Product Deviations

January 28, 2009
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Programs may use different terms in their SOPs, which is acceptable as long as the intent of FACT Standards are fulfilled.
8 Requirements for Product Deviations

- Detection
- Evaluation
- Investigation
- Documentation
- Reporting
- Follow-up Activities
  - Long-term Corrective Action
  - Short-term Corrective Action

Deviations
Incident Report

• Useful for:
  – Ensuring each required activity is completed
  – Documenting each step
  – Review by Director and QM committees
  – Preparing for FACT inspections
  – Trending purposes

• Can be simple and contain steps for all types of product deviations or can be specific for a specific type of deviation
UAB HOSPITAL
Bone Marrow Transplantation & Cell Therapy Program
Complaint/Adverse Event /Variance Form

______Variance: Planned _____Yes _____No

___Adverse Event ___Complaint ___Clinical ___Collection ___Processing

Date of Event __________________________ Patient Name: __________________________

Event:
________________________________________
________________________________________

Action:
________________________________________
________________________________________

Resolution: To Be Completed by BMT Program Leadership
________________________________________
________________________________________

Collection and Processing Facility Director __________________________ Date ______
Clinical and Collection Medical Director __________________________ Date ______
Program Director and Processing Medical Director __________________________ Date ______
UAB HOSPITAL
Bone Marrow Transplantation & Cell Therapy Program
Complaint/Adverse Event /Variance Form

Yes  ☑️  Variance: Planned  _____  No  _____  Adverse Event  ____  Complaint  ☑️  Clinical  ____  Collection  ____  Processing

Date of Event  1/01/01  Patient Name:  Cure, I. Wanna

Event:

Patient started on metronidazole for C. diff + stool during busulfan by on-call fellow. Busulfan levels returned high secondary to drug-drug interaction.

Action:

Patient informed. Physician recommended additional set of busulfan levels for drug monitoring/adjustment. Additional modifications and levels were required.

Resolution: To Be Completed by BMT Program Leadership

Patient out-come to be determined. Chemo protocols and nursing standards will be modified to include an order requiring Attending approval for non-standard drugs during chemo.
Variances

• **Planned** deviations from recommended practices or Standard Operating Procedures (SOPs).
• Must be pre-approved by the applicable Director.
• Example: A Clinical Program’s SOP requires that products must have TNC that equals the collection goals of the transplant physician. The transplant physician plans to proceed with administering a product with less than the TNC goal.
**Detect**
- Order Processing Facility to compare TNC to collection goals

**Investigate**
- Confirm any issues with donor or collection procedure

**Evaluate**
- Determine if benefits of the product outweigh the risk

**Document**
- Urgent Medical Need in recipient’s chart and product record
- Incident Report

**Report**
- Clinical Program Director
- Collection Facility Director
- QM Committee

**Short-term Action**
- Confirm Urgent Medical Need documentation
- Administer the product

**Long-term Action**
- Review donor criteria and/or collection goals

**Follow-Up**
- Conduct recipient outcome analysis
- Audit collection procedure
Errors and Accidents

• Unforeseen or unexpected deviations from applicable laws and regulations, established Standards, or specifications that may affect the safety, purity, or potency of a product.
• Must be reviewed (along with associated corrective actions) by the Director.
• Example: The Processing Facility freezer alarm sounded and personnel found the temperature to be outside of acceptable temperature range.
Errors and Accidents

Detect
- Audible alarm system

Investigate
- Low liquid nitrogen level

Evaluate
- Need to move products to functioning freezer to maintain temperature
- Determine products’ temperatures are acceptable

Document
- Product records
- Incident Report

Report
- Processing Facility Director
- QM Committee

Short-term Action
- Move products to back-up freezer
- Replenish liquid nitrogen

Long-term Action
- Adjust delivery schedule of liquid nitrogen

Follow-Up
- Audit delivery schedule
Adverse Events

- Any unintended or unfavorable sign, symptom, abnormality, or condition temporally associated with an intervention that may or may not have a causal relationship with the intervention, treatment, or procedure.
- Adverse reactions are a type of adverse event; however, programs are required to take action before this may be confirmed.
- Must be documented and reported.
- Example: A donor undergoing an apheresis procedure begins to have shortness of breath, chest pain, drop in blood pressure, and changes in mental status.
UAB HOSPITAL
Bone Marrow Transplantation & Cell Therapy Program
Complaint/Adverse Event /Variance Form

Variance: Planned _____ Yes _____ No

√ Adverse Event ___ Complaint ___ Clinical ___ Collection ___ Processing

Date of Event ___1/01/01______ Patient Name: ______ Help, I. Wanna______

Event:

Auto donor developed acute SOB, chest pain, hypotension and AMS during collection. Apheresis terminated. Patient found to have tension pneumothorax from line placement. Emergency Medical Team called and donor stabilized.

Action:

Chart reviewed. Appropriate pre-pheresis donor evaluation performed, signed consent (consent specifically mentioned risk of pneumothorax), and time out documented. Line placed without initial complications by IR under flouroscopy with review of post placement film documented. Risk management notified and donor and donor family aware.

Interventional Radiology Informed of line placement complication.

Resolution: To Be Completed by BMT Program Leadership

Personnel performance evaluated and found to be satisfactory. At next clinical practice meeting will review with team the incident and re-enforce adherence to SOP’s. Donor doing well.
# Adverse Events

<table>
<thead>
<tr>
<th>Step</th>
<th>Tasks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Detect</strong></td>
<td>Adequate collection personnel for supervision of donors</td>
</tr>
<tr>
<td><strong>Investigate</strong></td>
<td>List of symptoms and causes in Adverse Event SOP</td>
</tr>
<tr>
<td></td>
<td>Risk Management department analysis of kit and machine</td>
</tr>
<tr>
<td><strong>Evaluate</strong></td>
<td>Medical Director review of symptoms and donor’s chart</td>
</tr>
<tr>
<td><strong>Document</strong></td>
<td>Donor and recipient charts</td>
</tr>
<tr>
<td></td>
<td>Product record</td>
</tr>
<tr>
<td></td>
<td>Incident Report</td>
</tr>
<tr>
<td><strong>Report</strong></td>
<td>Donor’s and recipient’s physicians</td>
</tr>
<tr>
<td></td>
<td>Processing Facility</td>
</tr>
<tr>
<td></td>
<td>QM Committee</td>
</tr>
<tr>
<td><strong>Short-term Action</strong></td>
<td>Stop collection procedure</td>
</tr>
<tr>
<td></td>
<td>Stabilize donor</td>
</tr>
<tr>
<td><strong>Long-term Action</strong></td>
<td>Personnel training and competency</td>
</tr>
<tr>
<td><strong>Follow-Up</strong></td>
<td>Donor health outcomes</td>
</tr>
<tr>
<td></td>
<td>Audit of collection procedure</td>
</tr>
</tbody>
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Biological Product Deviations

• A deviation from applicable regulations, standards, or established specifications that relate to the prevention of communicable disease transmission or cellular therapy product contamination; or an unexpected or unforeseeable event that may relate to the transmission or potential transmission of a communicable disease or may lead to cellular therapy product contamination.

• United States FDA definition; involves communicable diseases

• Example: A contracted testing laboratory that provides IDM testing changed test kits and did not notify the Processing Facility of the change. The testing laboratory incorrectly thought approved IDM testing for blood donors and for diagnostic testing was acceptable for HPC/TC donors.
Biological Product Deviations

**Detect**
- Audit of contracted testing laboratory

**Investigate**
- Reason for use of inappropriate assay

**Evaluate**
- Determine which products were tested with inappropriate assay

**Document**
- Product record
- Incident report

**Report**
- FDA for distributed products
- Recipient’s physician
- QM Committee

**Short-term Action**
- Retest affected products with appropriate assay
- Update product records

**Long-term Action**
- Revise testing specifications to include cleared test kits

**Follow-Up**
- Re-audit of contracted testing laboratory
- Recipient outcome analysis

More information provided by the ISCT North America Legal and Regulatory Affairs Committee:
Complaints

- Any written, oral, or electronic communication about a problem associated with a product or with a service related to the collection, processing, storage, distribution, or infusion of a cellular therapy product.
- FDA requirements in 21 CFR 1271.320
- Example: Cord blood collection kit contained collection bags that were difficult to seal.
## Complaints

### Detect
- Provision of contact information within collection kit

### Investigate
- Defects in construction of collection bags

### Evaluate
- Determine that complaint is not reportable under 21 CFR 1271.320
- Identify kits with bags from the same lot as kit in question

### Document
- Complaint file (required by FDA)
- Incident Report
- Unit records for cord blood already collected with the bags

### Report
- Manufacturer of materials

### Short-term Action
- Send new kits with bags from a different lot to collection sites that were given faulty bags

### Long-term Action
- Remove affected lot from inventory

### Follow-Up
- Obtain certificate of analysis from manufacturer or choose new manufacturer
Example Method of Inspection

1. Ask for record for a product with microbial contamination.
2. Confirm documentation of sterility testing (detection).
3. Review documentation of the cause (investigation).
4. Review notes in donor and recipient charts and product records (evaluation).
5. Review documentation in product record, labels, and patient charts and of Urgent Medical Need (documentation).
6. Review written notification to recipient and recipient’s physician (as appropriate), FDA Form 3486, and donor’s physician and Collection and Processing Facilities as applicable (reporting).
7. Review documentation of corrective actions (short-term and long-term corrective actions).
8. Review evaluation of corrective actions, donor follow-up (if applicable), and recipient outcome analysis (follow-up).
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