IQPP Standard for Recording Donor Adverse Events

Version 2.0
Implemented April 1, 2018

PPTA
Plasma Protein Therapeutics Association

Background

The IQPP Standard for Recording Donor Adverse Events is part of a series of standards that comprise the Plasma Protein Therapeutics Association (PPTA) IQPP Standards Program. PPTA's Voluntary Standards Program provides global leadership for the plasma protein industry's goal of continuous improvement with a focus on safety and quality from the donor to the patient.

This voluntary IQPP Standard was developed by the PPTA IQPP Standards Committee, and was approved by the PPTA Source Board of Directors on February 8, 2018. This version supersedes version 1.0 in its entirety.

For questions about this PPTA Voluntary Standard contact IQPP@pptaglobal.org. For more information about the IQPP Standards Program or PPTA, visit www.pptaglobal.org.

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1. Introduction

In 2006, the United States Federal Advisory Committee for Blood Safety and Availability ("Committee") recommended that the federal government engage in efforts to enhance safety monitoring for blood products, cell and tissue products and solid organs in partnership with private sector initiatives.[1] These monitoring systems, collectively termed "biovigilance," were viewed by the committee as important tools for improving outcomes related to transfusion and transplantation therapy. Donor biovigilance is integral to the total biovigilance program since donors provide the "raw materials" for biologic treatments, and because safety of living donors is a related and important public health issue.[2]

All IQPP certified establishments have processes in place to monitor, manage, and document donor adverse events. This IQPP Standard serves as the foundation for establishing industry-wide requirements for adverse event definitions and classification.

This Standard is part of a series of standards that comprise the PPTA IQPP Voluntary Standards Program. For more information about the program, visit www.pptaglobal.org.

2. Scope

This standard applies to facilities that collect Source Plasma.

3. Terms and Definitions

3.1. BP

blood pressure

3.2. DAE

donor adverse event

3.3. LOC

loss of consciousness

[1] Letter dated February 9, 2007, from Chair, ACBSA, to ASH John O. Agwunobi, https://wayback.archive-it.org/3919/20140402193410/http://www.hhs.gov/ash/bloodsafety/advisorycommittee/recommendations/recommendations200608.pdf

[2] Biovigilance in the United States: Efforts to Bridge A Critical Gap in Patient Safety and Donor Health, report of PHS Biovigilance Task Group in Response to HHS ACBSA recommendations, https://www.researchgate.net/profile/James_Bowman3/publication/255703308_Biovigilance_in_the_United_States_Efforts_to_Bridge_a_Critical_Gap_in_Patient_Safety_and_Donor_Health/links/56b0c3d608ae8e372151f08a/Biovigilance-in-the-United-States-Efforts-to-Bridge-a-Critical-Gap-in-Patient-Safety-and-Donor-Health.pdf

4. Requirements

4.1. General

Companies shall have a documented process for recording known DAEs considered to be associated with any part of a Source Plasma donation program (this includes initial screening, donation, immunization for high titer collections, etc.) following company approved SOPs.

NOTE: The presence of an isolated sign/symptom/finding in Attachment A does not necessarily require the recording of a DAE if not associated with the donation/immunization process. Similarly, equipment issues (e.g. RBC spill, machine malfunction, AC run out) in the absence of associated donor signs/symptoms/findings, does not require recording of a DAE.

All DAEs listed in the DAE Classifications in Subclause 4.2 which have an asterisk (*) shall be classified in accordance with this IQPP Standard by a licensed physician or physician substitute utilizing the available information and best medical judgment.

Each DAE shall be assigned to a single category using the DAE Classifications list in Subclause 4.2. If the donor subsequently returns to the center with symptoms of another event, unrelated to the original DAE, the new event can be recorded and classified as a separate event but linked to the same donation. For example, on 5/10/2016, a new donor experiences a Hypotensive Event with LOC of less than 60 seconds. The donor returns to the center on 5/11/2016 exhibiting a large hematoma at the venipuncture site from the 5/10/2016 donation. These events may be recorded as separate DAEs linked to the 5/10/2016 donation.

All DAEs listed in the DAE Classifications list in Subclause 4.2 which do not have an asterisk (*) shall be managed according to company SOPs and are not subject to tracking and trending under this Standard.

DAEs, when occurring off-site and reported to the facility, shall be documented including whatever information is available, with the understanding that the information may be limited and not completely accurate.

Companies shall follow Attachment A, *Donor Adverse Event Classification Guide*, when reviewing and classifying each event in their process.

4.2. DAE Classifications

DAEs include the following:

Category	Recording Requirement (* = record)	Sub-Category
Hypotensive Event (vasovagal/Hypovolemia)		
		Prefaint, No LOC (Minor)
	*	Prefaint, No LOC (Moderate)
	*	LOC approximately less than 60 Seconds
	*	LOC approximately 60 Seconds or longer
	*	Severe (With or Without LOC)
	*	Injury
Major Cardiovascular or Respiratory Event	*	
Local Injury Related to Phlebotomy Event		
	*	Nerve Irritation
		Hematoma/Bruise (Uncomplicated)
	*	Hematoma/Bruise (Complicated)
	*	Infection
	*	Arterial Puncture
		Infiltration
	*	Major Blood Vessel Injury
Citrate Reaction Event		
		Minor
	*	Moderate
	*	Severe
Hemolysis/Hemoglobinuria Event		
	*	Uncomplicated
	*	Complicated
Air Embolus Event		
		Uncomplicated
	*	Complicated
Allergic Event		
	*	Local
	*	Generalized
	*	Anaphylaxis
Hyperventilation Event	*	

Category	Recording Requirement (* = record)	Sub-Category
Immunization Event		
		Local, mild
	*	Local, severe
		Systemic, mild
	*	Systemic, severe
	*	Hypotensive, no LOC
	*	Hypotensive, LOC
Other Event	*	

4.3. Donor Variables

The DAE recording process shall incorporate the following variables in accordance with company SOPs:

a) The donor's age

b) The donor's gender

c) The donor's weight

d) The donor's height

e) The date of donation (mm/dd/yyyy)

f) The time of donation (military or standard) (This is the time of venipuncture.)

g) The name and title of the staff member recording the reaction

h) The pre-donation Diastolic BP

i) The pre-donation Systolic BP

j) The pre-donation pulse

k) The timing when the reaction was first known to begin, either:

- Pre-donation;
- During Donation;
- Post-donation on-site;
- Post-donation off-site;
- Immunization – immediate (less than or equal to 15 minutes after immunization); or
- Immunization – delayed (more than 15 minutes after immunization)

l) Special observation relating to the donor reaction event (when applicable):
   - **o** Collected volume at the time of the DAE

m) Transport and/or hospitalization within 24 hours

4.4. Inspection and Compliance Verification

At the Corporate Audit, inspectors shall request the company SOPs related to DAE recording, and review the company's documented process for recording known DAEs.

ATTACHMENT A – Donor Adverse Event Classification Guide

DAE Classification	Description	Signs/Symptoms/Findings
1. Hypotensive (Vasovagal/Hypovolemia) Hypotensive reaction (vasovagal/hypovolemia) that falls into any of the following categories. *NOTE:* For the purposes of this IQPP Standard, "medical staff intervention" means the use of expertise from the physician or physician substitute to make decisions regarding management of the DAE.		
1.1 Hypotensive: Prefaint, No LOC (Minor)	This reaction: a. must resolve without medical staff (e.g., physician substitute) intervention, AND b. Involves signs and symptoms that resolved quickly (e.g. within approximately 10 minutes).	May include one or more of the following: a. Abdominal cramps; b. Auditory disturbance (e.g. sounds coming from a distance or "buzzing" in the ears); c. Chills or Shivering; d. Clammy; e. Cold extremities; f. Dizziness; g. Epigastric discomfort; h. Facial pallor (e.g. pale skin or lips); i. Feeling of Warmth; j. Headache or neck ache; k. Hypotension; l. Lightheadedness; m. Nausea; n. Palpitations; o. Sweating; p. Visual Disturbance (e.g. blurred or faded vision); or q. Weakness.

DAE Classification	Description	Signs/Symptoms/Findings
1.2 Hypotensive: Prefaint, No LOC (Moderate):	This reaction: a. requires medical staff (physician substitute) intervention, OR b. involves signs/symptoms that did not resolve quickly (e.g. within approximately 10 minutes), OR c. additional signs/symptoms may be present.	May include any in 1.1 AND a. Vomiting.
1.3 Hypotensive: LOC (brief)	In this reaction, LOC lasts approximately less than sixty seconds.	May include any in 1.1 or 1.2.
1.4 Hypotensive: LOC (prolonged)	In this reaction, LOC lasts approximately sixty seconds or longer.	May include any in 1.1 or 1.2.
1.5 Hypotensive; Severe (With or Without LOC):	This reaction may or may not include LOC.	May include any in 1.1 through 1.4 AND any of the following: a. Chest Pain; b. Convulsions/Seizures c. Loss of Bladder/Bowel Control; or d. Prolonged signs or symptoms that do not resolve.
1.6 Hypotensive; Injury	A hypotensive event that results in ANY type of injury such as: a. Closed Head Injury; b. Dental Injury; c. Fracture; d. Laceration; e. Soft Tissue Injury (not phlebotomy-related); or f. Other.	May include any of 1.1 – 1.5 as well as any signs/symptoms related to the injury itself.
NOTE: If the donor exhibits symptoms of a hypotensive event (1.1 through 1.6), in addition to "anxiety," then the event should be classified according to "1.1 – 1.6 Hypotensive."		

DAE Classification	Description	Signs/Symptoms/Findings
2. Major Cardiovascular or Respiratory Event Major cardiovascular or respiratory event that occurs within 24 hours of the completion of donation and which falls into the following.		
2.1 Major Cardiovascular or Respiratory Event	Major cardiovascular or respiratory event that occurs within 24 hours of the completion of donation.	May include any of the below: a. Angina Pectoris; b. Cardiac Arrest; c. Cerebrovascular Accident; d. Myocardial Infarction; e. Transient Ischemic Attack; or f. Respiratory Arrest.
3. Local Injury Related to Phlebotomy Local injury related to phlebotomy that falls into one of the following categories.		
3.1 Local Injury Related to Phlebotomy: Nerve Irritation	Persistent signs, symptoms, or findings in a peripheral nerve distribution associated with the venipuncture area, which began at venipuncture or later (in the absence of a visible hematoma).	May include any of the below: a. Immediate Intense Pain at Site; b. Paresthesias, Numbness/Tingling of Fingers, Hand, or Arm; c. Shooting Pain Down Arm; or d. Weakness of Arm.
3.2 Local Injury Related to Phlebotomy: Hematoma/Bruise (uncomplicated)	A hematoma/bruise that is approximately ≤ 2" x 2." **"≤ 2" x 2""** means that both dimensions are **≤ 2".** For example, a hematoma/bruise that is 2" x 2", in the absence of signs/symptoms/findings for "complicated," would be classified as "uncomplicated." However, a hematoma/bruise that is 3" x 1", would be	May include any of the below: a. Mild Pain; b. No Restriction of Movement; c. Skin Discoloration; or d. Swelling.

DAE Classification	Description	Signs/Symptoms/Findings
	classified as "complicated." If, following initial classification and prior to resolution, the hematoma/bruise is found to meet the classification requirements for "complicated," then it shall be reclassified as "complicated" and/or recorded appropriately in the facility's DAE documentation system.	
3.3 Local Injury Related to Phlebotomy: Hematoma/Bruise (complicated)	A hematoma/bruise that is approximately >2" x 2." **"(>2" x 2")"** means that at least one dimension is **>2".** For example, a hematoma/bruise that is 3" x 2" would be classified as "complicated." However, a hematoma/bruise that is 2" x 1", would be classified as "uncomplicated, unless also has signs/symptoms/findings for "complicated."	May include any of the below: a. Paresthesias, Numbness/Tingling of Fingers, Hand, or Arm; b. Pressure; c. Redness; d. Restricted Movement; e. Shooting Pain Down Arm; f. Significant Pain; g. Skin Discoloration; h. Swelling; i. Tenderness; j. Warmth; or k. Weakness of Arm.
3.4 Local Injury Related to Phlebotomy: Infection		May include any of the below: a. Drainage; b. Pain; c. Redness; d. Swelling; e. Tenderness; or f. Warmth.

DAE Classification	Description	Signs/Symptoms/Findings
3.5 Local Injury Related to Phlebotomy: Arterial Puncture	An apparent arterial puncture	May include any of the below: a. Bright Red Blood; b. Pulse Sensation in Tubing; or c. Pulsing Blood Flow.
3.6 Local Injury Related to Phlebotomy: Infiltration	An apparent infiltration in the absence of bruising or hematoma	May include any of the below: a. Pain; or b. Swelling.
3.7 Local Injury Related to Phlebotomy: Major Blood Vessel Injury		May include any of the below: a. Arteriovenous Fistula; b. Brachial Artery Pseudoaneurysm; c. Compartment Syndrome; d. Venous Thrombosis; e. Phlebitis; or f. Thrombophlebitis.
4. Citrate Reaction Citrate reaction that falls into one of the following categories.		
4.1 Citrate Reaction: Minor	Resolves quickly with or without reducing flow rate or providing calcium.	May include any of the below: a. Metallic Taste; b. Paresthesia (Perioral – Lips Tingling/Numbness); or c. Paresthesia (Peripheral - Hands/Feet Tingling/Numbness).

DAE Classification	Description	Signs/Symptoms/Findings
4.2 Citrate Reaction: Moderate		Any of 4.1 that progress to the rest of the body AND any of the below: a. Carpopedal Spasms; b. Chest Pressure; c. Cold Extremities; d. Chills/Shivering; e. Muscle Tightness and/or Cramping; f. Nausea; g. Pallor, Pale Skin or Lips; h. Shortness of Breath; i. Sneezing/Nasal Congestion; j. Tetany (Transient); k. Tremors (Sensation of Vibration); l. Twitching; or m. Vomiting.
4.3 Citrate Reaction: Severe		Any of 4.1 or 4.2 that progress to the rest of the body AND any of the below: a. Bluish Tint to Skin (Cyanosis); b. Chest Pain; c. Heart Arrhythmia; d. Hypotension (Severe); e. Incontinence; f. Mental Confusion; or g. Tetany (Severe).

5. Hemolysis/Hemoglobinuria Reaction that falls into one of the following categories.		
5.1 Hemolysis/ Hemoglobinuria: Uncomplicated		Red/brown colored urine as the only sign
5.2 Hemolysis/ Hemoglobinuria: Complicated		Red/brown colored urine and any of the below: a. Back/Flank Pain; b. Bluish Tint to Skin (Cyanosis); c. Mental Confusion; d. Pallor, Pale Skin or Lips; or e. Shortness of Breath.
6. Air Embolus Air embolus that falls into one of the following categories.		
6.1 Air Embolus: Uncomplicated		None
6.2 Air Embolus: Complicated		May include any of the below: a. Back/Flank Pain; b. Bluish Tint to Skin (Cyanosis); c. Chest Pain; d. Mental Confusion; e. Nausea; f. Shock; g. Shortness of breath; or h. Vomiting.
7. Allergic Allergic reaction that falls into one of the following categories.		
7.1 Allergic: Local	In the antecubital area.	May include any of the below: a. Itching; b. Rash/Hives; or c. Redness.

DAE Classification	Description	Signs/Symptoms/Findings
7.2 Allergic: Generalized		May include any of 7.1 AND any of the below: a. Itching, Generalized; b. Rash/Hives, Generalized; or c. Sneezing/Nasal Congestion.
7.3 Allergic: Anaphylaxis		May include any of 7.1 AND any of 7.2 AND any of the below: a. Anxiety; b. Arrhythmia; c. Bluish Tint to Skin (Cyanosis); d. Gastrointestinal Symptoms; e. Laryngeal Edema with Stridor; f. Restlessness g. Scratchy Feeling in Throat; h. Shortness of Breath; i. Swollen Tongue, Throat, Eyes, and Face; j. Wheezing; or k. Hypotension. *NOTE:* The term, "Anxiety," as used here, includes <u>significant</u> anxiety and is more than simply being "tense" or verbalizing nervous feelings a new donor may report, such as nervousness about: • needles; • blood; • pain or discomfort; • fainting; • being deferred; or • medical environments.

8. Hyperventilation Hyperventilation that results in any of the following signs and symptoms.		
8.1 Hyperventilation	This reaction: • Is more than simply being "tense" or verbalizing anxious feelings a donor may report, such as nervous about: - Needles; - Blood; - Pain or discomfort; - Fainting; - Being deferred; or - General environment. • Requires medical staff (physician substitute) intervention, OR • Involves signs/symptoms that do not resolve quickly with supportive care and reassurance (e.g. within 10 minutes)	May include any of the below: a. Anxiousness / Anxiety;[3] b. Carpopedal Spasms; c. Chest Tightness; d. Dry Mouth; e. Paresthesia (Perioral - Tingling/Numbness); f. Paresthesia (Peripheral - Hands/Feet); g. Respiration, Rapid; h. Restlessness; i. Shaking; j. Shortness of Breath; or k. Tetany.
[3] If the donor exhibits significant anxiety only resulting from hyperventilation, then classify the event as "8.1 Hyperventilation." If the donor exhibits symptom(s) of "8.1 Hyperventilation" and another event (e.g. citrate), then classify the DAE as the other event.		
9. Other Reaction that does not fall into any other category listed above or in section 10.		
9.1 Other	A reaction that does not fall into any other category listed above	Any

DAE Classification	Description	Signs/Symptoms/Findings
10. Immunization Immunization reaction that falls into one of the following categories.		
10.1 Immunization: Local, mild	Associated with the site of injection	May include any of the below: a. Induration (hardening); b. Itching; c. Nodule formation; d. Pain; e. Rash; f. Redness; g. Swelling; h. Tenderness; or i. Urticaria.
10.2 Immunization: Local, severe	Associated with the site of injection	May include any of 10.1 AND any of the below: a. Brachial Neuritis; b. Infection; or c. Necrosis
10.3 Immunization: Systemic, mild		May include any of the below: a. Arthralgia; b. Diarrhea; c. Dizziness; d. Fatigue; e. Fever; f. Flu-like symptoms; g. Headache; h. Lymphadenopathy (enlarged, sometimes tender lymph glands); i. Malaise; j. Myalgia (muscular pain); k. Nausea; l. Rash, disseminated, diffuse; or m. Vomiting

DAE Classification	Description	Signs/Symptoms/Findings
10.4 Immunization: Systemic, severe	Includes specific reactions related to administration of the vaccine or antigen and the complications that may result as well as life threatening reactions. Immediate medical care is necessary.	May include any of 10.3 AND any of the below: a. Anaphylaxis or anaphylactoid reactions; b. Hemolytic transfusion reaction (when human red blood cells are used as the antigen); or c. Serum sickness See package insert for information on adverse reactions specific to vaccine administered.
10.5 Immunization: Hypotensive (no LOC)	Onset of symptoms considered to be related to an immunization	May include any of 1.1 and 1.2
10.6 Immunization: Hypotensive (LOC)	Onset of symptoms considered to be related to an immunization	May include any of 1.3 and 1.4