

Guidance for Industry

Notifying FDA of Fatalities Related to Blood Collection or Transfusion

FINAL GUIDANCE

Additional copies of this guidance are available from the Office of Communication, Training and Manufacturers Assistance (HFM-40), 1401 Rockville Pike, Rockville, MD 20852-1448, or by calling 1-800-835-4709 or 301-827-1800, or from the Internet at <http://www.fda.gov/cber/guidelines.htm>.

For questions on the content of this guidance contact Lois Simmons at 301-827-6220.

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
September 2003**

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Guidance for Industry

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This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the appropriate FDA staff. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. PURPOSE

This document's goal is to help you, a blood collection or transfusion facility, report fatalities related to blood and blood component (blood) collection or transfusion to us, the Food and Drug Administration (FDA), Center for Biologics Evaluation and Research (CBER). This guidance finalizes the draft guidance of the same title dated June 2002.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA's guidances mean that something is suggested or recommended, but not required.

II. BACKGROUND

The current good manufacturing practice (CGMP) regulations for blood and blood components require that you report fatalities related to blood collection or transfusion to CBER (21 CFR 606.170(b)). Section 606.170(b) states:

When a complication of blood collection or transfusion is confirmed to be fatal, the Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research, shall be notified by telephone, facsimile, express mail, or electronically transmitted mail as soon as possible; a written report of the investigation shall be submitted to the Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research, within 7 days after the fatality by the *collecting facility* in the event of a donor reaction, or by the *facility that performed the compatibility tests* in the event of a transfusion reaction. (Emphasis added)

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Standard operating procedures for compatibility testing are required in 21 CFR 606.151 and 606.100(b)(8). Among other things, that regulation requires an establishment to have procedures both for collecting and identifying the blood samples of recipients, and for demonstrating incompatibility between the donor's cell type and the recipient's serum or plasma type. CBER is aware that some blood banks and transfusion services may enter into contracts with blood centers or other blood banks or clinical laboratories to perform testing on blood samples. If this is how your facility operates, the responsibility for compatibility testing is shared between the blood bank or transfusion service that collects and identifies the blood sample of the recipient, and the blood center or other blood bank or clinical laboratory that uses procedures to demonstrate incompatibility between the donated blood product and the recipient. If a transfusion-related fatality occurs, both the transfusing facility and the blood center or bank that performed the testing under contract would be responsible for reporting the death to CBER. Under these circumstances, the two facilities may make a joint report under § 606.170(b).

III. HOW TO NOTIFY FDA

Section 606.170(b) states that you may report a fatality by telephone, facsimile, express mail, or electronically transmitted mail (e-mail). We recommend that you submit the initial notification by e-mail, if possible, and if you do so, you will receive an e-mail confirmation receipt from us. If e-mail is not feasible, please notify us by telephone or facsimile. We cannot access notification outside of customary working hours unless you use e-mail or telephone. Similarly, we recommend that you submit 7-day follow up reports by e-mail, facsimile, or express mail.

- E-mail: fatalities2@cber.fda.gov
- Telephone/voice-mail number: 301-827-6220
- Fax number: 301-827-6748, Attn: CBER Fatality Program Manager
- Express mail address:
Office of Compliance and Biologics Quality/CBER
Attn: Fatality Program Manager (HFM-650)
1401 Rockville Pike, Suite 200N
Rockville, MD 20852-1448

IV. INITIAL NOTIFICATION

There is no required FDA form or format for notifying us of fatalities related to blood transfusion or blood collection. We recommend that you provide at least the following information so we can evaluate the potential public health significance of the event.

- Date and time of the notification.
 - Your name, title, telephone number with area code, and fax number (if available).
 - Your facility's name, mailing address, and FDA registration number (if applicable).
- NOTE:** Transfusion services that do not routinely collect or process blood or blood components are not required to register with FDA and, therefore, do not usually have a registration number.

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- Age and sex of the deceased.
- Date, time, and cause or suspected cause of death (briefly describe what happened).
- If an autopsy was or will be performed.
- Name and address of facility where the fatality occurred if different from your facility.
- Please also include in the initial notification the information listed in A, B, or C below, as appropriate:

A. Patient/Recipient Fatality

- Transfusion date(s),
- Blood/blood component(s) and unit number(s) of product(s) that may be implicated,
- Name and address of facility(ies) providing the blood, and
- Brief description of events that led to the fatality – include underlying medical condition or disease and circumstances necessitating this hospitalization, reason for transfusion, how the patient initially responded to the transfusion, any medical intervention taken or response to the reaction, and time from initiating the transfusion to patient’s death.

B. Donor Fatality

- Collection date,
- What product was collected or attempted to be collected,
- Whether this was a manual or automated collection,
- If automated, the name and model of collection device and device manufacturer, and
- Brief description of events that led to the fatality – include an overview of the donor’s previous donations/health history, approximate frequency of donation, any unusual events that occurred during this or any previous donation by the donor, any medical intervention taken or response to the reaction, and time from initiating the blood collection to donor’s death.

C. Fatality Associated with Therapeutic Apheresis or Certain Therapeutic Phlebotomies

- Date of therapeutic apheresis (e.g., therapeutic plasma exchange) or therapeutic phlebotomy,
NOTE: A report is required for a therapeutic apheresis fatality *only if* blood products (e.g., plasma, albumin), rather than products such as crystalloids or hydroxyethyl starch, were given as part of the procedure. A report is required for a therapeutic phlebotomy fatality *only if* a blood product was collected for manufacture into transfusable biologics.
- Whether product was collected, and the product’s disposition,
- Whether this was a manual or automated collection (if automated, include manufacturer, name, and model of collection device),
- If any blood product(s) was transfused, identify the product and the unit or lot number(s), and
- Brief description of events that led to the fatality – include underlying medical condition or disease and circumstances necessitating the therapeutic apheresis or

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therapeutic phlebotomy, any medical intervention or response to the reaction, and time from initiating the procedure to patient's death.

V. 7-DAY REPORT

You must submit a written report of the fatality investigation to CBER within 7 days after the fatality (§ 606.170(b)). We recommend that you identify this report as a follow-up on a fatality notification previously reported to CBER and include the initial notification date. We also recommend that this 7-day report provide any new findings or information relevant to the fatality that have become available since the initial notification, including your follow-up investigation and conclusions.

Section 606.170(a) requires that you conduct a "thorough investigation" of adverse reactions relating to blood collection or transfusion. Section 606.170(b) requires submission of a written report of such investigation within 7 days after an adverse reaction resulting in fatality. We recommend that a "thorough investigation," and an associated written report for a fatality, include:

- Discharge summary and/or death certificate,
- Autopsy report (if performed),
- Conclusions and follow-up actions (frequently referred to in the blood community as a corrective action plan), if appropriate, and
- Either A, B, or C listed below, as appropriate.

We understand that, due to the complexity of some fatality investigations, some of this information may not be available when you submit your 7-day report. In that event, you may amend your 7-day report by filing additional information as it becomes available.

A. Patient/Recipient Fatality

- Complete transfusion reaction report, including the manufacturer and lot number of the blood collection system and results of the clerical, serological, and visual re-checks performed.
- Additional relevant documents, include hematology reports; clinical chemistry reports for cardiac and/or liver enzymes, albumin, and bilirubin; viral marker tests; microbiology reports; reports of anti-HLA and/or anti-neutrophil antibody testing; tryptase levels; radiology reports; and physicians' consults/opinions.
- If replacement fluid(s) was given during the transfusion, indicate which fluid(s) and the unit or lot number(s), and include any other relevant information, manufacturer's notices, contamination warnings, or replacement fluid recalls.
- If responsibility for the fatality appears to be outside the blood bank, the nurses' and/or physicians' notes on the patient, radiology reports, and physicians' consults/opinions.
- Results of lookback investigation, including follow-up testing on implicated donor(s) when the fatality was the result of transfusion transmitted infectious disease such as hepatitis or HIV.

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- Meeting minutes or report from your transfusion committee when the fatality was reviewed and discussed. If this incident was reviewed by any other hospital oversight group(s) such as risk management or quality practices, include the report or summary of their findings.

B. Donor Fatality

- The deceased's donor record file that includes the donation just before the fatal incident and information on all donations during the past 2 years.
- Lot numbers and expiration dates of collection sets or harnesses; if replacement fluid(s) was given during the collection, indicate which fluid(s) and the unit or lot number(s) and include any other relevant information, such as manufacturer's notices, contamination warnings, or replacement fluid recalls.
- Performance log for the device and any other relevant performance logs, maintenance records, manufacturer's notices, or recalls on significant machine part(s) on the device/system during the past 2 years.
- If the donor was hospitalized due to the reaction, provide any relevant documents, e.g., reports of laboratory tests, which may help determine the cause of the fatality.

C. Fatality Associated with Therapeutic Apheresis or Certain Therapeutic Phlebotomies

- A summary of the deceased's history of previous therapeutic apheresis or therapeutic phlebotomy procedures, including any previous adverse reactions related to the procedures.
- Lot numbers and expiration dates of collection sets or harnesses; if replacement fluid(s) was given at any time during the procedure, indicate which fluid(s) and the unit or lot number(s) and include any other relevant information, such as manufacturer's notices, contamination warnings, or replacement fluid recalls.
- A summary of the performance log for the device and any other relevant performance logs, maintenance records, and manufacturer's notices or recalls on any significant machine part(s) on the device/system during the past 2 years.
- If the fatality followed therapeutic plasma exchange (TPE) and Fresh Frozen Plasma (FFP) was the replacement fluid, an abbreviated transfusion reaction work-up to rule out ABO incompatibility, bacterial contamination, anaphylactic reaction, or WBC antibody reaction may be useful.

VI. INQUIRIES

If you have any questions about reporting fatalities, please contact the CBER Fatality Program Manager at 301-827-6220.