Error Management and BPD Reporting for the Transfusion Service

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Objectives

• Define biological product deviation
• Explain what constitutes a BPD (and what does not)
• Describe how BPDs should be reported to the FDA
To Error is Human
To Forgive Divine

Alexander Pope
(1688-1744)
Discovery

Events may be discovered as the result of:

- Record Review
- Staff Observation
- Task Performance
- QA Audits
- External Audits
- Customer complaints
7 Steps of the Deviation/Error Management Process

1. Discovery
2. Document
3. Immediate Correction
4. Investigate (Reportable: Yes/NO)
5. Causal Analysis
6. Corrective Action
7. Effectiveness Evaluation
Do You Know to Who and What to Report?
Error Reporting

• Hospitals have internal policies to track, trend and report adverse events.

• *Required:*
  - FDA
  - OSHA

• *Voluntary*
  - Sentinel Event reporting for The Joint Commission
  - AABB if accredited
Reporting Adverse Events to the FDA

• Historically hospitals have reported fatalities due to Blood Transfusions
• Reasons for fatality
  • Mix-ups in samples resulting in ABO mismatch
  • Mix-up in identification process at time of transfusion
  • Technical error in the transfusion service
• Expanded reporting requirements in 2001
FDA Reported Fatalities: 2009 to 2013

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Effective 5/7/01 – 21CFR 606.171

• Requires reporting by all unlicensed blood establishments, including transfusion services and registered blood banks;
• Replaces “error and accident” with “biological product deviation”, includes near miss events;
• More clearly describes the types of events that must be reported
Effective 5/7/01 – 21CFR 606.171

- Limits reporting to those events that may affect the safety, purity, or potency of distributed products
- Establishes a reporting time frame of 45 days from the date the event was discovered
Who Must Report? 21 CFR 606.171(a)

- Licensed manufacturer of blood and blood components, including Source Plasma
- Unlicensed registered blood establishment
- Transfusion service

The manufacturer who had control over the product when the deviation or unexpected event occurred.
What Do I Report? 21 CFR 606.171(b)

• You must report any event associated with manufacturing of both licensed and unlicensed blood or blood components that

  Either:
  – Represents a deviation from CGMP, regulations, standards, or specifications that may affect safety, purity, or potency; or
  – Represents an unexpected or unforeseeable event that may affect the safety, purity, or potency; and

  Occurs in your facility or a facility under contract to you; and

  Involves a distributed biological product
But I Don’t Manufacture Products!!!!!!

Manufacture 21CFR607.3(d)

- The collection, preparation, processing, or **compatibility testing** or other procedures of any blood product that meets the definition of a drug and including manipulation, sampling, testing or control procedures applied to the final product
What Do I Report? 21 CFR 606.171(b)

Events pertaining to distributed products
- Left control of the blood bank
- Greatest risk to patients
- Potential for harm

- Deviation from cGMPs
  - Testing
  - Storage
- Deviations from SOPs
- Affect Safety, Purity, Potency, or Identity of the Product
  - Ex: Patient sample used for compatibility testing was collected from the wrong patient
Not Reportable

- A unit released from the BB for transfusion and not maintained at the appropriate temperature outside of BB before transfusion
- Physician/Nursing Staff transfuses the wrong patient (misidentification) or transfuses the wrong unit

Not Considered Manufacturing
Not Reportable

- No affected products are distributed
- It is determined prior to distribution that the safety, purity, or potency of the product was not affected
- An event is detected and appropriately corrected prior to distribution (near miss)
- An event is not reported to FDA within 45 days

BUT
These events should be investigated as part of your error management system
When Do I Report? 21 CFR 606.171(c)

- Report as soon as possible
- Must report within 45-calendar days from date of discovery
How Do I Report? 21 CFR 606.171(d)

Form FDA-3486

Biological Product Deviation Report Form
Where Do I Report? 21 CFR 606.171(e)

- Electronically
  eBPDR System
  www.fda.gov/cber/biodev/biodev.htm
  - Use FDA registration number
  - If not registered, use CLIA number
Where Do I Report? 21 CFR 606.171(e)

• By Mail

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Avenue
WO71-G112
Silver Spring, MD 20993-0002
FDA BPD Reporting Trivia

- FDA estimated reporting would be:
  6 To 299 beds - 0/BPDRs / hospital/ year
  300 to 500+ beds - 1/BPDRs / hospital/ year
- Reality (2013)
  664 hospitals reporting 2062 BPDRs
- 11.4% of all US hospitals report
  501 of 5810
Examples By System

• Testing
• Labeling
• Quality Control and Distribution
Biological Product Deviations

**REPORTABLE TESTING**

- Testing not performed in accordance with SOP
  - Incorrect incubation time or temperature
  - Incorrect reagent used/using reagents from different lots
  - Incorrect addition of reagents
  - Two drops of reagent when manufacturer says one drop
- Expired reagents used for testing
- Unsuitable sample used for testing
  - Sample improperly stored
  - Sample diluted
  - Sample not identified appropriately to relate back to patient
Biological Product Deviations

**NON-REPORTABLE**

**TESTING**

- A clerical error if there is other information to indicate that testing was performed appropriately
- Expired reagent used - if rare and no other reagent is available
Biological Product Deviations

**REPORTABLE**

**LABELING**

- Product labeled with incorrect ABO, Rh, antigen, antibody, product type, unit number, volume, weight
- Information missing: ABO, Rh, product type, expiration date, unit number, volume, weight
- Unit labeled with extended expiration date
- Additional information on autologous unit missing or incorrect
- SOP’s for labeling not followed or inadequate
  - Unit labeled with incorrect information regarding leukoreduction, irradiation or washing
  - Unit not labeled with biohazard when indicated
Biological Product Deviations

NON-REPORTABLE

LABELING

• Unit labeled with shortened expiration date
Biological Product Deviations

REPORTABLE

QUALITY CONTROL AND DISTRIBUTION

• Unsuitable unit distributed
  – Clotted unit or segment
  – Hemolyzed unit or segment
  – Outdated unit
  – Unit shipped or stored at incorrect temperature

• Failure to quarantine due to:
  – Incorrect or incomplete testing
  – Testing not performed or not documented
Biological Product Deviations

REPORTABLE

QUALITY CONTROL AND DISTRIBUTION

• Transfusion service received an order requiring special processing or testing and fails to meet that requirement
  – CMV negative
  – Leukoreduced
  – Irradiated
• Wrong unit issued for patient
• Improper ABO or Rh selected for patient
• SOP’s for quality control or distribution not followed or inadequate
Biological Product Deviations

NON-REPORTABLE

QUALITY CONTROL AND DISTRIBUTION

• Discrepancy between shipping form and shipment
• Unit shipped to incorrect facility
• Unit lost or shipment never received
• Disposition unknown
• Frozen product breaks during thawing and the product is discarded
• Product breaks or is damaged during shipment and the product is discarded
• Unit returned to blood bank, determined to be unsuitable and discarded (e.g., out of temperature range)
• Otherwise unsuitable unit released in accordance with emergency release procedures
Do You Know What to Report?
Scenario 1

Phlebotomist collected sample and didn’t initial the labels. Unit of blood crossmatched and transfused. Missing label information discovered second day when 2\textsuperscript{nd} unit being crossmatched. Phlebotomist was off that day and initialed label when he returned on day four after the second unit was transfused. No untoward affect for the patient.
Routine Testing
Sample ID; Sample used for testing was incorrectly or incompletely labeled.
Scenario 2

Daily QC performed on expired antisera for 3 days and lot numbers (A1, B, Screening cells I & II) and expiration dates recorded as no change (NC). QC was within range. All serological testing for three days used these reagents and units were transfused.
Routine Testing

Testing performed using reagents in which QC was unacceptable or not performed, or expired reagents were used.
Scenario 3

A unit of red blood cells was requested and issued for patient, B.S. When the nurses performed the bedside check with the patient and the unit, they discovered a problem. They had intended to transfuse LS but had requested blood for BS.
The unit was issued correctly by the Transfusion Service, since the patient care area had requested blood for patient BS.
Scenario 4

Two patient BB ID's were on a unit of blood that was dispensed. Patient #1 was crossmatched and didn’t get the unit and it was returned to inventory. The ID wasn’t removed and it was crossmatched for Patient #2. Double tag was not discovered until nursing was checking identification at patient bedside. It was returned to the blood bank.
ANSWER

YES

Labeling
Crossmatch tag or tie tag incorrect or missing information; recipient identification incorrect or missing.
Scenario 5

A unit of blood was issued to the nursing floor. The BB order had indicated that the patient needed CMV negative, irradiated blood. The units were returned, neither unit was CMV negative nor irradiated.
Quality Control and Distribution
Distribution procedure not performed in accordance with BB transfusion service specifications; product not irradiated and CMV negative as required.
Scenario 6

A unit of red blood cells was returned to the Blood Bank from the patient care area. The temperature was taken and read 15C.
The error occurred when the unit was on the patient care area and was no longer under the control of the Blood Bank.
Scenario 7

6 units of RBC’s and a platelet pheresis were issued to the OR. The technician dispensed the RBC’s but forgot to dispense the platelets in the LIS system. The mistake was discovered when the unused RBC’s and platelet pheresis were returned from the OR to the Blood Bank.
Quality Control and Distribution

Distribution procedure not performed in accordance to BB transfusion service’s specifications; product not documented or incorrectly documented as issued in the computer.
Scenario 8

- A patient’s antibody screen was negative.
- Doctor ordered a DAT, which was positive.
- The technologist did not request a transfusion history, since antibody screen was negative.
- The patient transfused a few days earlier at another hospital.
- An elution was not ordered.
Scenario 8 cont’d...

• Doctor ordered a unit of RBC’s, it was transfused.
• Patient had a transfusion reaction.
• An elution ordered on the pre- and post-transfusion samples, since DAT was positive on both samples.
• Anti-Jka was detected in both eluates.
ANSWER

YES

Quality Control and Distribution
Testing not performed, incompletely performed or not documented for antibody screen or identification.
Scenario 9

A patient was discharged from the hospital, but returned to the ER the next day. A T&XM was ordered. The BB tech added on two units of RBC’s using a blood bank sample from the previous admission which had not expired. The patient’s armband was still on from the previous admission.
Quality Control and Distribution
Distribution procedure not performed in accordance with blood bank transfusion service’s specifications: product released before obtaining current sample for ABO,RH, antibody screen and/or compatibility testing
Scenario 10

You are a transfusion service that received a unit of Red Blood Cells from your blood supplier. You crossmatched the unit for a patient and issued it to the floor for transfusion. A few minutes later the nurse called to report the unit was clotted.
ANSWER

YES

Quality Control and Distribution
You are required to report for failing to follow your SOP, which would have detected the clotted unit.
Survey Results

- Scenarios sent to 176 participants.
- Compiled from actual past experiences.
- Individuals worked in hospitals from 100 to 500+ beds and blood centers collecting 500 to 5,000 donation/mo.
- 5.7% (10 of 176) got all scenarios correct.
  - No knowledge advantage for subset taking survey.
Lessons To Learn

Evaluate every error as a potential biological product deviation

Even if it isn’t a BPD, investigate and learn from near misses
Questions to Ponder

When determining if an event is a BPDR:

1. Is there a specific regulation or violation of your own SOP that applies to the action?
2. Did the product leave your control?
3. Was it a pre-approved deviation by the Medical Director?
When in doubt…

• How to contact FDA/CBER for questions regarding reportability?
• bp_deviations@cber.fda.gov
Thank you!!!

Questions…
References

• Guidance for Industry: Biological Product Deviation Reporting for Blood and Plasma Establishments, Food and Drug Administration October 2006

• R Lamb, B.J. Bryant: Knowledge of food and drug administration reportable deviations: Transfusion Vol 51, No 7, Part II, pg 1619-23, July 2011.