Washington State Department of Health
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Blood Bank/Transfusion Product Deviation Reports

The Food and Drug Administration (FDA) published guidance to assist blood and plasma establishments with identifying and submitting Blood and plasma Product Deviations (BPD).

This publication guides the site in determining:
- when a report is required
- who should submit the report
- what information to submit in the report
- when to submit the report,
- how to submit the report

This article discusses scenarios that may occur in a Transfusion Services site. For detailed information about transfusion services, donor collection and donor testing, please see the full guidance.

(Please Note: This revised guidance explains that the FDA does not consider post-donation information events to require BPD reports.) [1]

For more information, please refer to the complete guidance at: FDA guidance

WHEN IS A REPORT REQUIRED?

Under 21 CFR 606.7, you must report certain events associated with the following that may affect the safety, purity or potency of a distributed blood or blood component:
- manufacturing (including testing, processing, packing and labeling)
- storage
- holding or distribution

Safety, purity, and potency are defined in 21 CFR 600.3(p), (r), and (s), respectively as follows:
- "The word safety means the relative freedom from harmful effect to persons affected, directly or indirectly, by a product when prudently administered, taking into consideration the character of the product in relation to the condition of the recipient at the time."
- "Purity means relative freedom from extraneous matter in the finished product, whether or not harmful to the recipient or deleterious to the product. Purity includes but is not limited to relative freedom from residual moisture or other volatile substances and pyrogenic substances."
- "The word potency is interpreted to mean the specific ability or capacity of the product, as indicated by appropriate laboratory tests or by adequately controlled clinical data obtained through the administration of the product in the manner intended, to effect a given result." Code of Federal Regulations, 4/2020. [2]

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Practice Guidelines

The following practice guidelines have been developed by the Clinical Laboratory Advisory Council. They can be accessed at the LQA website.

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Bleeding Disorders
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Diabetes
Group A Strep Pharyngitis
Group B Streptococcus
Hepatitis
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Intestinal Parasites
Lipid Screening
PAP Smear Referral
Point-of-Care Testing
PSA
Rash Illness
Red Cell Transfusion
Renal Disease
STD
Thyroid
Tuberculosis
Urinalysis
Wellness

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WHO MUST REPORT A BIOLOGICAL PRODUCT DEVIATION (BPD)?

Individuals or establishments with "responsibility for maintaining the continued safety, purity and potency of the product and for compliance with applicable product and establishment standards, and for compliance with current good manufacturing practices." FDA Guidance [3]

WHAT INFORMATION DO I REPORT TO THE FDA?

Under 21 CFR 606.171(b), you must report any event, and information about the event, associated with the manufacturing, including testing, processing, packing, labeling, or storage. You must also report any event associated with the holding or distribution, of both licensed and unlicensed blood or blood components, including Source Plasma, if that event meets all the following criteria:

(1) Either:

- Represents a deviation from CGMP, applicable regulations, applicable standards, or established specifications that may affect the safety, purity, or potency of that product,
- Represents an unexpected or unforeseeable event that may affect the safety, purity, or potency of that product,

(2) occurs in your facility or a facility under contract with you,
(3) involves distributed blood or blood components. FDA guidance [3]

WHEN DO I SUBMIT A REPORT?

Under 21 CFR 606.171(c), you should report a BPD as soon as possible, but you must report at a date not to exceed 45 calendar days from the date of acquiring information that reasonably suggests a reportable event has occurred. To simplify reporting, the FDA has developed a standardized reporting format that you may submit electronically or in paper form, by mail. FDA guidance [3]

HOW AND WHERE DO I SUBMIT A REPORT?

Under 21 CFR 606.171(d), you must use Form FDA-3486 to report BPDs. You must submit the completed report either electronically through CBER's web site or by mail to:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Avenue
Silver Spring, Maryland 20993-0002 [3]

Note: Use the FDA's list of BPD Codes to assign a specific code to a reportable event when you submit the report to FDA. [4]

The FDA has listed the following examples of reportable and non-reportable events (please see the full guidance for additional examples and information) [3]:

1) TESTING

Testing events include those that occur during the testing process that you did not discover until after you distributed the product. Testing includes all tests to assure the safety, purity, and potency (e.g., testing requirements in 21 CFR 610.40, 640.5, and 606.151). Using unsuitable or inappropriate samples may be testing deviations or unexpected events.

Under 21 CFR 606.171(b), you must submit a report when there is an event (a deviation or unexpected or unforeseeable event) during testing that may affect a **distributed** product's safety, purity, or potency.

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REPORT TO FDA:
When testing was not performed according to the test manufacturer's instructions, such as:

- An incorrect incubation time or temperature was used,
- An incorrect reagent was used/licensable components from two different test kit lots were used,
- The incorrect addition of reagents (incorrect sequence, volume, or concentration).
- Testing was incomplete, not performed, or not documented.
- The sample wasn't tested according to the manufacturer's package insert (e.g., repeated testing until you obtained a negative result).
- Test results were inappropriately invalidated.
- The sample did not meet the specifications for the testing used, such as a sample that was improperly stored,
- The sample was labeled with the wrong donor or patient identifier.
- Testing was performed using a reagent or test kit in which QC was unacceptable or not documented. This may include situations in which QC testing was not performed or was not documented on one day, even if the QC testing the day before and the day after was acceptable.
- Testing was performed using expired reagents.
- Patient samples were mislabeled or collected from the wrong patient and were used to perform pretransfusion testing and a product was distributed based on that testing. This may include samples collected by transfusion service personnel and personnel outside of the blood establishment.
- Patient typing results or compatibility testing results were misinterpreted, and a product was distributed based on that testing.
- Antibody screen or identification testing on the recipient, as set forth in your procedures, was not performed or was incomplete before the distribution of the product.
- Product with no historical antigen typing was not tested for an antigen that corresponds to the patient's antibody, as set forth in your procedures.
- Immediate spin crossmatch was performed when a patient's history or testing results indicated that an indirect antiglobulin test was needed.

DO NOT REPORT:

- You appropriately invalidated the assay results and retested samples and they tested negative before the product was distributed.

2) QUALITY CONTROL (QC)

Under 21 CFR 606.171(b), you must submit a report when

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there is an event (a deviation or unexpected or unforeseeable event) during or related to QC procedures or in the quarantine and distribution process that may affect the safety, purity, or potency of a product you distributed.

REPORT TO FDA:

- A product distributed after it was processed using an instrument or reagent for which QC was unacceptable, not documented or not performed. For example:
- No documentation that weekly QC was performed, even if daily QC tasks were performed and documented;
- No documentation of daily QC of trip scales used to weigh whole blood collections, unless the product was weighed before distribution and found acceptable.

DO NOT REPORT:

- There was no documentation of instrument or reagent QC if data from another source showed the instrument or reagent was acceptable.

3) DISTRIBUTION

REPORT TO FDA:

- The distribution of a product in which QC testing was unacceptable, not performed, not documented, or incomplete. For example:
- pH (monthly QC of platelets).
- Platelet count.
- Inappropriate release from quarantine, and distribution of, a product that was identified as not meeting specifications due to a deviation or unexpected event in donor eligibility, collection, component preparation, testing, or labeling. For example:
- Failure to quarantine and distribution of a unit collected from a donor that was determined to be ineligible due to unacceptable donor medical history;
- Failure to quarantine and distribution of a unit/component that was overweight or underweight;
- Failure to quarantine and distribution of a component prepared from a whole blood unit, in which one of the components was clotted or hemolyzed.
- The product was released from electronic or physical quarantine and distributed before determining whether the product was suitable for distribution.
- The distribution of a product before resolving a discrepancy in manufacturing, such as testing, labeling, or donor eligibility.
- The inappropriate distribution of a unit with a positive test result.
- The distribution of an outdated product.
- Events associated with the storage or shipment of the product, for example: - The product was not shipped at the appropriate temperature (e.g., the product was

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packed without ice for shipment).
- The product was not stored at the appropriate temperature prior to distribution.
- No documentation that the product was stored at the appropriate temperature, including reissuance of the product without a record of proper temperature maintenance.
- Visual inspection was not performed or documented before distribution.
- Incorrect product or unit issued for a specific patient (unless the transfusion service notified the hospital staff that the product ordered was unavailable and that the transfusion service was providing a substitute.)
- Special processing or testing was requested, such as leukoreduced, irradiated, cytomegalovirus (CMV) negative, but the product didn't meet the specifications
- The product issued was designated for a different patient
- Incorrect product type issued, such as platelets instead of fresh frozen plasma
- A product with the improper ABO or Rh type was selected for a patient.
- A visual check of the product was not performed or not documented prior to distribution.
- The product was received from a blood establishment, accepted into the transfusion service's inventory and subsequently discovered to be hemolyzed after distribution.

DO NOT REPORT:
- If the transfusion service issued a product from the laboratory to the nursing floor, operating room, emergency room, etc., for transfusion and the product was not held at the appropriate temperature outside of the transfusion service before transfusion. However, the transfusion service must report if the product was returned and the transfusion service reissued the product despite determining it to be unsuitable.
- If the hospital staff, outside of the transfusion service, transfused the wrong patient or transfused a patient with the wrong unit, provided the unit was labeled appropriately and the transfusion service conducted compatibility testing properly. If a transfusion complication was confirmed to be fatal, the facility that performed the compatibility testing must submit a fatality report to us in accordance with 21 CFR 606.170(b).
- If the transfusion service issued a filter with the product and the hospital staff did not use the filter at the bedside.
- If the patient has a transfusion reaction unrelated to an event in manufacturing. Fatalities due to Transfusion Related Acute Lung Injury (TRALI) or other transfusion complications must be reported to CBER in accordance with 21 CFR 606.170(b). We also accept voluntary reports of non-fatal TRALI as a serious adverse reaction to transfusions. You can submit a voluntary report via MedWatch. For additional information related to TRALI and biologics safety, see the "Dear Colleague" letter published October 19, 2001.
- The product was shipped to the incorrect facility.
- The product is properly labeled but the shipping invoice differs from the actual shipment.
- The frozen product (e.g., fresh frozen plasma) container broke during thawing and the product was discarded.
- The product broke or was damaged during shipment and the product was discarded.*
- A segment was clotted or hemolyzed, but the product was subsequently evaluated for clots or hemolysis and found acceptable.
- Small residual clots were found in the filter after the product was completely transfused, unless you did not adequately evaluate the unit for clots before issuing unit for transfusion.
- No documentation of instrument or reagent QC if there was data from another source that showed the instrument or reagent was acceptable.

*Broken or damaged products are rarely identified as system problems in manufacturing and are generally tied to an unusual event in the shipment.

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REFERENCES

1. **Biological Product Deviation Reporting for Blood and Plasma Establishments Guidance for Industry March 2020**.

2. **Electronic Code of Federal Regulations April 22, 2020**.

3. **Biological Product Deviation Reporting for Blood and Plasma Establishments
Guidance for Industry U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research, March 2020**.

4. **FDA: Biological Product Deviation Reporting and HCT/P Deviation Reporting Deviation Codes**.

Calendar of Events

Training Classes:

2022 NWMLS
October 12-14
(VIRTUAL)

2022 Clinical Laboratory Conference
November (date TBD)

Contact information for the events listed above can be found on page 2. The Calendar of Events is a list of upcoming conferences, deadlines, and other dates of interest to the clinical laboratory community. If you have events that you would like to have included, please mail them to ELABORATIONS at the address on page 2. Information must be received at least one month before the scheduled event. The editor reserves the right to make final decisions on inclusion.

Washington State Department of Health

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For persons with disabilities, this document is available upon request in other formats. To submit a request, please call 1-800-525-0127 (TTY/TDD 1-800-833-6388).

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