

Requirements for Blood and Blood Components Intended for Transfusion or for Further Manufacturing Use

**Office of Blood Research and Review
CBER, FDA**

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Outline

- Overview
 - Historical Background
 - Intent of the Rule
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 - Relevant Transfusion-Transmitted Infection
 - Control of Bacterial Contamination of Platelets
 - Medical Supervision
 - Donor Acknowledgement
 - Alternative Procedures
 - Donor Eligibility
- Implementation

GAO Oversight and FDA Concerns

- Publish in the form of regulations the guidelines that FDA deems essential to ensure the safety of the blood supply
- Concern about the delay in requiring testing for emerging infectious agents, e.g. HTLV
- Concern about blood safety and the regulations being out-of-date
- Concerns about donor safety

Intent of the Final Rule

- To better assure the safety of the blood supply and to help protect donor health
- To make donor eligibility and testing requirements more consistent with current practices and to provide flexibility with regard to emerging infectious diseases
- To accommodate technological advances
- To establish requirements for donor education, donor history, and donor testing

Organization of the Final Rule - 1

- A. General
- B. Definitions (§§ 606.3, 610.39, 630.3, 640.125)
- C. Standard Operating Procedures (§ 606.100)
- D. Control of Bacterial Contamination of Platelets (§ 606.145)
- E. Records (§ 606.160)
- F. Test Requirements (§§ 610.40, 640.5, 640.71(a))
- G. Donor Deferral (§ 610.41)

Organization of the Final Rule - 2

- H. Purpose and Scope (§ 630.1)
- I. Medical Supervision (§ 630.5)
- J. General Donor Eligibility Requirements (§ 630.10)
- K. Donor Eligibility Requirements Specific to Whole Blood, Red Blood Cells and Plasma Collected by Apheresis (§ 630.15)
- L. General Exceptions from Donor Eligibility Requirements (§ 630.20)

Organization of the Final Rule -3

- M. Exceptions from Certain Donor Eligibility Requirements for Infrequent Plasma Donors (§630.25)
- N. Donation Suitability Requirements (§ 630.30)
- O. Requalification of Previously Deferred Donors (§630.35)
- P. Requirements for Notifying Deferred Donors (§630.40)

Organization of the Final Rule - 4

- Q. Platelets: Eligibility of Donors (§ 640.21)
- R. Source Plasma: Plasmapheresis (§ 640.65(b))
- S. Source Plasma: General Requirements (§640.69)
- T. Source Plasma: Records (§ 640.72)
- V. Alternative Procedures (§ 640.120)

Relevant Transfusion- Transmitted Infection (RTTI)

- Regulatory framework to provide for testing, screening, educational material
- Identifies specific agents
- Provides for the addition of new agents
- Flexible approach
 - Allows for removal of testing and screening
- Incorporates current recommendations

RTTI Definition

§ 630.3 (h) (1) -

- (i) Human immunodeficiency virus, types 1 and 2 (referred to, collectively, as HIV);
- (ii) Hepatitis B virus (referred to as HBV);
- (iii) Hepatitis C virus (referred to as HCV);
- (iv) Human T-lymphotropic virus, types I and II (referred to, collectively, as HTLV);
- (v) *Treponema pallidum* (referred to as syphilis);
- (vi) West Nile virus;
- (vii) *Trypanosoma cruzi* (referred to as Chagas disease);
- (viii) Creutzfeldt-Jakob disease (referred to as CJD);
- (ix) Variant Creutzfeldt-Jakob disease (referred to as vCJD); and
- (x) *Plasmodium* species (referred to as malaria).

RTTI Definition (part 2)

§ 630.3 (h)(2) -

- A transfusion-transmitted infection not listed in paragraph (h)(1) of this section when the following conditions are met:
- (i) Appropriate screening measures for the transfusion-transmitted infection have been developed and/or an appropriate screening test has been licensed, approved, or cleared for such use by FDA and is available; and
- (ii) The disease or disease agent:
 - (A) May have sufficient incidence and/or prevalence to affect the potential donor population; or
 - (B) May have been released accidentally or intentionally in a manner that could place potential donors at risk of infection.

New RTTIs

- FDA would issue draft guidance for public comment to address
 - Appropriate donor screening measures, including medical history assessments, in accordance with § 630.10(e)
 - Appropriate donor testing in accordance with § 610.40(a)(3)
 - Educational materials in accordance with § 630.10(b)

Testing

- An establishment that collects blood and blood components for transfusion or for use in manufacturing a product, including donations intended as a component of, or used to manufacture, a medical device, must comply with the following requirements
 - Test for HIV, HBV, HCV
 - Test for HTLV, syphilis, West Nile virus, and Chagas disease
 - Source Plasma donations do not have to be tested for HTLV, West Nile virus or Chagas disease
 - Source Plasma donors must be tested for syphilis in accordance with 640.65(b)

Flexible Approach to Testing

- Allows for alternate testing schemes when approved by FDA, e.g. one time testing for Chagas disease
- FDA may allow testing to be discontinued for a specific relevant transfusion transmitted infections other than HIV, HBV, and HCV, if testing is no longer necessary to reduce adequately and appropriately the risk of transmission of such infection
 - Factors FDA would consider include epidemiology, geography, or pathogen reduction technology

Control of Bacterial Contamination of Platelets

- Blood collection establishments and transfusion services must assure that the risk of bacterial contamination of platelets is adequately controlled using FDA approved or cleared devices or other adequate and appropriate methods found acceptable for this purpose by FDA
- Allows for use of testing or pathogen reduction technology to control risk
- Donors must be notified of a bacterial infection likely to be endogenous to the blood stream of the donor

Medical Supervision - 1

- Definitions provided for responsible physician, physician substitute, trained person
- *Who must determine the eligibility of a donor?*
The responsible physician must determine the eligibility of a donor of blood or blood components in accordance with this subchapter.

Medical Supervision - 2

- The responsible physician may delegate certain activities to a physician substitute or other trained person
 - The responsible physician need not be present at the collection site provided that the responsible physician has delegated oversight of these activities to a trained person who is adequately trained and experienced in the performance of these activities and is also adequately trained and experienced in the recognition of and response to the known adverse responses associated with blood collection procedures

Medical Supervision - 3

Must rapid emergency medical services be available?

- Establishments that collect blood or blood components must establish, maintain, and follow standard operating procedures for obtaining rapid emergency medical services for donors when medically necessary. In addition, establishments must assure that an individual (responsible physician, physician substitute, or trained person) who is currently certified in cardiopulmonary resuscitation is located on the premises whenever collections of blood or blood components are performed

Donor Acknowledgement

- Prior to each donation, you must provide information to the donor to address:
 - Donor has reviewed educational materials
 - Donor agrees not to donate if potential risk to recipient
 - Sample of blood testing for RTTI
 - Donor will be notified of unsuitable donation
 - Risks and hazards of donation procedure
 - Donor has opportunity to ask questions and withdraw from donation procedure

Donor Acknowledgement

- Information on risks and hazards may be provided in donor educational materials
- Must not include exculpatory language through which donor is made to waive legal rights
- You must establish procedures to assure donor has reviewed materials and provide for donor signature or other documented acknowledgement (electronic signature acceptable)
- Is in addition to informed consent requirements in § 630.15 and § 640.21

Alternative Procedures

- FDA may issue an exception or alternative to any requirement in subchapter F of chapter I of title 21 CFR regarding blood, blood components, or blood products in response to a written or oral request from an establishment. (§640.120 (a))
- To respond to a public health need, the Director CBER may issue a notice of exception or alternative, if a variance is necessary to assure availability (§640.120 (b))
 - To address an urgent and immediate need for blood
 - To provide for appropriate donor screening and testing

Donor Eligibility

- What factors determine the eligibility of a donor?
 - The donor must be in good health and
 - Free from diseases transmissible by blood as required in this chapter
- What factors make the donor not eligible?
 - The donor is not in good health or
 - If you identify any factor(s) that might affect the
 - (1) The health of the donor; or
 - (2) The safety, purity, or potency of the blood or blood component

When Must You Determine the Eligibility of a Donor?

- On the day of donation, and before collection
 - Except if the component cannot be stored for more than 24 hours, you may determine eligibility no more than 2 days before donation
- Incomplete responses regarding the donor's medical history may be clarified within 24 hours of collection
 - Does not include failure to perform or document part of the physical assessment

How Must You Determine the Eligibility of a Donor?

- You must consult the records of deferred donors
 - If you cannot check the cumulative record prior to collection, you must do so before release of the product
- Assure donation interval is appropriate
- Assess the donor's medical history
- Perform a physical assessment of the donor

How Do You Assess the Donor's Medical History?-1

- Before collection, you must conduct a medical history interview
- Assess and identify risk for, or evidence of, a relevant transfusion-transmitted infection
 - Behaviors associated with an RTTI
 - Receipt of blood or blood components or other medical treatments
 - Signs and/or symptoms of an RTTI

How Do You Assess the Donor's Medical History? -2

- Assess and identify risk for, or evidence of, a relevant transfusion-transmitted infection
 - Institutionalization for 72 hours or more consecutively in the past 12 months
 - Intimate contact with risk for a relevant transfusion-transmitted infection
 - Nonsterile percutaneous inoculation

Other Factors Affecting the Donor's Health or Blood Product

- Symptoms of a recent or current illness
- Certain medical treatments or medications
- Travel to, or residence in, an area endemic for a transfusion-transmitted infection
- Exposure to accidentally or intentionally released disease or disease agent
- Pregnancy at the time of, or within 6 weeks prior
- Unreliable answers
 - Donor appears to be under the influence or test seeking
- Xenotransplantation product recipient (products with exposure to *live*, nonhuman cells, tissues or organs)

How Do You Perform a Physical Assessment of the Donor?

- On the day of donation and before collection
- Temperature
 - Not to exceed 37.5 C (99.5F)
- Blood pressure
 - Systolic between 90 and 180 mmHg
 - Diastolic between 50 and 100 mmHg
- Hemoglobin
 - Males \geq 13.0 gm/dL or 39% hematocrit
 - Females \geq 12.5 gm/dL or 38% hematocrit
 - Females \geq 12.0gm/dL or 36% hematocrit with FDA approval

How Do You Perform a Physical Assessment of the Donor?

- Pulse
 - Must be regular and between 50 and 100 beats per minutes
 - A donor with measurements outside these limits may donate only when responsible physician determines and documents that the health of the donor would not be adversely affected by donating
 - Procedures for one time determination by responsible physician for athletic donors with pulse rate less than 50 beats per minute may be acceptable to qualify the donor for future donations
- Weight \geq 110 lbs
- Skin examination

When Must Donors Be Weighed?

- Plasmapheresis donors must be weighed at each donation (630.15 (b)(3))
 - Applies to all plasmapheresis donors, including infrequent plasma donors and when plasma is co-collected with other apheresis components
 - A current weight measurement permits the collecting establishment to calculate accurately the plasma volumes to be collected based on a weight specific nomogram

Exceptions for Certain Ineligible Donors

- Permits donation from certain ineligible donors provided
 - The donation is for autologous use only as prescribed by the donor's physician;
 - The donor has a hemoglobin level no less than 11 grams of hemoglobin per dL of blood or a hematocrit value no less than 33 percent; and
 - The responsible physician determines and documents that the donor's health permits the collection procedure
 - Responsible physician may make this determination by telephonic or other offsite consultation
 - Responsible physician is the best person to determine that the donor's health permits the collection procedure

Implementation of the Rule

- Rule becomes effective May 23, 2016
- If a new requirement is more stringent than the current requirement, you may implement prior to effective date
- Licensed blood establishments
 - We recommend that required submissions be sent to FDA as soon as possible
 - Refer to FDA Guidance for Industry: Changes to an Approved Application: Biological Products: Human Blood and Blood Components Intended for Transfusion or for Further Manufacture (November 2014)
 - For implementation questions, please contact your CSO