



**DukeMedicine**  
Division of Cellular Therapy



## ADULT AND PEDIATRIC BLOOD AND MARROW TRANSPLANT PROGRAM

**DOCUMENT NUMBER:** APBMT-COMM-030

**DOCUMENT TITLE:**

Recording and Reporting of Adverse Events

**DOCUMENT NOTES:**

### Document Information

**Revision:** 08

**Vault:** APBMT-Common-rel

**Status:** Release

**Document Type:** Common

### Date Information

**Creation Date:** 06 Jun 2019

**Release Date:** 19 Jul 2019

**Effective Date:** 19 Jul 2019

**Expiration Date:**

### Control Information

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**Previous Number:** APBMT-COMM-030 Rev 07 **Change Number:** APBMT-CCR-159

## APBMT-COMM-030 RECORDING AND REPORTING OF ADVERSE EVENTS

### 1 PURPOSE

- 1.1 To describe the procedure to document and report severe adverse events and infusion reactions, as applicable, for cellular therapy product infusions, collection procedures, and extracorporeal photopheresis (ECP).
- 1.2 To ensure comprehensive documentation, as applicable, and timely reporting in order to ensure patient safety and compliance with requirements of regulatory agencies and research protocol requirements.

### 2 INTRODUCTION

- 2.1 Timely documentation and reporting of adverse events and cellular therapy product infusion reactions is paramount in order to protect the patient and minimize risk of injury.
- 2.2 Reporting originates from point of care and/or procedures where the adverse event occurs.
- 2.3 **Adverse Event (AE)** is as any unintended or unfavorable sign, symptom, abnormality, or condition temporarily associated with an intervention that may or may not have a causal relationship with the intervention, medical treatment, or procedure. This may include new illness or injuries or a worsening of existing illnesses, and a causal relationship between the treatment and the adverse event need not be established. AE is synonymous with adverse drug experience, adverse biological experience, adverse product experience, and adverse event.
- 2.4 **Adverse Reaction** is a type of adverse event and includes a noxious unintended response suspected or demonstrated to be caused by the collection or administration of a cellular therapy product or by the product itself. Adverse reactions may be specific to a procedure or infusion. (See related procedure APBMT-COMM-035 *Detection and Management of Adverse Events* for additional details around identifying adverse reactions related to apheresis, bone marrow harvest, or extracorporeal photopheresis procedures.)
- 2.5 **Expected Adverse Event** is any event listed in current FDA approved labeling of a licensed product or a known transplant or procedure related risk or side effect.
- 2.6 **Unexpected Adverse Event** is any event that is not listed in current FDA approved labeling of a licensed product or the investigator's brochure for an IND sponsored product/drug, an adverse event that has not been seen in prior patients or an adverse event that has been seen in prior patients but has a different level of severity.
- 2.7 **Serious Adverse Event (SAE)** is any experience that suggests a significant medical hazard and includes any event that is fatal, life threatening, requires or prolongs hospitalization or is permanently disabling. SAE is any event which:
  - 2.7.1 Is fatal

- 2.7.2 Is immediately life threatening
- 2.7.3 Is permanently/significantly disabling
- 2.7.4 Requires or prolongs hospitalization
- 2.7.5 Causes a congenital anomaly
- 2.7.6 Requires intervention to prevent impairment or damage

### **3 SCOPE AND RESPONSIBILITIES**

- 3.1 Any clinical staff member, working within the Adult Blood and Marrow Transplant Program (ABMT) or the Pediatric Blood and Marrow Transplant (PBMT) program including the Brain Injury Program, are responsible to ensure that any severe adverse events or infusion reactions are properly documented and reported.
- 3.2 Reporting to the appropriate staff members executing CIBMTR (Center for International Blood and Marrow Transplant Research) reporting is an essential component of reporting. CIBMTR reporting staff members are required to submit SAEs, infusions reactions, and product sterility testing as described below.

### **4 ACRONYMS**

- 4.1 AE Adverse Event/Adverse Experience
- 4.2 ABMT Adult Blood and Marrow Transplant
- 4.3 CIBMTR Center for International Blood and Marrow Transplant Research
- 4.4 EMR Electronic Medical Record
- 4.5 FDA Food and Drug Administration
- 4.6 IRB Institutional Review Board
- 4.7 PBMT Pediatric Blood and Marrow Transplant
- 4.8 QSU Quality Service Unit
- 4.9 SAE Serious Adverse Event/Serious Adverse Experience
- 4.10 SRS Safety Reporting System
- 4.11 STCL Stem Cell Laboratory

### **5 MATERIALS**

- 5.1 N/A

### **6 EQUIPMENT**

- 6.1 Computer for electronic submissions and documentation (As applicable)

### **7 SAFETY**

- 7.1 N/A

## 8 PROCEDURE

### 8.1 Clinical Events

- 8.1.1 All fatal adverse events will be recorded in the EMR and reported to the team responsible for CIBMTR reporting. In addition, the following are designated as qualifying events and will be recorded in the EMR and reported to research staff, who will then report the event in FormsNet per NMDP/CIBMTR guidelines found at <https://network.bethematchclinical.org/education/transplant-center/operational/adverse-events-and-product-complaint-reporting/>:
  - 8.1.1.1 Grade 3 or greater cellular therapy infusion reactions
  - 8.1.1.2 Positive infectious testing from a cellular therapy product
  - 8.1.1.3 Any patient-specific positive infectious testing after receiving a contaminated product.
- 8.1.2 If a patient is on a clinical trial and experiences an SAE (for example: readmission, transfer to ICU or death), the research team must be notified the same day. The research staff will then assess if the event requires IRB, sponsor and/or FDA reporting per the IRB, sponsor's and FDA's guidelines.
- 8.1.3 Certain AEs will be reported to leadership and presented in the APBMT Quality Assurance Committee Meeting. (See APBMT-COMM-027 *Adult and Pediatric Blood and Marrow Transplant Program Quality Management Plan*.)
- 8.1.4 Certain AEs and process controls may require inclusion in quarterly QA meeting minutes and/or annual reports prepared by members of the QSU team. The following AEs are reported in annual reports prepared by members of the QSU team:
  - 8.1.4.1 Deaths
  - 8.1.4.2 Product contamination
  - 8.1.4.3 Infections related to the product

### 8.2 Safety Reporting System

- 8.2.1 Clinically significant medication reactions, medication related adverse events, and/or medication errors will be reported, in compliance with hospital policy, by the clinical staff via the Duke safety reporting system (SRS).
- 8.2.2 Specific SRS reports will be presented at the APBMT Quality Assurance Committee (see APBMT-COMM-027 *Adult and Pediatric Blood and Marrow Transplant Program Quality Management Plan*.)

### 8.3 Infusion Reactions

- 8.3.1 The STCL-SOP-050 *Infusion Form* should be completed for all patients who receive a cellular therapy infusion. The form should be completed within 24 hours after receiving the infusion and should be faxed to the

Stem Cell Laboratory (STCL) where a staff member will review the document for completeness. All infusion forms are stored in patient's specific product file.

- 8.3.1.1 PBMT: If Grade 3 or higher toxicities are noted, the STCL will notify the PBMT research staff and PBMT physicians by sending an email to the following email group: CanCtr-pbmt\_md\_np@dm.duke.edu. The PBMT research staff will review and determine need for reporting in FormsNet (as described above) and/or more reporting if on a clinical trial.
- 8.3.1.2 ABMT: If Grade 3 or higher toxicities are noted, the STCL will notify the ABMT nursing staff and ABMT physicians. ABMT research staff will receive verbal communication from clinical staff regarding research related reports. The ABMT research staff will review and determine need for reporting in FormsNet (as described above) and/or more reporting if on a clinical trial. Written notification of a research related report will occur via the SRS system.
- 8.3.1.3 CIBMTR reporting staff will review the medical record for adverse event reports.
- 8.3.1.4 Instructions for completing STCL-SOP-050 *Infusion Form* are described below:
  - 8.3.1.4.1 Ensure ISBMT 128 barcodes are present on all pages of the form. If missing, contact the STCL.
  - 8.3.1.4.2 Record the infusion date in the "Date of Infusion" Prompt.
  - 8.3.1.4.3 Record the time the infusion started in the "Start Time of Infusion" field and record the time the infusion was complete in the "End Time of Infusion" field.
  - 8.3.1.4.4 Check the applicable Yes or No box regarding the administration of pre-infusion medications. If yes, record medications that were administered.
  - 8.3.1.4.5 Check the applicable Yes or No box regarding the use of emergency medications. If yes, record the medications that were administered.
  - 8.3.1.4.6 For each toxicity listed on the form, record the highest grade of complication/toxicity occurring within 24 hours of the infusion.
  - 8.3.1.4.7 If needed, provide additional comments as applicable to the event on the form.



- 8.3.1.4.8 The person completing the form will sign and date the form in the space provided at the end of the form.
    - 8.3.1.4.9 Once the form is completed in its entirety, fax the form to the STCL representative reflected on the bottom of the form or provide a scanned copy.
- 8.4 Reporting for Collection Procedures and Extracorporeal Photopheresis (ECP)
  - 8.4.1 Errors, accidents, and adverse reactions are all types of adverse events (AE). This procedure will allow staff to assess, detect and manage any AE that may occur while undergoing an apheresis, photopheresis or bone marrow harvest procedure.
  - 8.4.2 Patients who have a clinically significant adverse event during a procedure will be followed post the event by a physician knowledgeable in the care of the patient. The patient may also be followed by a transplant coordinator and/or other staff such as advance practice providers in the outpatient setting. Follow-up care will be coordinated with the donor's home physician for donors who live out of the Duke Hospital vicinity. For information regarding side effects and reactions related to these procedures, see SOP: APBMT-COMM-035 *Detection and Management of Adverse Events*.
  - 8.4.3 A Duke Hospital Safety Reporting System (SRS) report may be completed for those collections that result in a severe or unexpected adverse event related to the procedure. Reporting is at the discretion of the clinical team and in compliance with institution recommendations and policy. A serious adverse event is any experience that suggests a significant medical hazard and includes any event that is fatal, life threatening, requires or prolongs hospitalization or is permanently disabling.
    - 8.4.3.1 A SRS report will be completed for any procedure that results in equipment failure or tubing set failure occurring while a patient/donor is undergoing collection.
  - 8.4.4 APBMT-COMM-030 FRM1 *Adverse Event Form* will be completed within 24 hours if there is a procedure-related event Grade 3 or greater with the exception of these events below, which will also be reported on the form:
    - 8.4.4.1 APBMT-COMM-030 FRM1 *Adverse Event Form* will be completed within 24 hours for any event occurring that will effect product sterility; and also reported to STCL staff.
    - 8.4.4.2 Apheresis and ECP patients: Fever, which will be reported for Grade 1 or greater; and also reported to the attending physician responsible for the apheresis patient.

- 8.4.4.3 Apheresis and ECP patients: Rigors and Chills, which will be reported for Grade 2 or greater; and also reported to the physician responsible for the apheresis patient.
- 8.4.5 Completing the APBMT-COMM-030 FRM1 Adverse Event Form:
  - 8.4.5.1 Enter the donor number in the boxes provided in addition to the date of the collection.
  - 8.4.5.2 Circle the type of procedure and the type of donor, as applicable.
  - 8.4.5.3 For each toxicity that occurs, place a check in the box that best describes the side effects and symptoms experienced by the donor.
  - 8.4.5.4 Record any appropriate treatments given in the electronic medical record.
  - 8.4.5.5 Record any comments in the comment section provided to further explain any side effects.
  - 8.4.5.6 The person completing the form will sign and date the form in the space provided at the end of the form. The following person is responsible for form completion:
    - 8.4.5.6.1 Apheresis: apheresis nurse
    - 8.4.5.6.2 Bone Marrow Harvest: attending physician or advanced practice provider
    - 8.4.5.6.3 Extracorporeal Photopheresis: photopheresis nurse
    - 8.4.5.6.4 Surgical nurses, as applicable.
  - 8.4.5.7 The completed form will be faxed to the number on the bottom of the form for centralized storage of all AE forms.
  - 8.4.5.8 After the fax is received, a designated APBMT staff member will place the document in a centralized APBMT binder housed in North Pavilion.
- 8.4.6 External Reporting Regarding NMDP Donors:
  - 8.4.6.1 Any adverse event related to apheresis or any unexplained adverse event grade 3 or greater will be reported to the National Marrow Donor Program (NMDP)/CIBMTR through FormsNet within 2 working days.
- 8.4.7 Errors and Accidents:
  - 8.4.7.1 Report any cellular product labeling errors immediately to the Stem Cell Laboratory Manager and Nurse Manager and document the error in the SRS.

- 8.4.7.2 Report any apheresis or ECP procedural errors or equipment or tubing malfunction to the apheresis coordinator, nurse manager and attending physician and document in SRS. The apheresis coordinator will provide re-training, educational in-service and review of the procedure. The apheresis coordinator or Nurse Manager will place equipment or supplies out of service or quarantine if needed.
  - 8.4.7.2.1 Any accidents occurring due to apheresis or ECP machine malfunction during collection will be documented in the patient record and reported to the hospital online Safety Reporting System (SRS). The machine will be taken out of service until it can be repaired and approved for service by the Duke Clinical Engineering Department.
  - 8.4.7.2.2 Performance Qualification (PQ) must be done on the equipment after each repair by the apheresis coordinator or designee before placing back into use.
  - 8.4.7.2.3 Any accidents occurring as a result of tubing set problems such as leaks will be documented in the SRS and will be reported to the manufacturer.
- 8.4.7.3 Report any error or accident occurring during the bone marrow harvest procedure to the attending physician responsible for the patient's care. Document the event in the SRS and medical records in accordance with hospital policy.

## **9 RELATED DOCUMENTS/FORMS**

- 9.1 APBMT-COMM-027 Adult and Pediatric Blood and Marrow Transplant Program Quality Management Plan
- 9.2 APBMT-COMM-030 FRM1 Adverse Event Form
- 9.3 APBMT-COMM-035 Detection and Management of Adverse Events
- 9.4 STCL-SOP-050 Infusion Form

## **10 REFERENCES**

- 10.1 MedWatch Continuing Education Article: The Clinical Impact of Adverse Event Reporting – [www.fda.gov/medwatch/articles/med.pdf](http://www.fda.gov/medwatch/articles/med.pdf)
- 10.2 U.S. Food and Drug Administration – [www.fda.gov/medwatch](http://www.fda.gov/medwatch)
- 10.3 U.S. Food and Drug Administration MedWatch – [www.fda.gov/medwatch](http://www.fda.gov/medwatch)



**11 REVISION HISTORY**

Revision No.	Author	Description of Change(s)
08	Sally McCollum	This heavily updated document should be viewed as a new document as the contents have been revised almost in their entirety to collectively capture the revised workflows of all areas in APBMT.

**Signature Manifest****Document Number:** APBMT-COMM-030**Revision:** 08**Title:** Recording and Reporting of Adverse Events

All dates and times are in Eastern Time.

**APBMT-COMM-030 Recording and Reporting of Adverse Events****Author**

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**Document Release**

Name/Signature	Title	Date	Meaning/Reason
Betsy Jordan (BJ42)		11 Jul 2019, 11:09:02 AM	Approved