Qualification and Validation

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Webinar Presenters

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In accordance with the standards of the Accreditation Council for Continuing Medical Education (ACCME), all speakers are asked to disclose any real or apparent conflicts of interest, which may have a direct bearing on the subject matter they will be presenting.

These speakers have indicated no conflict of interest to disclose.

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QUALIFICATION AND VALIDATION

Dennis Gastineau, MD; Olive Sturtevant, MHP, MT(ASCP), SBB, SLS; and Michele Carbone, MS, CLS, MT(ASCP)
Presentation Outline

• Background information
• Performing qualification
• Conducting validation studies
• Optimizing Studies to Achieve Synergies
BACKGROUND INFORMATION
Definition and Purpose of Qualification

- Definition: “The establishment of confidence that equipment, supplies, and reagents function consistently within established limits.”
- Purpose: Strengthen control of processes by establishing minimal acceptance criteria and performance for materials used in those processes.
- Note: Some local terminology refers to qualification as “validation” . . . this is acceptable as long as intent is met
Definition and Purpose of Validation

- **Definition:** “Confirmation by examination and provision of objective evidence that particular requirements can consistently be fulfilled.”
- **Purpose:** Confirm that a process consistently produces a cellular therapy product or cord blood unit that meets predetermined specifications.
What is the difference?
(Or, more importantly, what is the same?)

**Qualification:**
- Focus on materials
- Focus on performance *before* or *during* process

**Validation:**
- Reliance on predetermined requirements and specifications
- Ability to assess quality of a process
- Impact on quality of product or unit

- Focus on processes
- Focus on consistent *results* of process
FACT Requirements for Qualification and Validation

☑️ Inclusion in Quality Management (QM) Plan
  - Both qualification and validation
  - All details in QM Plan OR a summary in QM Plan with reference(s) to the details

☑️ Oversight
  - Review and approval by appropriate Director or QM representative
    - Qualification studies (cord blood banks)
    - Validation studies (cord blood banks and processing facilities)
FACT Requirements for Qualification and Validation

✓ Qualification of:
  – Equipment
  – Supplies
  – Reagents
  – Vendors (cord blood banks and processing facilities)
  – Facilities (cellular therapy)

✓ Validation of:
  – Critical or significant procedures
    • Specific list for collection and processing facilities
    • Decided upon by CBB Director/Medical Director and QM representatives in cord blood banks
  – Changes to a procedure (including new equipment, supplies, or reagents!)
FACT Requirements for Qualification and Validation

✓ Maintain records of studies and results
✓ Follow-up and evaluation
  – If predetermined specifications or requirements are not met
  – Corrective actions if necessary
  – Re-evaluate
Inspecting Qualification and Validation

• Review of applicable Standard Operating Procedures (SOPs)
  – Evidence of collection, analysis, evaluation, and follow-up of data

• Review of specific qualification and validation studies
  – Appropriateness of study design
  – Conformance to applicable SOP(s)
  – Evidence of oversight
Qualification Deficiencies

- Not included in the QM Plan
- Summarized in QM Plan but no reference to details
- Included in QM Plan but not actually performed
- Not all required qualifications performed
- Results of qualifications not evaluated
Validation Deficiencies

- Not included in the QM Plan
- Summarized in QM Plan but no reference to details
- Included in QM Plan but not actually performed
- Not all required validation studies performed
- Changes to processes not validated
- No acceptance criteria
- Unable to locate documentation
- No documentation of results
Quality Management Tools

Quality Management Plan

Standard Operating Procedures

Supporting Documents
QUALIFICATION
Why Each Type is Important

- **Installation Qualification (IQ)**
  - Usually applicable to equipment
  - Equipment appropriately assembled, programmed, placed, functioning

- **Operational Qualification (OQ)**
  - Verify all predetermined specifications or requirements are met (can also be documented with manufacturer’s Certificate of Analysis)
  - Include worst-case scenarios and normal variations

- **Performance Qualification (PQ)**
  - Verify predetermined specifications or requirements are met during intended use
  - Perform actual procedure with the material being qualified
    - Demonstrate acceptable results
When to Perform Qualification

- New equipment
- New vendor
- New lot of supplies and/or reagents
- New or remodeled facility
- Relocation of equipment
- Change to a procedure in which the material is used
Qualification of Flow Cyometer

• Move of a piece of equipment that reasonably has the potential to change the function of the equipment.

• Outline of the Qualification Process

• Purpose:
  – This qualification will be performed to ensure that the FACSCalibur Flow Cytometer is in proper working condition after it is moved within the HCTL.

• System Description:
  – Currently the flow cytometer is in Hi 261 and is scheduled to be moved to Hilton 278. The cytometer is being moved to make room for the new FacsCalibur.
Qualification of Flow Cytometer

• **Study Summary:**
  – After the cytometer is moved, calibrations will be performed to ensure that the cytometer is in proper working condition prior to performing patient samples.

• **Responsibilities:**
  – The qualification outline will be approved by the Supervisor, Medical Director and QA prior to initiation of the validation. The qualification will be performed by HCTL. The qualification summary will also be approved by laboratory management.
Qualification of Flow Cytometer

• Qualification Plan:
  – The cytometer will be moved from Hi 261 to Hi 278.
  – Perform the FACSComp calibration per SOP 5528.
  – Perform the Rainbow Particle calibration per SOP 5528.

• Acceptance Criteria:
  – The FACSComp calibration must Pass all criteria.
  – The Rainbow Particle calibration results must have $R^2$ values of $>0.98$. 
Qualification of Flow Cytometer

• **Deviations:**
  – Rainbow Calibration did not pass for FL4. However, this problem was discovered in June with the new lot of Rainbow Calibration Beads all three cytometers did not pass FL4. BD has been contacted about the problem see event report 07-09-016. This appears to be reagent, not equipment, related.

• **Summary of Findings:**
  – FacsComp passed.
  – Rainbow Calibration passed FL1, FL2, and FL3.
Qualification of Flow Cytometer

• Conclusions:
  – Document overall interpretation of qualification studies (acceptable and ok to implement, modify, or reject).
    – Acceptable, OK to implement
    – Acceptable, with Limitations (describe below)
    – Modify, Define modifications in comments section
    – Reject
VALIDATION
Validation versus Verification

• Validation confirms process performs as expected on a consistent basis
  – Example: Ensure collection or processing procedure consistently results in acceptable number of cells
  – Can include verification

• Verification confirms accuracy or that requirements have been fulfilled
  – Example: Ensure a product or unit contains the desired number of cells
  – Can be outside of a validation study
When to Perform Validation

• Prospectively
  – Example: New procedure or change to existing procedure

• Concurrently
  – Example: New equipment, supplies, reagents, or facility

• Retrospectively
  – Example: Existing procedure that has not yet been validated
Important Steps During Validation

• Design and planning
• Writing the objectives for the study
• Perform a risk assessment of the process
• Determining what to measure and what are acceptable outcomes
• Having documentation in place (SOP, worksheets, etc.)
• Writing conclusion based on data obtained
• Formal sign-offs
• Training
• Review/audits
Validation Plan

- Written plan stating how validation will be conducted:
  - Test parameters
  - Product or unit characteristics
  - Production equipment
  - Acceptable results
  - Variables
  - Worst-case scenarios, upper and lower limits
Validation Plan Outline

• Purpose
• System Description
• Study Summary
• Responsibilities
• Validation Plan
• Acceptance Criteria
Concurrent Validation
New Bone Marrow Collection Kit

Plan:

1. Initial steps
   - New marrow collection kits are received, evaluated, and approved for use
   - Documents (SOP and forms) revised and reviewed
   - Training plan developed

2. Plan to evaluate the new kits with predetermined evaluation criteria in two phases
   - The marrow collection kit and revised SOP were assessed initially during the next three marrow collections performed using one collection team
   - Additionally, after the first 15 collections were obtained, another review of performance documented
Acceptable Outcomes

• Ease of use – comparable to previous
• Sterility outcome equal or less than historical data
• Cell counts / volume – amount acceptable based on historical data
• Cell viability equal to historical data
• Engraftment data within 2 SD of mean for patient group
• No unexpected Donor events
• No unexpected deviations
Product Verification

• Kits received were intact, complete and labeled appropriately
• Certificate Conformance & Sterility on-file for the kit lot number used
• Kits were placed in-stock in the OR
SOP Verification and Training

• Physician and PA read procedure before, during and after the collection to assess accuracy of the SOP and data forms (x3)
• SOP tweaked to reflect actual practice
• Additional Staff trained
  – Read SOP
  – Direct observation by trainer
Outcome After Initial 3 Collections

- Sterility cultures – No growth
- Cell counts / volumes – No difference
- Ease of use - Acceptable
- No negative Donor outcome
- No significant deviations
- SOP revised after 1st collection
  - Supplies and Lot number documentation form
- Engraftment – to follow
Outcome After 15 Collections

• Sterility cultures – positive rate less historical rate (13 vs 15%)
  – No sign of infection in donors with positive cultures
• No negative Donor outcomes.
• Cell counts / volumes (2.71 x10^6 CD34+/Kg)
  – One collection had a low volume – unrelated to collection kit
• No deviations
• Supply and Lot number form filled out correctly
• Engraftment – to follow
Outcome - Engraftment

• ANC Engraftment data for the patients who received HPC-Marrows collected with the new kits were comparable to previous findings for the donor type (Auto vs. MRD vs URD) and patient disease category (100%)

• Time to ANC engraftment 12-22 days
Validation Summary

• Results attached (may be quite numerous and bulky with multiple graphs)
• Deviations from plan (almost nothing goes completely as planned)
• Summary of findings
• Assessment
  – Acceptable
  – Acceptable with limitations
  – Reject
• Comments
• Review and Approvals
OPTIMIZING STUDIES TO ACHIEVE SYNERGIES
A procedure cannot be sufficient if inadequate materials are used.

Materials cannot perform as expected if used inappropriately during a procedure.
Timing of Qualification and Validation

- Qualification
- Validation

Sequential:
- Qualification
- Validation

Concurrent:
- Qualification
- Validation

Separate:
- Qualification
- Validation
Acceptable Ways to Combine Processes

• Include qualification as a step in the validation procedure
• Conduct performance qualification at the same time as process validation
• Use retrospective studies in conjunction with a new one
• Perform validation studies of both collection procedures and processing procedures in the Processing Facility
Prioritizing Studies

1. Focus on aspects for which failure to meet specifications could result in adverse event
2. Conduct all specific studies in the Standards
3. Assess where your program or bank is at particular risk for nonconformance
4. Fill in the gaps
Related Educational Sessions

• [www.factwebsite.org](http://www.factwebsite.org) > Training and Development > Related Opportunities
  – Retrospective and Prospective Validation of Processes (ISCT)
  – Validation and Qualification of Equipment and Reagents (ISCT)
  Free!  – Qualification of Vendors, Equipment, and Supplies (PACT)
Thank you for joining us today.

- This was the first session of the QM Series Module 2: Quality Assessment Activities.

- Join us for the upcoming sessions in this module:
  - Outcome Analysis Webinar: March 5, 2009 at 2 pm ET
  - Audit Webinar: April 20, 2010 at 2 pm ET
  - Virtual Roundtable, Example Assessment Programs: TBD

- Join us for the upcoming inspection and accreditation workshops:
  - Cellular Therapy: February 23, 2010 in Orlando, FL
  - Cellular Therapy: May 23, 2010 in Philadelphia, PA
  - Cellular Therapy Collection Facility: May 25, 2010 in New Orleans, LA
  - Cord Blood: June 6, 2010 in San Francisco, CA
Evaluations and Continuing Education Credit

- All inspectors can obtain CME/CNE certificates free of charge via the online Inspector Area.
- Program and bank personnel requesting CME/CNE credit can purchase credit for $20 via the FACT webinar web page.
- Evaluations will be distributed to participants not wishing to receive CME/CNE credit.
QUESTION AND ANSWER SESSION