**TRAINING UPDATE**

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|---|---|---|---|
| **Lab Location:** | SGAH and WAH | **Date Implemented:** | 3.28.2014 |
| **Department:** | Blood Bank | **Due Date:** | 4.15.2014 |

**DESCRIPTION OF PROCEDURE REVISION**

## Name of procedure:

Biological Product Deviation Reporting—FDA Reportable Event

## Description of change(s):

- CQA revised this corporate procedure.
- Major changes have to do with the way in which the responses are written and approved.
- For your purposes, understand what types of events are reportable and the process that must be taken when an FDA-reportable event is identified.

Non-Technical SOP

| | |
|---|---|
| **Title** | **Biological Product Deviation Reporting –FDA Reportable Event** |
| **Prepared by** | Hospital Transfusion Services Working Group **Date: March 6, 2014** |

| **Laboratory Approval** | **Effective Date:** | |
|---|---|---|
| **Print Name and Title** | **Signature** | **Date** |
| **Laboratory Director** | | |
| | | |
| | | |
| | | |

| **Review** | | |
|---|---|---|
| **Print Name and Title** | **Signature** | **Date** |
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| **Corporate Approval** | **Corporate Issue Date:** March 6,2014 | |
|---|---|---|
| **Print Name and Title** | **Signature** | **Date** |
| Jill Hittinger, MT(ASCP), CQA(ASQ) **Owner** | *Approval on file* | **February 11, 2014** |
| Lee Hilborne, M.D., MPH **BPT Medical Advisor** | *Approval on file* | **February 11, 2014** |

| | |
|---|---|
| **Retirement Date:** | |
| **Reason for retirement/replacement:** | |

## TABLE OF CONTENTS



## 1. PURPOSE

This document sets forth the process for recognition, classification, and reporting of biological product deviations, as prescribed by 21 CFR 606.171, for all Quest Diagnostics manufacturing and/or transfusion service departments. This process will ensure timely investigation of exceptions in service and FDA notification of subsequent corrective actions, as described in 21 CFR 606.100, 211.192, and 211.198. This process describes specific activities related to the filing of reportable events with the FDA and is to be used in concert with the corporate reportable quality issue SOP that describes internal notification, investigation, root cause analysis, corrective actions, and preventive actions.

## 2. SCOPE

This process applies to all Quest Diagnostics hospital laboratories that are staffed with Quest Diagnostics employees and that offer donor or transfusion services.

## 3. RESPONSIBILITY

| Responsible Party | Task |
|---|---|
| **Laboratory Director** | • Approves the initial document and revisions.<br>• Ensures that nonconforming events (Biological Product Deviations or BPDs) are investigated and corrected when encountered.<br>• Ensures that Biological Product Deviations are appropriately reported to the FDA. |
| **Laboratory Operations Director or Manager** | • Ensures implementation of this Standard Operating Procedure (SOP)<br>• Communicates the SOP to relevant laboratory areas. |

| Responsible Party | Task |
|---|---|
| **Manager/ Supervisor** | • Implements and maintains this SOP as part of local procedure manuals.<br>• Ensures applicable training and competency.<br>• Ensures departmental compliance with this process.<br>• Participates in the investigation and correction of nonconforming events.<br>• Completes the RQI and FDA Reportable Event documents in conjunction with the Quality Assurance Personnel. |
| **Testing Personnel** | • Comply with procedure.<br>• Report nonconforming events immediately.<br>• Participate in the investigation and correction of nonconforming events. |
| **Quality Assurance Personnel** | • Ensure the completion of the RQI and FDA Reportable Event documents.<br>• Facilitate in the investigation and correction of nonconforming events.<br>• Monitor the effectiveness of the corrective action implemented.<br>• Submit the RQI to DGX RQI and FDA Reportable Event Form to the FDA. |

## 4. DEFINITIONS

**Accident:** an event that is not expected, foreseen, or intended.

**Adverse event:** any complication experienced by a donor or patient. Adverse events may occur in relation to blood donation, transfusion, diagnostic procedures, or therapeutic procedures.

**Biological Product Deviation (BPD):** an event that could affect the safety, purity, or potency of a biological product. It may represent a deviation from current "good manufacturing practices", applicable regulations, applicable standards, or established specifications, or it may be unforeseen and unexpected.

**Blood Bank:** a facility that performs any of the following: collection, processing, storage, and distribution of human blood and/or components that is intended for transfusion or transplantation.

**Corrective Action:** any action or combination of actions taken to mitigate the severity of an adverse event that has occurred.

**CQA:** the Corporate Quality Assessment group within Quest Diagnostics.

**Error:** a mistake resulting from carelessness, inattention or misunderstanding by a person or persons.

**Event:** when used in the context of this document, is a nonspecific term intended to convey recognition that something has occurred that requires further investigation.

**Non-Conformance Event**: An event that results in deviations from approved policies, processes and procedures or in failures to meet requirements, as defined by the facility, or applicable regulations.

**Preventive Action:** any combination of actions taken to prevent or diminish the probability that an event might recur in the future.

**QA:** an abbreviation for the Quality Assurance department.

**Reportable Quality Issue (RQI):** A quality issue with known or potential effect on current patient care that is of sufficient priority to require the notification of Corporate Quality Assessment (CQA), Medical Quality Assurance (MQA), Corporate Medical Quality (CMQ) or National Referral Testing (NRT).

**Transfusion Service:** a facility that performs one or more of the following activities: compatibility testing, storage of blood or components, or selection and issuance of blood or components to intended recipients. Transfusion services do not routinely collect blood for transfusion or process Whole Blood into components.

## 5. PROCESS

### A. Recognition of a Non-Conformance Event

<table>
<tr><th>Step</th><th colspan="2">Action</th></tr>
<tr><td colspan="3">All department personnel will:</td></tr>
<tr><td>1.</td><td colspan="2">Notify the Manager/Supervisor or Lab Administrator on call IMMEDIATELY. The manager/supervisor is responsible for notifying the Medical Director and local QA team.</td></tr>
<tr><td></td><td>If</td><td>Then</td></tr>
<tr><td></td><td>the event resulted in injury or harm to a patient (alleged or realized),</td><td>notify the Laboratory Director or delegated M.D. CLIA Technical Supervisor and QA manager, IMMEDIATELY.</td></tr>
<tr><td></td><td>AND the event resulted in a fatality,</td><td>o notify CQA Mentor via phone IMMEDIATELY.<br>o Notify the FDA IMMEDIATELY via phone (301-827-6220).<br>o See special instructions in Section F for filing a written report within 7 days of the fatality.</td></tr>
<tr><td>2.</td><td colspan="2">Document the event on a PI/variance form.</td></tr>
<tr><td colspan="3">Manager/Supervisor will:</td></tr>
<tr><td>3.</td><td colspan="2">Notify the QA manager, as soon as possible.</td></tr>
</table>

| Step | Action | |
|---|---|---|
| 4. | Collect relevant information, evidence, and personnel interviews as soon as possible. | |
| **QA Manager will:** | | |
| 5. | Notify CQA Mentor via phone as soon as possible. | |
| 6. | Consult with CQA to determine the event classification. | |
| | **If the event involves** | **Then** |
| | o a deviation that **does not** require correction to patient results<br>o **and** the event is corrected prior to any associated blood product distribution, | o follow local procedures for corrective and preventive actions of occurrences and/or non conformance events;<br>o **do not** initiate the FDA reportable event process;<br>o **do not** submit an RQI. |
| | o a deviation that requires correction to patient results,<br>o **and** the event is corrected prior to any associated blood product distribution, | o submit an RQI;<br>o **do not** initiate the FDA reportable event process. |
| | o a deviation that has the potential to affect the safety, purity, or potency of a biological product<br>o **and** is not corrected prior to blood product distribution, | o initiate the FDA reportable event process;<br>o **and** submit an RQI. |
| 7. | Consult with the *Guidance for Industry – Biological Product Deviation Reporting for Blood and Plasma Establishments* (http://www.fda.gov/cber/gdlns/devbld.pdf) to determine the event classification. Examples of Biological Product Deviations (BPDs) are provided in Addendum A. | |

**B. Initiate the FDA Reportable Event Process**

| Step | Action |
|---|---|
| **QA Manager will:** | |
| 1. | Complete the Initial Notification of a Suspected BPD Template (Form QDHBB301) and email to CQA Mentor within **3 days** of discovery.<br>**NOTE**: Required information includes:<br>o Date of occurrence<br>o Date of discovery<br>o Statement of initial deviation<br>o Brief description of what happened<br>o Who discovered the deviation<br>o How it was discovered<br>o Type of blood products involved<br>o If products were transfused<br>o If the clinician was notified<br>o If a transfusion reaction occurred<br>o Laboratory Director assessment of patient impact |
| 2. | Initiate the RQI form. |
| **CQA Mentor will:** | |
| 3. | Notify senior corporate staff via email of the FDA reportable event. |
| 4. | Notify senior corporate staff via phone if the event resulted in injury or harm to the patient (alleged or realized). |

**C. Perform Investigation and Corrective Actions**

| Step | Action |
|---|---|
| **CQA Mentor/QA Manager/Manager/Supervisor will:** | |
| 1. | Perform root cause analysis as soon as possible, using collected information, evidence and interviews. The CQA Mentor, QA Manager, Laboratory Manager/Supervisor, and other involved individuals will participate in the analysis. Often many causal factors are identified, in addition to a root cause. |
| 2. | Evaluate all potential or realized risks identified during the event investigation for appropriate corrective and preventive actions. |
| 3. | Determine steps to adequately correct the problem, prevent recurrence, and include monitoring to ensure the continued effectiveness of the actions taken. |
| 4. | Obtain the Laboratory Director's approval for the outcome of the investigation, including the determination of cause(s), corrective actions, and preventive actions. |
| 5. | Initiate actions in a timely manner to ensure patient safety and to ensure the safety, purity, and potency of blood and blood products. |

## D. Complete the BPDR 3486

| Step | Action |
|---|---|
| 1. | The final report version is due to CQA within **30 days** of discovery. |
| **CQA Mentor/QA Manager/Manager/Supervisor will:** | |
| 2. | Obtain a current BPDR 3486 form and instructions from the FDA website (http://www.fda.gov/opacom/morechoices/fdaforms/CBER.html) |
| 3. | Write the report together with input from the Laboratory Director. |
| 4. | Adhere to the following report writing instructions:<br>o There must be only one version of the report while in draft form. This draft version must reside on a designated local laboratory shared drive and be labeled with the local naming convention and the word DRAFT.<br>**NOTE:** Do not email draft versions. Do not save previous drafts.<br>o Collaborations must be performed using WebEx, LYNK, etc.<br>o **DO NOT** include donor, patient, or employee personal identification information or other confidential information.<br>o Use concise, declarative statements. Do not include opinions.<br>o Choose the most appropriate BPDR Product Deviation Code from the current list found at (http://www.fda.gov/cber/biodev/devcode.pdf)<br>o List the products affected using the appropriate BPDR Blood Product Codes found (http://www.fda.gov/cber/biodev/bldcode.pdf)<br>o When complete, change the report label from DRAFT to FINAL and add the current date. |
| **QA Manager will:** | |
| 5. | Generate a printed copy of the FINAL version and obtain the Laboratory Director's signature indicating approval of the root cause analysis and corresponding corrective actions. |
| 6. | Email the final report to the CQA Mentor.<br>o The CQA Mentor will distribute the report to Corporate Quality Assessment, Corporate Medical Regulatory Affairs and the Corporate Legal Department for approval.<br>o When approved, the CQA Mentor will email the QA Manager to submit the BPDR 3468 to the FDA. |

| Step | Action |
|---|---|
| 7. | Submit the BPDR 3486 to the FDA within **45 days** of event discovery (with the exception of a fatality; see Guidance for Industry: (http://www.fda.gov/cber/gdlns/devbld.pdf) |
| 8. | The report can be submitted<br>o electronically at: (https://www.accessdata.fda.gov/scripts/cber/CFApps/Login)<br>o or by mail: : Director, Office of Compliance (HFM-650)<br>Center for Biologics Evaluation and Research<br>1401 Rockville Pike<br>Rockville, MD 20852-1448 |

## E. Documentation

Document and compile all activities related to the event. Activities can include but are not limited to:

Initial information and evidence
Interviews
FDA reportable Event Template
Root Cause Analysis
RQI report
Correspondence between lab and hospital administration, if required
BPD report

## F. Notification Guidelines

1. If a complication of a transfusion was confirmed to be fatal, the facility that performed the compatibility testing must notify the FDA
   - **regardless of whether or not a BPD occurred**
   - immediately by phone: 301-827-6220
   - within 7 days by submitting **a fatality report** to:
     Center for Biologics Evaluation and Research
     Director, Office of Compliance
     Attn: Fatality Program Manager (HFM-650)
     1401 Rockville Pike 200N
     Bethesda, MD 20852-1448

2. Event reporting must be reviewed by the laboratory management, the QA Manager and the CQA Mentor, and approved by the Laboratory Director, prior to submission to the Medical Regulatory and Legal Departments.

3. Report contents must be reviewed by Corporate Quality Assessment, Corporate Medical Regulatory Affairs and the Legal department before submission to the FDA.

4. Deadlines for reporting include:
   - Initial notification to CQA—**as soon as possible**

- FDA Reportable Event Template to CQA—within **3 days of discovery**
- BPD Final Report to CQA—**within 30 days of discovery**
- BPD Final Report to FDA—**within 45 days of discovery**

5. The FDA must be notified of any changes to information contained in BPD reports already filed. This includes changes to patient outcomes, corrective actions, etc. Send relevant information by email with reference to the original confirmation number or tracking number to:
   - CBER BP_Deviations [BP_Deviations@fda.hhs.gov]

## 6. RECORDS MAINTENANCE

Records are maintained according to the requirements published in the Quest Diagnostics *Records Management Program Reference Guide.*

## 7. RELATED DOCUMENTS

- BPDR Product Deviation Codes (http://www.fda.gov/cber/biodev/devcode.pdf)
- BPDR Blood Product Codes (http://www.fda.gov/cber/biodev/bldcode.pdf)
- BPDR Form 3486 (http://www.fda.gov/opacom/morechoices/fdaforms/CBER.html)
- Initial Notification of a BPD Template(QDHBB301)
- *Process for Notification of Reportable Quality Issues (*QDMED708)
- *Notification of Federal and State Agency Laboratory Performance Investigations, Inspections, Complaints or Adverse Media (*QDMED724)

## 8. REFERENCES

1. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research, Guidance for Industry – Biological Product Deviation Reporting for Blood and Plasma Establishments, Oct. 2006.
2. Guidance for Industry – Biological Product Deviation Reporting for Blood and Plasma Establishments (http://www.fda.gov/cber/gdlns/devbld.pdf)
3. Code of Federal Regulations, 21, parts 600.14 and 606.171, 607.3(d), 606.3(k), 606.3(l), 640.74, 211.192, 211.198, June 8, 2000.
4. AABB Standards for Blood Banks and Transfusion services, 28th Edition, 2012.
5. AABB Technical Manual, 17th Edition, 2011.

## 9. DOCUMENT HISTORY

| Version | Date | Section | Revision | Revised By | Approved By |
|---|---|---|---|---|---|
| 2 | 2-1-2014 | All | Updated to current corporate template | J. Hittinger | L. Hilborne, M.D. |
| | | 1 | Reworded Purpose; removed "tracking and trending" | J. Hittinger | L. Hilborne, M.D. |

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|---|---|---|---|---|---|
| | | 3 | Changed Laboratory Director responsibilities to include approval of SOP revisions and to ensuring that BPDRs are reported to the FDA;<br>Removed "tracking and trending" from the Laboratory Operations Director/Manager's responsibility | J. Hittinger | L. Hilborne, M.D. |
| | | 4 | Changed NQA to CQA | J. Hittinger | L. Hilborne, M.D. |
| | | 5 | Process rewritten. Initial notification template changed. New process for writing the report described. Added Laboratory Director approval of corrective actions. Added instructions for amended reports. Moved Examples of BPDs to Addendum A. | J. Hittinger | L. Hilborne, M.D. |
| | | 7 | Updated. Moved FDA information from References to Related Documents | J. Hittinger | L. Hilborne, M.D. |
| | | 8 | Updated. | J. Hittinger | L. Hilborne, M.D. |
| | | 10 | Removed Process Flow and Event Template; Added Examples of BPDs. | J. Hittinger | L. Hilborne, M.D. |

## 10. ADDENDA

| Addendum | Title |
|---|---|
| **A** | **Examples of Reportable and Non-Reportable Biological Product Deviations** |
| **B** | **FDA Electronic Submission Tips** |

**ADDENDUM A**

| **BPD is NOT REPORTABLE** | **BPD is REPORTABLE** |
|---|---|
| • The affected product was not distributed.<br>• Prior to distribution, it was determined that the safety, purity, or potency of the product was not affected.<br>• The event was detected and corrected prior to distribution of product.<br>• Timeframes for lookback, retrieval or consignee notification were not met. (i.e., proper notification procedures were followed but were not completed in the timeframe established in the procedure.) | |
| COMPONENT PREPARATION<br>• A recordkeeping deviation, such as a missing signature of the person preparing the unit, or other documentation that would not affect the safety, purity, or potency of the product. | COMPONENT PREPARATION<br>• The component was not prepared within the allotted time frame after collection.<br>• Air contamination or bacterial contamination occurred.<br>• The SOP for component preparation is inadequate or was not followed.<br>• The platelet count or yield was not acceptable.<br>• The collection time was extended beyond that allowed.<br>• Freezing time requirements were not met.<br>• The resting time requirement for platelets was not met.<br>• Specific procedures (irradiation or leukoreduction) were not performed or were improperly performed.<br>• The incorrect dosage was used for irradiation.<br>• The product was not washed/deglycerolized properly. |

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| TESTING<br>• A documentation deviation, if other information indicates that testing was performed appropriately.<br>• Appropriately invalidated assays (run failures or QC failures) for which the affected samples were retested in an acceptable run and tested negative. | TESTING<br>• Testing was not performed in accordance with instructions.<br>• An incorrect incubation time or temperature was used.<br>• Incorrect reagents were used or reagents from different lots were used without appropriate QC testing prior to use.<br>• Reagents were added incorrectly.<br>• Incorrect testing for ABO, Rh, antibody screen, antigen type, or compatibility.<br>• The incorrect sample was tested or the sample was misidentified.<br>• An initially reactive sample was not repeated in duplicate (viral marker).<br>• An unsuitable sample was used for testing.<br>• The sample was improperly stored.<br>• The sample was diluted (by IV fluids, for example).<br>• The sample was not identified appropriately and could not be traced back to the donor or patient.<br>• Testing was performed using expired reagents.<br>• Patient samples were mislabeled or collected from the wrong patient.<br>• Mistyped or misinterpreted patient samples if the sample was used in crossmatching a product that was distributed.<br>• Only an immediate spin crossmatch is performed when a patient's history or testing protocol indicate that an indirect antiglobulin test is required. |

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| LABELING<br>• A unit is labeled with a shortened expiration date.<br>• Any of the following information is missing or incorrectly stated on the label (provided that the product is otherwise acceptable):<br>o collection date (provided that the expiration date is correct)<br>o facility identification.<br>• An unlicensed product is labeled with a license number. | LABELING<br>• A product is labeled with an incorrect ABO, Rh, antigen, antibody, product type, anticoagulant, volume, weight or unit number.<br>• Information is missing for ABO, Rh, product type, expiration, date, unit number, weight, volume or platelet count (for platelet products).<br>• Unit is labeled with an incorrectly extended expiration date, even if the product was transfused within the correct dating period.<br>• Additional information on an autologous unit is missing or incorrect.<br>• The SOP for labeling was not followed or is inadequate.<br>• The unit is labeled with incorrect information regarding leukoreduction, irradiation, washing, crossmatch, antigen/antibody, donor number or recipient number.<br>• Unit is not labeled as a biohazard, when indicated. |

| | |
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| QUALITY CONTROL & DISTRIBUTION<br>• There is a discrepancy between the shipping form and the shipment.<br>• A unit was shipped to the incorrect facility.<br>• A unit was lost or the shipment was never received.<br>• The final disposition of the unit is unknown.<br>• A frozen product breaks during thawing and the product is discarded.<br>• A product breaks or is damaged during shipment and the product is discarded.<br>• An allogeneic unit is issued when an autologous unit is available.<br>• A unit is returned to the blood bank, is determined to be unsuitable, and is discarded (e.g., out of temperature range).<br>• Unlicensed product was distributed labeled with a license number. | QUALITY CONTROL & DISTRIBUTION<br>• An unsuitable unit is distributed.<br>• A unit or segment is clotted.<br>• A unit or segment is hemolysed.<br>• An outdated unit is distributed.<br>• A unit is shipped or stored at an incorrect temperature.<br>• Failure to quarantine a unit due to incorrect, incomplete, or positive testing.<br>• Required testing is not performed or not documented.<br>• The donor has an unsuitable medical history.<br>• SOPs for quality control or distribution are not followed or are inadequate.<br>• Product specifications are unacceptable or not documented.<br>• An incorrect product is issued for a specific patient.<br>• The wrong unit is issued for a patient.<br>• An improper ABO or Rh is selected for a patient.<br>• The wrong filter was issued for use in transfusion or a filter was not issued when required.<br>• Visual check of the product was not performed prior to distribution.<br>• Product was distributed based on testing that was not performed on a current sample (sample too old for testing). |

## ADDENDUM B

### FDA Electronic Submission Tips

### Establishing an eBPD Account:

An account can be established using a FDA Registration Number or a CLIA Number.

- The FDA requires a blood bank to register if it routinely collects or processes blood or blood components. Processing includes, but is not limited to, preparing components, irradiation, leukoreduction, washing of red cells, viral marker testing of blood donors (21 CFR 607.7).
- Contact the local FDA district office to obtain a registration number from the appropriate Registration Monitor (Blood, Device, or Drug). A listing of the Registration Monitors is available at: http://www.fda.gov/ICECI/Inspections/IOM/ucm124063.htm[7].
- Only use your CLIA Number if you do not have a registration number

Enter the Establishment Identification Number and select the Establishment Identification Number Type then press the **Add to My Establishments** button.

- A confirmation screen will appear if you have entered a valid Identification Number and Number Type. By pressing the **Yes** button, you are agreeing that you are a valid representative of this establishment and may legally submit Biological Product Deviation reports for this establishment. Press the **No** button to cancel your association request and return to the previous page.
- Repeat this process for each establishment with which you want to request an association.
- The establishment information corresponding to the Establishment Identification Number selected is automatically populated. Verify that this information is correct. If an incorrect establishment identification number was entered, return to Select Establishment page. If the establishment identification number is correct, but the information displayed is incorrect, Contact eBPDR Technical Support.

Upon selecting "New Report" for a CLIA facility, the system asks, "Is this facility actively registered with FDA? The user answering NO can proceed with creating the new report and is not required to answer the question again for that facility for 90 days. The user answering YES will see a screen requesting that registered facilities submit BPD Reports using their FEI number instead of their CLIA number.

### Account Maintenance

Periodically check the **List of Active Users.** This page will display other users that are associated to the same establishment you have listed on your "My Establishments" page.

- Contact eBPDR Technical Support if you find unfamiliar names listed or need names removed.

- If one of your establishments is not listed, it means that you are the only user account associated to that establishment.
- If one of your establishments is listed it will display the following information:
  - Establishment Identification Number and Type
  - Establishment Name
  - Full Name (Last Name, First Name, MI) of other users associated with that establishment.

To remove your association with an establishment, select the establishment and press the **Remove From List** button.

- A confirmation screen will appear asking if you are sure you want to remove your association to this establishment. Press **OK** to remove the establishment or press **Cancel** to cancel your request.

To remove or change the name of an establishment:

- Contact eBPDR Technical Support.