Experiences with a Failure Investigation Program for Apheresis Blood Products

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AGENDA

- Apheresis Program – Overview
- Sources of Product Quality Failures
- Product QC Program - Essential Components
- Monthly Quality Control Monitoring
- Conducting a QC Failure Investigation
- Product Quality Communications
- QC Testing Challenges

Apheresis Program - Overview

The American Red Cross has 262 registered facilities that collect and distribute approximately 630,000 Apheresis Platelets, 321,000 Apheresis Red Cells, and 1,000 Granulocytes annually.

Fenwal

- **ALYX:** leukoreduced double red cells
- **Amicus:** leukoreduced platelets (single, double, triples), concurrent plasma
- **Autopheresis-C:** plasma
- **CS3000:** granulocytes

Gambro

- **Spectra:** leukoreduced platelets (single, double), concurrent plasma, granulocytes
- **Trima:** leukoreduced platelets (single, double, triples); concurrent plasma, concurrent non-leukoreduced apheresis red cells

Haemonetics

- **MCS+ LN8150:** leukoreduced double red cells

Apheresis Program – Product QC Testing

The volume of product QC testing performed within the American Red Cross:

- Apheresis Red Cells
  - > 100,000 per year for component hemoglobin and mean total component hemoglobin
  - > 3,200 per year for residual leukocyte counts and percent recovery
- Apheresis Platelets (Platelets pheresis)
  - > 30,000 per year for pH and platelet yield
  - > 4,000 per year for residual leukocyte counts

Apheresis Program – Product QC Testing

Average results - Apheresis Red Cells

- Mean total component hemoglobin
  - Trima – 66 g
  - Haemonetics 832F – 53 g
  - ALYX – 57 g
- Residual leukocyte counts
  - ALYX 99% $<3.5X10^5$
  - Haemonetics 94% $<3.5X10^5$

Apheresis Program – Product QC Testing

Average results - Apheresis Platelets

- pH = 7.4 $\pm$ 0.2
- Volume = 255 $\pm$ 69 mLs
- Platelet concentration = 1545 $X10^3$ $\pm$ 255
- Platelet yield = 3.8 X 10^{11} $\pm$ 0.6

Sources of Product Quality Failures

Failures can be discovered:

- During validation of equipment or process control
- During routine processing
- Result of a customer complaint
- Result of product QC testing

Sources of Product Quality Failures - Examples

During validation of equipment or process control

- New technology introduced
- Additional testing outside of the validation process – such as QC testing at the time of distribution

Sources of Product Quality Failures - Examples

During routine processing

- Collection process
- Manufacturing Process
- Routine QC
- Multiple processes or technology at one site

Sources of Product Quality Failures - Examples

Result of a customer complaint

- Platelets implicated in adverse reaction
- Hemolyzed RBCs

Product Quality Control Program

Tracking: Regional Monthly Schedule for Finished Product QC

- Type of product to be tested
- Apheresis instrument type
- Specific site location, as applicable
- Number of collected products (per site)
- Number of product to be tested (per site)

Product Quality Control Program

Clear Procedures

Ongoing Monitoring

Process for Failure Investigation and Corrective Actions

Product Quality Control Program

Responsibility and Accountability

- **Maintaining** the Regional Monthly Schedule for Finished Product Quality Control
- **Tracking** and **trending** Product Quality Control results
- **Notifying** key staff when monthly Quality Control fails
- **Compiling and initiating** the Product QC Summary reports
- **Routing** the QC Summary reports and data for review
- **Reviewing** the QC Summary Data

Product Quality Control Program

Reviews and Documentation

Review QC forms for:

- Transcription of test results from analyzer printouts
- Completeness of the form
- Correctness of any calculations
- Correctness of any interpretations

If a failure on an individual product:

- Staff notify the supervisor
- Staff conduct an evaluation
- Product suitability for release is evaluated

Monthly Quality Control Monitoring

Routine review of monthly QC reports ensures:

- An adequate number of products are sampled and tested
- The QC results meet or exceed the acceptability criteria
- Track and trend results to include process improvement opportunity where possible

Standardized Failure Investigation

- **Accuracy of the sample tested**
- **Accuracy of the test result**
- **Process related critical control points**

ACTION	Performed	Record Results, if applicable	Initials and Date, if performed	Further Corrective Action
Quality Control Laboratory				
Was the product tagged for *Machine QC, %, or R1*? (if so, no further action is necessary)	☐			
Repeat calculations	☐			
Verify Sample Integrity				
Presence of clots	☐			
Presence of hemolysis	☐			
Was sample collected appropriately?	☐			
Verify the following equipment is functioning properly:				
Scale				
QC performed with passing results	☐			
Verify that correct tare bag was used	☐			
Recheck weights and/or confirm weights from other documents	☐			
Verify that segments are removed from RBC bag before weight measurement was taken	☐			
Automated Hematology Analyzer				
QC performed with passing results	☐			
Review maintenance/PM stickers	☐			
Check reagents	☐			
Perform electronic & mechanical checks	☐			
Clean instrument/check waste	☐			
Troubleshoot equipment as necessary	☐			
Document maintenance performed	☐			
Collections Equipment				
[Region Defined]	☐			

Individual Product Quality Control Failure

Product Safety and Risk Evaluation – Product Disposition

- Released as non-standard product code
- Released as another product type
- Released through the Material Review Board process – medical exceptions
- Discarded

Conducting a QC Failure Investigation

Investigation

When a monthly QC failure occurs, actions include:

- Review of the individual product failure checklist(s)
- Look at historical results
- Look at previous failures

Conducting a QC Failure Investigation

Investigation (cont'd.)

- Critical components of the process
  - Procedures
  - Equipment
  - Supplies
- Observe staff
- Other – environmental/facility

Conducting a QC Failure Investigation

Investigation Evaluation

- Information gathering
  - Data
  - Observations and interviews
  - Brainstorming, etc.
- Root cause / failure mode analysis
- Isolated vs. process failures

Actions Outside of the Investigation

Product Safety and Risk Evaluation

- Impact to the individual product only
- Scope of impact to time and product type
- Potential risk to a potential recipient

Actions Outside of the Investigation

Regulatory Actions

- Blood Product Deviation Report
- Recall of product(s)
- Limit or cease production
- Other reporting requirements...

Concluding a QC Failure Investigation

Investigation Documentation

- Must stand on its own
  - Over time
  - Independent of audience
  - Be clear and concise
- Must include key information
  - What happened
  - What actions were taken
  - Why
- Follow-up with outcomes of actions

Concluding a QC Failure Investigation

Effectiveness Check

- Perform additional testing if changes are made to process, procedure or training
- Review by the Quality Assurance Department and Medical Director for impact
- Reinstate routine QC testing
- Ensure standard operating procedures are revised to reflect any changes, if applicable

Concluding a QC Failure Investigation

What Happens When You Can Not Determine the Cause…

?

Concluding a QC Failure Investigation

When is testing of additional samples needed…

- Gather additional data
- To confirm actions taken are effective

Product Quality Communications

Communication

- For Failures:
  - To affected staff - change or enhancement in a process, procedure, or training
  - To affected staff - discuss investigations of failed product QC
  - Supplier, customer (as applicable) – discuss failure investigation and outcome
  - To FDA as appropriate
- For Routine Product QC Outcomes
  - Internally and externally- share information regarding product quality data
  - Discuss potential process improvement opportunities

QC Testing Challenges

- Sampling Criteria and Random Sampling – representative sampling
- Timing constraints
- Requirements carried over from one product type or technology to another

Tracking	**Reviews and Documentation**	**Ongoing Monitoring**	**Investigation**
Corrective Actions	**Clear Procedures**	**Responsibility Accountability**	**Communication**
Standardized Failure Investigation	**Product Safety**	**Effectiveness Check**	**Regulatory Actions**