confirmation that the system meets all user requirements as intended by the manufacturer
    - Operator training and documentation
    - Assay configurations
    - Assay performance and interpretation
    - Maintenance processes
  - Usually performed by the vendor
    - Plan should address who will perform this

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## *How* is it being Validated?

- **Performance Qualification (PQ)**
  - Confirmation that the system consistently produces acceptable outcomes under routine operating conditions and functions according to laboratory, regulatory, and accrediting agency requirements
  - Developed and performed by the facility
    - Should include routine and non-routine samples
    - Facility must determine the number and types of samples to run
      - How many is statistically meaningful?
      - Consider what current volumes are
      - Types of samples

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## Policy Validation Example

| | |
|---|---|
| Personnel to conduct the validation | Phlebotomy personnel |
| Criteria for acceptability | All questions should be answered "YES" except #8 and #9 |
| Method of assessment | Actual performance of the process |

**VALIDATION STEPS**

| | | |
|---|---|---|
| 1. Is the title clearly defined and specific? | ☐ N/A ☐ YES | ☐ YES ☐ NO ☐ See comments |
| 2. Is the purpose clearly defined and specific? | ☐ N/A ☐ YES | ☐ YES ☐ NO ☐ See comments |
| 3. Is the "Equipment & Reagents" list complete? | ☐ N/A ☐ YES | ☐ YES ☐ NO ☐ See comments |
| 4. Is the test sufficiently detailed to be understood and followed by staff? | ☐ N/A ☐ YES | ☐ YES ☐ NO ☐ See comments |
| 5. Do any procedural steps need to be put in a different order so that you could perform the more easily? | ☐ N/A ☐ YES | ☐ YES ☐ NO ☐ See comments |
| 6. Do any steps appear to be missing? | ☐ N/A ☐ YES | ☐ YES ☐ NO ☐ See comments |
| 7. Is the purpose of the SOP accomplished? | ☐ N/A ☐ YES | ☐ YES ☐ NO ☐ See comments |
| 8. Does the policy "clearly" describe how to fill out the worksheet and log? | ☐ N/A ☐ YES | ☐ YES ☐ NO ☐ See comments |
| 9. Does the policy identify the causes for rejection of blood bank specimens? | ☐ N/A ☐ YES | ☐ YES ☐ NO ☐ See comments |

| VALIDATION ASSESSMENT | | |
|---|---|---|
| ☐ Procedure has passed all Validation steps and may be entered.<br>☐ Procedure has NOT passed all Validation steps and may not be performed. | SIGNED | Validated By |
| ☐ Procedure has passed all Validation steps and may be entered.<br>☐ Procedure has NOT passed all Validation steps and may not be performed. | SIGNED | Blood Bank Supervisor |

Comments may be documented on the back of this form.

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Test Form (rev. 092006) Galileo Echo Serial Number:

| | |
|---|---|
| Test Case Number: | |
| Function: | Run the Group assay, i.e. the Run Test in place on 1 sample for a total of 5 times. Calculate the Precision for the ABO assays, a retrospective assay. |
| Attachments Required? | YES<br>a. Printed copies of each run of the patient sample. |

Operator:

| Operator Signature | Date of Validation |
|---|---|
| | |

Test Method:

| Step | Action Description | Expected Outcome(s): | Actual Outcome(s): Pass / Fail / Comments |
|---|---|---|---|
| 1 | Select a patient sample of an appropriate expected result. Using the Group assay, run the sample a total of 5 times. | One patient sample has from antibody of test results and representative of a normal patient sample should be on a total of 5 times. The results should be identical to each other. No hesitation / loss of the sample should occur during the repeated testing process. | |
| 2 | Print and attach the Group reports generated by this test case. | Group Reports printed and attached. In order for the results to be determined to be precise, all 5 runs must show the same results / interpretation. | |

The operator must refer to the Problem Resolution Form for test case number ___ in the instance of failure(s).

Reviewer:

| Reviewer Signature | Review of Actual Outcome(s): Accept / Reject / Comments | Date of Review |
|---|---|---|
| | | |

The reviewer must refer to the Problem Resolution Form for test case number ___ in the instance of rejection.

NOTE: This is not an immucor approved procedure. Any case studies that are not written, tested, and validated by immucor must be written and validated by the customer.

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## *How* is it being Validated?

- **Performance Qualification (PQ)**
  - Usually presented in Test Case scenarios
  - Challenge for a single validation task
    - E.g. is the instrument reading the barcode properly?
  - Challenge for multiple associated validation tasks
    - E.g. Is the instrument consistently performing correct ABO/Rh typing?

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## *How* is it being Validated?

- **Performance Qualification (PQ)** considerations:
  - Hemolyzed, icteric, lipemic samples
  - Unexpected results
  - Challenges to using expired reagents
  - Challenges to reporting results if QC is not valid or hasn't been performed
  - Sample identification issues (illegible barcodes, manual entry, etc)
  - Carry over studies
  - Accuracy/Precision studies, Sensitivity & Specificity studies
  - Stress loading
  - Turn around times

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## *How* is it being validated?

- Careful consideration should be given to how many samples are included in the validation and what the reference method is when determining how many is enough.
  - If there is a discrepancy between the old and the new, will a tie-breaker method be used?
    - How will you determine which result is "correct"
  - How will you determine which results are acceptable?

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## *How* is it being Validated?

- Freezing and thawing samples for validation:
  - –Manufacturer's limitations and expected effects
  - –Freeze thaw may affect the reactivity of antibodies
    - Test thawed samples on both new and reference methods to assure reactivity

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## *How* is it being Validated?

- Example 1: A lab is switching from tube method to an new automated analyzer . The methodology as well as the instrumentation will be new to the lab. They run approximately 500 antibody screens a week.
- Example 2: A lab has been using an automated analyzer for testing for 5 years and are adding a second analyzer of the same type into their lab in anticipation of increased volume. They currently run 1000 antibody screens a week

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## *How* is it being Validated?

- When validating an Antibody Identification method:
  - – What specificities will you choose or will you specify what they are
    - Will passively acquired antibodies be included (i.e. Anti-D from RhIG)
  - – How many antibodies do you get in the course of a week or a month

    Ex: a facility has written their plan to test 20 antibody positive samples. They only do 2 antibody work-ups in a month.

    Ex: a facility has written their plan to include testing reactivity of Anti-N and Anti-JK3. The lab typically sees these antibodies once or twice a year.

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## *How* is it being Validated?

- Result definitions
  - True Positive
  - True Negative
  - False Positive
  - False Negative
- Acceptance Criteria
  - Sensitivity
  - Specificity
  - Concordance
  - Accuracy
  - Precision/Reproducibility

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## *How* is it being Validated?

- Training
  - Who will be trained and by whom, by what methods?
  - When will competency be assessed?
    - Remember that CLIA requires competency on tests/methods must be assessed before reporting patient results
- Describe conditions which require re-validation


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## *How* is it being Validated?

- Remember that policies and procedures should be written so that they, too, can be evaluated for clarity and effectiveness during the validation process.
- Consider your laboratory's general validation SOP that may require certain formats and content of the final new SOP.

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## Approving the Plan

- The plan should be approved BEFORE validation begins:
  - Review for completeness
  - Assure there is agreement with acceptance criteria
  - Are the test cases in the PQ sufficient ?
  - Helps to assure expectations of those writing the plan and those who will have final sign off on the system are in sync with each other

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## Executing the Plan

- Document at every step of the process
  - Validation records must be maintained (21 CFR 211.68(b), 211.100(b), 606.160(b)(5)(ii))
- Document any problem resolutions that were performed as a result of failed test cases
- Document changes in the validation plan and approvals for the changes made

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## Executing the Plan

- **DOCUMENT**
  - **DOCUMENT**
    - **DOCUMENT**
    - **And then DOCUMENT SOME MORE!**

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## Final Review & Acceptance

- There should be clear documentation as to:
  - *Who* performed the final sign-off
    - Assure with your regulating agencies that it is an appropriate individual
  - *When* the sign-off was done
    - It is important that the documentation shows that final sign-off was done PRIOR to the process being moved into production
  - *What* was signed off
    - Regulatory agencies may require approval of EACH test for clinical use, make sure the documentation is clear

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## Other requirements

- Additional proficiency test platforms may be required.
  - For example, if adding on automated blood banking testing, CAP/API require a specific 'automated' proficiency assessment.
  - Various state agencies may also have specific requirements for new methods.

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## In review….

- The validation process should include:
  - Writing a plan
  - Approving the plan
  - Executing the plan
  - Final review/acceptance
  - Implementation of the new system/process
  - After implementation, the new method or process should be evaluated for acceptable performance.
    - **RQ** Re-Validation Qualification?

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## Reminder…

- The ultimate responsibility for writing and executing a validation protocol is the facility's responsibility … but certain 'rules' need to be followed.
- Consider checking with regulatory agencies or peer facilities for criteria that would be acceptable or examples of validation plans.

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## The **Validation** Plan

- You have now written out your roadmap to success and have covered all of your basic needs as defined by regulatory agencies.
- Now it is time to see if your new method works for your laboratory.

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## Some plans may seem a little hard to visualize clearly at first…

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Some plans you cannot see at all how they are going to work…

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And some best laid plans still cause problems you did not see coming…

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Take a walk, clear your head, go back to the plan, try again,…

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When successful and the Validation plan worked…***CELEBRATE!***

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## References


- aabb.org
- CAP.org
- fda.gov


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Planning ahead

helps you

to succeed

Thank you!!!

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## QUESTIONS??

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