



e-Network Forum

CALIFORNIA BLOOD BANK SOCIETY

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Does QA Review All Manufacturing Records Prior to Release of Blood Products?

The following question was sent to the e-Network for discussion:

"Prior to the release of products into distribution, are blood collecting facilities (both donor centers and hospital-based donor centers) requiring the QA unit to review all records prior to the release (refer to 21 CFR 211.192)? If so, are you willing to share the description of how this process is performed?"

Here are replies from some **hospital transfusion services** (some may also collect blood):

Hospital #1: We do not have a QA person review all the records before release. This is in the CFR 212's and largely impractical for a hospital. We could not get a syringe out the door before it outdated unless we made every person on staff the QA person for everyone else.

Hospital #2: YES - all records are reviewed prior to issue although not by the QA unit per se (one might say by individuals serving as QA unit agents).

Hospital #3: I work as the Laboratory Coordinator for Quality Assurance at a large hospital complex in Texas. The section of Code of Federal Regulation, Title 21, **Section 211** refers to "Current Good Manufacturing Practice for Finished Pharmaceuticals", and in our opinion does not apply to the production of blood components. Below you'll find the text of the regulation we feel is the appropriate guideline for blood banks. Please let us know if you hear from others with similar, or differing opinions regarding this area, we're always open to learning new things.

[Code of Federal Regulations] [Title 21, Volume 7, Parts 600 to 799] [Revised as of April 1, 2000]
From the U.S. Government Printing Office via GPO Access [CITE: 21CFR606] [Page 42-44]

TITLE 21--FOOD AND DRUGS

PART 606--CURRENT GOOD MANUFACTURING PRACTICE FOR BLOOD AND BLOOD COMPONENTS
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Subpart F--Production and Process Controls

Sec. 606.100 Standard operating procedures.

(a) In all instances, except clinical investigations, standard operating procedures shall comply with published additional standards in part 640 of this chapter for the products being processed; except that, references in part 640 relating to licenses, licensed establishments and submission of material or data to or approval by the Director, Center for Biologics Evaluation and Research, are not applicable to establishments not subject to licensure under section 351 of the Public Health Service Act.

(b) Written standard operating procedures shall be maintained and shall include all steps to be followed in the collection, processing, compatibility testing, storage, and distribution of blood and blood components for transfusion and further manufacturing purposes. Such procedures shall be available to the personnel for use in the areas where the procedures are performed. The written standard operating procedures shall include, but are not limited to, descriptions of the following, when applicable:

- (1) Criteria used to determine donor suitability, including acceptable medical history criteria.
- (2) Methods of performing donor qualifying tests and measurements, including minimum and maximum values for a test or procedure when a factor in determining acceptability.
- (3) Solutions and methods used to prepare the site of phlebotomy to give maximum assurance of a sterile container of blood.
- (4) Method of accurately relating the product(s) to the donor.
- (5) Blood collection procedure, including in-process precautions taken to measure accurately the

quantity of blood removed from the donor.

- (6) Methods of component preparation, including any time restrictions for specific steps in processing.
- (7) All tests and repeat tests performed on blood and blood components during manufacturing.
- (8) Pretransfusion testing, where applicable, including precautions to be taken to identify accurately the recipient blood samples and crossmatched donor units.
- (9) Procedures for investigating adverse donor and recipient reactions.
- (10) Storage temperatures and methods of controlling storage temperatures for all blood products and reagents as prescribed in Secs. 600.15 and 610.53 of this chapter.
- (11) Length of expiration dates, if any, assigned for all final products as prescribed in Sec. 610.53 of this chapter.
- (12) Criteria for determining whether returned blood is suitable for reissue.
- (13) Procedures used for relating a unit of blood or blood component from the donor to its final disposition.
- (14) Quality control procedures for supplies and reagents employed in blood collection, processing and pretransfusion testing.
- (15) Schedules and procedures for equipment maintenance and calibration.
- (16) Labeling procedures, including safeguards to avoid labeling mix ups.
- (17) Procedures of plasmapheresis, plateletpheresis, and leukapheresis, if performed, including precautions to be taken to ensure reinfusion of a donor's own cells.
- (18) Procedures for preparing recovered plasma, if performed, including details of separation, pooling, labeling, storage, and distribution.
- (19) Procedures in accordance with Sec. 610.46 of this chapter to look at prior donations of Whole Blood, blood components, Source Plasma and Source Leukocytes from a donor who has donated blood and subsequently tests repeatedly reactive for antibody to human immunodeficiency virus (HIV) or otherwise is determined to be unsuitable when tested in accordance with Sec. 610.45 of this chapter. Procedures to quarantine in-house Whole Blood, blood components, Source Plasma and Source Leukocytes intended for further manufacture into injectable products that were obtained from such donors; procedures to notify consignees regarding the need to quarantine such products; procedures to determine the suitability for release of such products from quarantine; procedures to notify consignees of Whole Blood, blood components, Source Plasma and Source Leukocytes from such donors of the results of the antibody testing of such donors; and procedures in accordance with Sec. 610.47 of this chapter to notify attending physicians so that transfusion recipients are informed that they may have received Whole Blood and, blood components at increased risk for transmitting human immunodeficiency virus.

(c) All records pertinent to the lot or unit maintained pursuant to these regulations shall be reviewed before the release or distribution of a lot or unit of final product. The review or portions of the review may be performed at appropriate periods during or after blood collecting, processing, compatibility testing and storing. A thorough investigation, including the conclusions and follow-up, of any unexplained discrepancy or the failure of a lot or unit to meet any of its specifications shall be made and recorded.

(d) In addition to the requirements of this subpart and in conformity with this section, any facility may utilize current standard operating procedures such as the manuals of the organizations, as long as such specific procedures are consistent with, and at least as stringent as, the requirements contained in this part.

- (1) American Association of Blood Banks.
- (2) American National Red Cross.
- (3) Other organizations or individual blood banks, subject to approval by the Director, Center for Biologics Evaluation and Research.

[40 FR 53532, Nov. 18, 1975, as amended at 49 FR 23833, June 8, 1984; 55 FR 11013, Mar. 26, 1990; 61 FR 47422, Sept. 9, 1996; 64 FR 45370, Aug. 19, 1999] [[Page 44]]

Sec. 606.110 Plateletpheresis, leukapheresis, and plasmapheresis.

(a) The use of plateletpheresis and leukapheresis procedures to obtain a product for a specific recipient may be at variance with the additional standards for specific products prescribed in this part provided that: (1) A physician has determined that the recipient must be transfused with the leukocytes or platelets from a specific donor, and (2) the procedure is performed under the supervision of a qualified licensed physician who is aware of the health status of the donor, and the physician has certified in writing that the donor's health permits plateletpheresis or leukapheresis.

(b) Plasmapheresis of donors who do not meet the donor requirements of Secs. 640.63, 640.64 and 640.65 of this chapter for the collection of plasma containing rare antibodies shall be permitted only with the prior approval of the Director, Center for Biologics Evaluation and Research.

[40 FR 53532, Nov. 18, 1975, as amended at 49 FR 23833, June 8, 1984; 55 FR 11013, Mar. 26, 1990]



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Ira A. Shulman, MD
CBBS e-Network Forum Editor & Moderator

Posted: December 14, 2000

Addenda: Dec. 15, 2000

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Blood Collection Center replies: (some of these centers may also issue blood for transfusion)

Center #1: We do not have the QA Unit review all results, temperatures and other paperwork before batch review. We have been thinking of doing this but have not devised a system to accomplish this. We would like to know what the other facilities are doing concerning this subject.

Center #2: The QA unit at a very large blood collection center does not perform a review of all records (lot release) prior to the release of blood products. Rather, they do require an **operational review** of the following records prior to product release:

- Donor Registration records
- Hemapheresis donor records
- Apheresis run sheet
- RBC and Plasma Cumulative donation record
- Hemapheresis QC
- QC records-collections, components and hospital services
- Collection packing record
- Laboratory testing records and QC
- Daily record review worksheet
- Quarantine/destruction/ release notification
- SCD record and QC
- Component transformation record
- Automated RBC collection record
- Irradiator log

The QA unit audits this record review process on a regular basis.

Center #3: Processing records are reviewed only by Processing Supervisory staff prior to release for labeling.

Center #4: Yes, actually, we do review all records. Because we send out viral marker testing, we actually have organized the "process of processing the units" such that all reviews are able to be completed prior to the labeling of the unit. An overview of the review process includes:

1. Review of the Donor History cards (this is a second review by staff in the Transfusion Service; the first review occurred by Senior Nursing staff in the Donor Center on the day of collection). If a donor took an aspirin containing medication and platelet concentrates were prepared, that they are appropriately labeled with a "aspirin pool only" label (so they won't be used as a single unit transfused to a neonate, they will only be used in a pool.) All units needing irradiation (DD, etc) are labeled as "to be irradiated" / appropriate "flags" in the computer.
2. Review of Quality Control for reagents used to perform ABO/Rh, antibody screen - QC complete and results are acceptable.
3. Review of the Fractionation log - time of preparation of all components is acceptable; (FFP prepared/frozen solid in appropriate time; platelet concentrates prepared in appropriate time / volume / time on the rotator / etc.); complete tracking of who performed which step in processing / fractionating the unit and when.
4. Comparison of ABO/Rh information provided by the viral marker testing laboratory, as compared to the serologic results obtained from the segment (tested by our laboratory).
5. Review of on-line data; data entered into the computer for ABO/Rh, antibody screen, historical ABO/Rh of the donor; if an antibody screen is positive, that FFP is made into recovered plasma/ appropriate disposition of platelets; appropriate labeling of RBC unit.
6. Review of the Transport log of all coolers delivering the blood from collection site to fractionation area; time of transport and temperature upon receipt / which units arrived in which cooler / all units accounted.
7. Online review and comparison of viral marker test results (this is actually a third review); Verification of data entry.

8. Review of Plateletpheresis QC to verify total platelet yield for all products; verification of preparation of appropriate products (single product has appropriate count, double products truly meet requirements to be a double, etc).
9. Quarantine check - verification that the units in quarantine have a documented reason to be there; all units accounted - no excess units; all documentation complete. Then we go to the labeling process. Disclaimer -- we also have an approx. 40-step process in reviewing the viral marker test results -- looking for prior donations that are in stock that now need to be quarantined, appropriate biohazard labeling of Autologous units, etc, etc. that is on ANOTHER checklist; the "final" processing checklist includes verification that this viral marker checklist has been completed.

Center #5: We require a second person or a computer to review every critical process (including but not limited to history cards, records, product labels).

ADDENDA Dec. 15, 2000

We are a donor center with a centralized transfusion service, collecting about 32,000 units yearly. We recently implemented a standardized format for review of all records prior to release for labeling. Essentially we have created a Process Control form. The donor area signs off after they have reviewed all donor records for the previous day, as well as all QC (scales, temps, Hemacue etc) for each collection site such as mobile and in-house. This form then is forwarded to the lab where another person makes sure that temp QC was done on all blood storage units and centrifuges, and scales were QC'd etc (all equipment that could affect the quality of the component prep or product storage process). After all QC is reviewed this information is passed to the lab staff responsible to review and release donor units based on testing, so that any products deemed unsuitable can be quarantined until investigated.

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Addenda: Dec. 15, 2000