DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 606, 610, 630, 640, 660, 820, and 1270

[Docket No. 2006N–0221]

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

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) proposes to revise and update the regulations applicable to blood and blood components, including Source Plasma and Source Leukocytes, to add donor requirements that are consistent with current practices in the blood industry, and to more closely align the regulations with current FDA recommendations. FDA is taking this action to help ensure the safety of the national blood supply and to help protect donor health by requiring establishments to evaluate donors for factors that may adversely affect the safety, purity, and potency of blood and blood components or the health of a donor during the donation process.

DATES: Submit written or electronic comments on the proposed rule by February 6, 2008. Submit comments regarding information collection by December 10, 2007 to OMB (see **ADDRESSES**). See section IV of this document for the proposed effective date of a final rule based on this proposal.

ADDRESSES: You may submit comments, identified by Docket No. 2006N–0221, by any of the following methods:

Electronic Submissions

Submit electronic comments in the following ways:

- Federal eRulemaking Portal: *http://www.regulations.gov*. Follow the instructions for submitting comments.
- Agency Web site: *http://www.fda.gov/dockets/ecomments*. Follow the instructions for submitting comments on the agency Web site.

Written Submissions

Submit written submissions in the following ways:

- FAX: 301–827–6870.
- Mail/Hand delivery/Courier [For paper, disk, or CD–ROM submissions]: Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

To ensure more timely processing of comments, FDA is no longer accepting comments submitted to the agency by e-mail. FDA encourages you to continue to submit electronic comments by using the Federal eRulemaking Portal or the agency Web site, as described previously, in the **ADDRESSES** portion of this document under *Electronic Submissions*.

Instructions: All submissions received must include the agency name and Docket No(s). and Regulatory Information Number (RIN) (if a RIN number has been assigned) for this rulemaking. All comments received may be posted without change to *http://www.fda.gov/ohrms/dockets/default.htm*, including any personal information provided. For additional information on submitting comments see the ''Comments'' heading of the **SUPPLEMENTARY INFORMATION** section of this document.

Docket: For access to the docket to read background documents or comments received, go to *http://www.fda.gov/ohrms/dockets/default.htm* and insert the docket number(s), found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Information Collection Provisions: Submit written comments on the information collection provisions to the Office of Information and Regulatory Affairs, Office of Management and Budget (OMB). To ensure that comments on the information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, FAX: 202–395–6974.

FOR FURTHER INFORMATION CONTACT: Brenda R. Friend, Center for Biologics Evaluation and Research (HFM–17), Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852–1448, 301–827–6210.

SUPPLEMENTARY INFORMATION:

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I. Introduction

A. The Blood Initiative

For a variety of reasons we, FDA, decided to review comprehensively and, as necessary, revise our regulations to include definitions, policies, guidance,

and procedures related to the licensing and regulation of blood products. In the **Federal Register** of June 3, 1994 (59 FR 28821 and 28822, respectively), we issued two documents, ''Review of General Biologics and Licensing Regulations'' (Docket No. 1994N–0066) and ''Review of Regulations for Blood Establishments and Blood Products'' (Docket No. 1994N–0080). These documents announced our intent to review biologics regulations (parts 600, 601, 606, 607, 610, 640, and 660 (21 CFR parts 600, 601, 606, 607, 610, 640, and 660)), and requested written comments from the public. We gave interested persons until August 17, 1994, to respond to the documents. In response to requests for additional time, we twice extended the comment period, as announced in the **Federal Register** of August 17, 1994 (59 FR 42193), and November 14, 1994 (59 FR 56448). In addition, we responded to requests for a public meeting to allow the public to present comments regarding our review of the biologics regulations. At the public meeting on January 26, 1995, interested individuals presented their comments, which assisted us in determining whether certain regulations should be revised, rescinded, or continued without change. Since the time of the regulation review, we have implemented a number of changes to the regulations and policies applicable to the general biologics and licensing requirements, some of which applied to blood products as well as other biological products.

The United States House of Representatives Committee on Government Reform and Oversight, Subcommittee on Human Resources and Intergovernmental Relations (the Subcommittee) and other groups such as the Government Accountability Office (previously, the General Accounting Office GAO), and the Institute of Medicine (IOM), have reviewed our policies, practices, and regulations. Reports issued following the respective reviews made a number of recommendations to improve the biologics regulations, particularly as they apply to assuring the continued safety of blood products. The relevant reports are:

- ''Blood Supply Generally Adequate Despite New Donor Restrictions'' by GAO (July 22, 2002);
- ''Protecting the Nation's Blood Supply From Infectious Agents: The Need for New Standards to Meet New Threats'' by the Subcommittee (August 2, 1996);
- ''Blood Supply: FDA Oversight and Remaining Issues of Safety'' by GAO (February 25, 1997);
- ''Blood Supply: Transfusion-Associated Risks'' by GAO (February 25, 1997); and,
- ''HIV and the Blood Supply: An Analysis of Crisis Decisionmaking'' by IOM (July 13, 1995).

These reports are on file with the Division of Dockets Management (see **ADDRESSES**) under the docket number found in the heading of this document.

We have reviewed these reports and agree with the majority of the recommendations contained within them. We are not describing all the specific recommendations we received and the numerous objectives of the Blood Initiative in this document. However, in response to the GAO recommendations, FDA has completed rulemakings, including the following: (1) Requirements for Testing Human Blood Donors for Evidence of Infection Due to Communicable Disease Agents (66 FR 31146; June 11, 2001); (2) General Requirements for Blood, Blood Components, and Blood Derivatives; Donor Notification (66 FR 31165; June 11, 2001); (3) Revisions to the Requirements Applicable to Blood, Blood Components and Source Plasma, Confirmation in Part and Technical Amendment (66 FR 1834; January 10, 2001); (4) Current Good Manufacturing Practice for Blood and Blood Components; Notification of Consignees and Transfusion Recipients Receiving Blood and Blood Components at Increased Risk of Transmitting HCV Infection (''Lookback'') (65 FR 69378; November 16, 2000); and (5) Biological Products: Reporting of Biological Product Deviations in Manufacturing (65 FR 66621; November 7, 2000, and 65 FR 67477; November 9, 2000 (Correction)). This rulemaking and other notices describe and discuss specific recommendations and regulatory objectives as they apply to each rulemaking.

Through the years, we issued a number of guidance documents containing recommendations intended to assure a safe, pure, and potent blood supply. One objective of this rulemaking is to make more visible the connections between the regulations and current recommendations. In many cases in this preamble, we will describe the general intended meaning of the proposed regulations and will also discuss those recommendations, contained in current guidance, which fall under a proposed regulation. Although it is neither possible nor desirable to codify all the specific details contained in recommendations, we believe the proposed rule will more explicitly describe donor eligibility standards and will clarify the relationship between the regulations and the applicable recommendations.

The Secretary of the Department of Health and Human Services (HHS) seeks to maximize blood safety and blood availability and has designated the Assistant Secretary of Health to be responsible for these issues. The supply of blood is generally adequate to meet medical needs; however, only about 6 percent of the U.S. general public donates blood each year. Periodically, local, regional or national shortages can occur. Although blood establishments are primarily responsible for recruiting and retaining blood donors, HHS plays a key role in monitoring the blood supply to identify potential shortages. Also, the Secretary of HHS has developed a number of initiatives to encourage individuals to donate routinely and during times of shortage or national disasters. In times of acute blood shortage, HHS has sponsored national appeals for blood donation.

Under the HHS Blood Action Plan, HHS and the Public Health Service agencies of HHS act to increase blood availability by removing unnecessary restrictions to blood donation while maintaining the highest level of safety for the recipient. HHS brings donor eligibility issues for discussion at scientific workshops and at FDA scientific advisory committees, including the Blood Products Advisory Committee and the Transmissible Spongiform Encephalopathies Advisory Committee, where we seek advice and scientific-based recommendations. Additionally the HHS Advisory Committee on Blood Safety and Availability provides advice on global public health, economic, social, and ethical issues related to FDA policies on donor eligibility. These discussions have often focused on the impact of donor deferrals on blood availability as well as the safety of blood for the recipient. During the development of policies on donor eligibility, including donor screening, testing and deferral, FDA considers the impact of candidate policies on blood availability and tries to balance anticipated donor loss with safety gained. One example of this balancing approach may be found in FDA's development of a guidance recommending deferral of persons who may have been exposed to the Bovine Spongiform Encephalopathy (BSE) agent (the agent that causes Mad Cow Disease) and thus create an increased risk of transfusion transmission of variant Creutzfeldt-Jakob Disease (vCJD). FDA commissioned the studies that produced the first available data regarding donor travel patterns and used the data to optimize the balance between a

reduction in the risk of transfusion-transmitted vCJD (estimated at 91 percent) and donor loss (estimated at 7 percent).

In developing this proposed rule, FDA has reviewed the proceedings of numerous workshops and advisory committee meetings, mindful of the goals of the HHS Blood Action plan: increasing blood availability by removing unnecessary restrictions to blood donation, while maintaining the highest level of safety for the recipient. For example, we have tried to achieve those goals by our proposal to change labeling requirements for certain donations from patients with hereditary hemochromatosis. This provision would remove a barrier to safe blood collection from these individuals. FDA welcomes comments on the risks and benefits of the donor eligibility criteria proposed in this rulemaking with regard to potential donor loss versus gains in blood product safety and donor safety.

B. Existing Donor Screening Requirements

We have developed five ''layers of safety'' to help ensure a safe blood supply:

- Donor suitability standards (part 640);
- Donor deferral lists (§ 606.160(e));
- Testing blood for communicable disease agents (§ 610.40);
- Quarantining unsuitable blood and blood components (§ 606.40(a)(6)); and
- Monitoring establishments by requiring the investigation of problems in manufacturing (21 CFR 211.192), reporting of fatalities (§ 606.170) and reporting of product deviations (§ 606.171).

The five layers of safety are designed to overlap and help prevent the distribution of blood and blood components that are at increased risk for transmitting infectious agents such as human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV).

In addition to safeguarding against transmission of disease agents from donor to recipient, the current donor suitability standards are designed to prevent harm to a donor from the donation process, and to help ensure the safety, purity, and potency of blood and blood components. Usually, collecting establishments review donor deferral lists to identify, before donation, individuals not eligible to donate. Collecting establishments conduct a prescribed limited physical examination and medical history interview for each donor. These steps are performed to:

- Establish that the donor is in good health;
- Rule out relevant disease infection; and,
- Identify any risk factors that would increase the possibility of transmitting a transfusion-transmitted infection through the donation.

In addition, under § 610.40, a blood sample collected from the donor at the time of donation must be tested for evidence of infection due to communicable disease agents such as HIV and viral hepatitis. By performing these steps, the collecting establishment helps assure the safety, purity, and potency of blood and blood components.

C. Proposed Regulations for Determining Donor Eligibility (Proposed Part 630)

Although we currently have donor suitability requirements applicable to blood and blood components, including Source Plasma and Source Leukocytes, parts 606, 610, 640, and 660, we intend to reorganize and revise current regulations, to make more visible the connections between the regulations and current FDA recommendations, to make them consistent with current practices in the blood industry, and to remove unnecessary or outdated requirements. Based on the recommendations of the 1997 GAO report, ''Blood Supply: FDA Oversight and Remaining Issues of Safety,'' we are issuing in the form of regulations provisions of the memoranda and guidance on donor eligibility that we believe are essential to help ensure the safety of the national blood supply.

Subsequent to the February 1997 GAO report, we conducted numerous workshops to obtain public input. The subjects discussed included for example:

- Screening and testing for evidence of infection due to communicable diseases;
- Donor history of hepatitis;
- Use of a donor deferral registry;
- Donor blood volume;
- Donor deferral based on cancer; and,
- Streamlining the donor history questionnaire.

We have consolidated information from memoranda, guidances, other workshops, advisory committee meetings, current § 630.6 requiring donor notification, and the donor suitability requirements in § 640.3 and 640.63 in developing the requirements for donors of blood and blood components intended for transfusion or for further manufacturing use in proposed part 630. For the purpose of this proposed rulemaking, when the term ''blood and blood components'' is used, Source Plasma and Source Leukocytes are included. We also use the term ''donor eligibility'' when referring to criteria to permit donation. This proposed rule uses the term ''suitability'' only when discussing the acceptability of the donated blood and blood components for transfusion or for further manufacturing use. (For further discussion, see section III.E of this document.)

II. Legal Authority

FDA is proposing to issue this new rule under the authority of sections 351 and 361 of the Public Health Service Act (PHS Act) (42 U.S.C. 262 and 264), and the provisions of the Federal Food, Drug, and Cosmetic Act (the act) that apply to drugs and devices (21 U.S.C. 201 *et seq.*).

The establishment of these criteria for determining the eligibility of a donor of blood and blood components and the suitability of blood and blood components for transfusion or for further manufacturing, is intended to prevent unsafe units of blood or blood components that may transmit a relevant transfusion-transmitted infection from entering the blood supply, while safeguarding the health of donors.

FDA has been delegated authority under section 361 of the PHS Act to make and enforce regulations necessary to prevent the introduction, transmission, or spread of communicable disease from foreign countries into the States or possessions, or from one State or possession into any other State or possession. Intrastate transactions affecting communicable disease transmission may also be regulated under section 361 of the PHS Act (see *Louisiana* v. *Mathews*, 427 F. Supp. 174, 176 (E.D. La. 1977)). FDA recently exercised this authority when the agency issued three rules requiring tissue establishments to register and list the human tissues manufactured; to conduct donor screening and testing; and to manufacture tissues in accordance with good tissue practices, including manufacturing practices, SOPs, recordkeeping, and other practices designed to prevent the transmission of communicable disease (66 FR 5447 (January 19, 2001), 69 FR 29786 (May 25, 2004), 69 FR 68612 (November 24, 2004)).

It is important to recognize that blood manufacturing presents significant risks of communicable disease transmission. As FDA has previously noted, section 361 of the PHS Act authority ''is designated to eliminate the introduction of communicable disease, such as hepatitis, from one state to another. Of

necessity, therefore, this authority must be exercised upon the disease causing substance within the state where it is collected, manufactured, or otherwise found. Thus, the Commissioner of Food and Drugs may promulgate current good manufacturing practice regulations for intrastate blood banking, pursuant to the act, as hepatitis is a communicable disease. Without proper controls, it is likely to spread on an interstate basis.'' (39 FR 18614, May 28, 1974). These statements are equally true today, where the spectrum of disease agents has increased to include, for example, HIV–1 and –2, agents that cause AIDS, and HCV, an additional cause of hepatitis. We understand communicable diseases to include, but not be limited to, those transmitted by viruses, bacteria, fungi, parasites, and transmissible spongiform encephalopathy agents. Preventing the spread of communicable disease is the important purpose underlying the comprehensive regulations for blood establishments now in place, which this proposed rule would somewhat modify and modernize.

Under section 361 of the PHS Act, FDA is authorized to enforce the regulations it issues to prevent the introduction, transmission, or spread of communicable disease interstate through such means as inspection, disinfection, sanitation, destruction of animals or articles found to be so infected or contaminated as to be sources of dangerous infection in human beings, and other measures that may be necessary. In addition, under section 368(a) of the PHS Act, any person who violates a regulation prescribed under section 361 of the PHS Act may be punished by imprisonment for up to 1 year. Individuals may also be punished for violating such a regulation by a fine of up to $100,000 if death has not resulted from the violation or up to $250,000 if death has resulted. For organizational defendants, fines range up to $200,000 and $500,000. Individuals and organizations also face possible alternative fines based on the amount of gain or loss (18 U.S.C. 3559 and 3571(b) through (d)). Federal District Courts also have jurisdiction to enjoin individuals and organizations from violating regulations implementing section 361 of the PHS Act. (See *Califano* v. *Yamasaki*, 442 U.S. 682, 704-05 (1979); *United States* v. *Beatrice Foods Co.*, 493 F.2d 1259, 1271-72 (8th Cir. 1974), cert. denied, 420 U.S. 961 (1975).)

Blood and blood components introduced or delivered for introduction into interstate commerce are subject to section 351 of the PHS Act, which requires that such products be licensed (42 U.S.C. 262). Section 351 of the PHS Act further authorizes FDA, by delegation, to establish requirements for such biologics licenses (42 U.S.C. 262(a)(2)(A)). In addition to its authority under section 361 of the PHS Act, FDA relies on this authority when the proposed regulations would be applied to products subject to biologics license. To obtain a license, applicants must show that the manufacturing establishment meets all applicable standards designed to assure the continued safety, purity, and potency of the blood and blood components, and that the product is safe, pure, and potent. FDA's license revocation regulations provide for the initiation of revocation proceedings if, among other reasons, the establishment or the product fails to conform to the standards in the license application or in the regulations designed to ensure the continued safety, purity, or potency of the product (§ 601.5). Violations of section 351 are punishable by a 1-year term of imprisonment, a fine as described in the preceding paragraph, or both (42 U.S.C. 262(f), 18 U.S.C. 3571).

Blood and blood components are also drugs or devices, as those terms are defined in sections 201(g)(1) and (h) of the act (21 U.S.C. 321(g)(1) and (h); see *United States* v. *Calise*, 217 F. Supp. 705, 708–09 (S.D.N.Y. 1962)); 42 U.S.C. 262(j) (''The Federal Food, Drug, and Cosmetic Act applies to a biological product subject to regulation under this section, except that a product for which a license has been approved * * * shall not be required to have an approved [new drug] application''). Since blood and blood components are drugs or devices generally subject to the act, in issuing these regulations, FDA relies on the act's grant of authority to issue regulations for the efficient enforcement of the act (21 U.S.C. 371(a)). The act requires collecting establishments to comply with the act's current good manufacturing practice provisions and related regulatory scheme. Under section 501 of the act (21 U.S.C. 351), drugs, including blood and blood components, are deemed ''adulterated'' if the methods used in their manufacturing, processing, packing, or holding do not conform with current good manufacturing practice (21 U.S.C. 351(a)(2)(B)). Devices are deemed ''adulterated'' if the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformity with good manufacturing practice requirements established by FDA in regulations (21 U.S.C. 351(h) and 360j(f)(1)). We propose to specify that the provisions of the proposed rule are critical aspects of good manufacturing practice. The proposed rule would require collecting establishments to assure that donors of blood and blood components meet the essential criteria for eligibility, and that blood and blood components are suitable for transfusion or further manufacturing. Blood and blood components not manufactured in accordance with good manufacturing practice, including the provisions of the proposed rule, would be considered adulterated under 21 U.S.C. 351(a)(2)(B) or 21 U.S.C. 351(h) and 360j(f)(1), and collecting establishments and blood and blood components would be subject to the act's enforcement provisions for violations of the act. These include seizure of violative products (section 304 of the act) (21 U.S.C. 332)), injunction against ongoing and future violations, and criminal penalties (section 303 of the act) (21 U.S.C. 333 and 18 U.S.C. 3571)). The act punishes both misdemeanor and felony violations of the act. Misdemeanor violations are punishable by a term of imprisonment of up to 1 year, a fine as described previously, or both. (21 U.S.C. 333(a)(1), 18 U.S.C. 3571). Individuals convicted of felony violations may be sentenced to a term of imprisonment of up to 3 years, a fine of up to $250,000, or both. Organizations convicted of felony violations may be sentenced to a fine of up to $500,000. Individuals and organizations also face possible alternative fines based on the amount of gain or loss (18 U.S.C. 3571(b) through (d)).

III. Summary of the Proposed Rule

A. General Description

The proposed regulations in subparts A, B, and C of part 630 would apply to you, establishments that collect and process blood and blood components. The proposed rule would add donor requirements for blood and blood components, including Source Plasma and Source Leukocytes, to make them consistent with current practices in the blood industry. The proposed regulations also would assemble into one part certain current provisions applicable to determining the eligibility of a donor. These general regulations would apply to any blood and blood component intended for transfusion or for further manufacturing use, including Source Plasma and Source Leukocytes, and those blood and blood components used in the manufacture of a medical device. We are proposing a new title for part 630 to reflect this application. For purposes of this document, whenever

we discuss blood and blood components, the source is human.

B. Standard Operating Procedures (SOPs) (Proposed § 606.100(b))

We propose to clarify current § 606.100(b) to state that you must not only establish and maintain, but must also follow written procedures, in accordance with all applicable regulations for all steps in the collection, processing, compatibility testing, storage and distribution of blood and blood components intended for transfusion and for further manufacturing use. We propose to distinguish the types of transfusions as ''allogeneic'' and ''autologous.'' We also propose to add, to current § 606.100(b), language making explicit the requirement that you establish, maintain, and follow SOPs for investigating product deviations (§ 606.171), and for recordkeeping related to current good manufacturing practice requirements (part 606) and biological product standards (part 610).

C. Records (Proposed § 606.160(e))

Current § 606.160(e) requires collecting establishments to have records available to identify unsuitable donors and prevent the distribution of blood and blood components collected from such individuals. This is sometimes accomplished by establishing a coding system, which allows personnel to identify a donor as ineligible without revealing the reason for the deferral to those who do not have a need to know the information. We propose to continue this requirement in § 606.160(e), which would require establishments to maintain a record of donors determined to be ineligible to donate in order to prevent the collection of blood or blood components from such individuals while they are ineligible or deferred. We also are proposing in § 606.160(e)(2) that all donor screening locations of a collecting establishment operating under a common organization, e.g., under the same license number, use a collective master list of donors determined at each location to be ineligible to donate. This list is also known as a donor deferral registry. Under proposed § 630.10(d)(1), the collecting establishment would be required to review the donor deferral registry before collection to prevent the collection of blood and blood components from donors deferred from donation temporarily (when the temporary deferral is in effect when the donor presents), indefinitely, or permanently.

Under proposed § 606.160(e)(2), we are proposing to limit entry into the shared donor deferral registry to those donors who are determined to be ineligible to donate due to a possible exposure to a relevant transfusion-transmitted infection (proposed § 630.10(f)), or to certain other factors that may adversely affect the health of the donor, or the safety, purity, or potency of the blood or blood component (proposed § 630.10(g)(1) through (g)(6)). We are interested in receiving comments on:

- The information that should be included on a donor deferral registry used in common by all donor screening locations of a collecting establishment operating under a common organization (e.g., under the same license number);
- The adequacy of the criteria listed in proposed § 630.10(f) and (g)(1) through (g)(6) to prevent the collection of blood and blood components that may be harmful to the donor or that may result in an unsuitable product due to possible exposure of the donor to a transfusion-transmitted infection; and
- The technical feasibility of complying with the proposed requirement.

We are also seeking comments on the feasibility of sharing donor deferral lists between licensed establishments for deferrals required by the FDA. Such national deferral registries have existed for Source Plasma collections for many years.

Proposed § 606.160(e) would help prevent the collection of unsuitable blood and blood components and reduce recipients' exposure to blood and blood components with an increased risk of transmitting an infectious agent. For example, under proposed § 606.160(e)(2), if a collecting establishment collected blood at four locations and three mobile sites, donors deferred from further donation at any of the seven sites would be listed on a donor deferral registry available at all seven sites. The requirement to review the record of ineligible donors before collection and to make the record of ineligible donors available to collecting establishments operating under a common organization would improve blood safety by reducing the likelihood of accidental release of potentially infectious units. We discussed the practice of reviewing a donor deferral registry before the collection of blood and blood components at the Blood Product Advisory Committee meeting of October 20, 1994, and recommended the practice in the guidance document entitled ''Guideline for Quality Assurance in Blood Establishments'' (60 FR 36290, July 14, 1995).

We are considering whether to include, in the final rule, a provision requiring that donor deferral records be used and disclosed only for purposes consistent with subchapter F of 21 CFR Chapter I.

- We request comment on this proposal, including the following specific issues:

Whether the current practices and protections adequately protect the confidentiality of donor records;

Whether those current practices and protections will still be adequate if FDA requires that establishments make donor deferral records available at all collection sites operating under the same license or common management; and

Whether a regulation limiting the use and disclosure of such records would actually further the goal of protecting the confidentiality of the records.

In addition, we request comment on the following:

We believe that few, if any, blood collection establishments are HIPAA-covered entities under the HIPAA Privacy Rule. However, to evaluate the impact of this rule on any such HIPAA-covered entities, we are seeking public comment from any facilities that may be covered by the HIPAA Privacy Rule, regarding whether or how HIPAA requirements may impact their ability to comply with this proposed rule.

D. Testing Requirements (Proposed § 610.40(a) and (e) and § 630.30(a)(5))

1. Testing for Relevant Transfusion-transmitted Infections

Section 610.40(a) requires that a collecting establishment test each donation of blood or blood component intended for transfusion or for further manufacturing use in preparing a product for evidence of infection due to the listed communicable disease agents. We are proposing to revise § 610.40(a) by replacing ''communicable disease agents'' with ''relevant transfusion-transmitted infections described in § 630.3(g).'' This change would require testing and, where appropriate, screening, for additional relevant transfusion-transmitted infections that present a potential risk to the health of the recipient and for which appropriate testing methods are available. Donor screening or testing for a relevant transfusion-transmitted infection may vary based on the characteristics of the blood product. For example, we do not currently require testing of Source Plasma for human T-lymphotropic virus (type I or II) because the virus is cell-associated and readily removed and inactivated during manufacturing. Similarly, testing for another relevant transfusion-transmitted infection may

not be required if viral inactivation or removal procedures have been validated to ensure inactivation or removal of the infectious agent and screening for risk factors is available, unless the risk of harm from transmission is too great to rely solely on viral inactivation procedures and screening for risk factors.

2. Testing Further With One or More Supplemental (Additional, More Specific) Test(s)

When a donation is found to be reactive by a screening test, § 610.40(e) currently requires that the establishment further test the donation with a supplemental (additional, more specific) test approved for such use by FDA. In proposed § 610.40(e), we are proposing to require that additional testing may be performed with additional tests that are not necessarily ''more specific'' provided that the additional test(s) is appropriate to determine the donor's infection status prior to notification. At a meeting of the Blood Products Advisory Committee (BPAC) on March 18 and 19, 2004, the committee heard presentations on alternative algorithms for additional testing for HIV and HCV after an initially reactive screening test. The committee recommended that FDA reconsider its requirement that supplemental testing be performed using more specific tests. At that meeting, industry representatives provided information on the need for and the use of alternative testing algorithms to confirm the deferred donor's infection status that involved the use of more than one enzyme immunoassay (EIA) screening test, including the use of multiple EIA screening tests in lieu of a supplemental test. A Public Health Service (PHS) working group reviewed the data presented at the March 2004 BPAC and all available data and concluded that when donor screening tests were reactive for antibody to HIV and reactive on an individual HIV–1 nucleic acid test (NAT) test, supplemental testing for HIV antibody was not necessary. A similar conclusion that supplemental testing for HCV was not necessary was reached for donor screening tests that were reactive for antibody to HCV and reactive on an individual HCV NAT test. However, the PHS working group was unable to recommend the use of multiple EIA screening tests in lieu of the HIV–1 or HCV supplemental tests when the individual HIV–1 or HCV NAT test was non-reactive.

The intent of this section is to allow for the use of multiple screening tests to ''confirm'' infection or to provide additional information on the presence of the analyte when described in guidance, as appropriate. It is not FDA's intention to move away from confirmatory or supplemental testing where such an approved test exists, but rather to recognize that under certain circumstances alternative testing schemes may provide confirmatory or supplemental testing information. In the case of HIV NAT, FDA has allowed the HIV–1 Western Blot not to be performed when the HIV EIA is reactive and HIV NAT is positive. If the HIV NAT is negative, the Western Blot must still be performed. If this rule is finalized, we intend to make initial recommendations for additional testing algorithms in draft guidance issued for public comment.

3. Testing for Bacterial Contamination for Platelets and Other Transfusible Blood Components

Bacteria remain a significant contaminant in blood and blood components (Ref. 1). Bacterial contamination of platelets has been discussed at an FDA workshop held on September 24, 1999, at the December 2002 BPAC meeting, and at the April 2004 meeting of the Public Health Service Advisory Committee on Blood Safety and Availability. AABB (formerly known as the American Association of Blood Banks) established an accreditation standard, effective March 2004, requiring accredited blood banks and transfusion services to have methods to limit and detect bacterial contamination in all platelet components. Currently, bacterial detection is being performed using a variety of methods, including FDA-approved quality control tests. However, we are proposing in § 630.30(a)(5) that a platelet component would not be suitable until tests for bacterial contamination are found negative. (See section III.L of this document.) In some instances, specific bacteria identified as contaminants in a blood component could indicate an underlying bacteremia or serious illness in the donor. Therefore, we are also soliciting comments on: (1) Whether to require, in the context of testing of platelet components prior to release, the identification of the species of the bacterial contaminant and (2) whether to require donor deferral and notification when identification of the contaminant indicates possible endogenous bacteremia, and not contamination during collection and processing. Additionally, we are also considering whether to extend, to other blood components for transfusion, the requirement for testing for bacterial contamination, and donor deferral and notification based on the results. We also invite comment on this issue.

E. Purpose and Scope (Proposed § 630.1)

The proposed rule would require that a blood establishment make two determinations: (1) The donor is eligible to donate and (2) the donation is suitable for use in transfusion or further manufacturing use. The proposed requirements in part 630 would provide criteria for the collecting establishment to use to determine the eligibility of the donor to donate. We would require that the collecting establishment determine on the day of donation that the donor is in good health and is not deferred from donating. Proposed § 630.1 also makes reference to previously issued requirements in part 630 that describe the process for notifying donors of their deferral due to failure to satisfy the eligibility criteria or test results for relevant transfusion-transmitted infections required under § 610.40.

This proposed rule would apply to any establishment or facility that collects any blood or blood component from donors:

- For transfusion, including autologous use;
- For further manufacturing use; or
- For use as a component of a medical device.

Creating this separate part for donor eligibility requirements for donors of blood and blood components would allow for a consistent set of criteria for all individuals participating in various collection programs.

F. Definitions (Proposed § 630.3)

Section 630.3(a) through (l) of the proposed rule contains proposed definitions of terms specifically used in this rulemaking.

We are proposing in § 630.3(a) and (b) to define *blood* and *blood component* as used in part 630. We would define blood as a product and describe the product as a fluid containing dissolved and suspended elements, which circulates in a human's vascular system. *Blood component* also would be defined as a product, and described as containing a part of blood separated by physical or mechanical means.

In proposed § 630.3(e), the definition for *intimate contact* is intended to help you determine whether the donor is at risk for contracting a transfusion-transmitted infection from another individual who may be infected with a transfusion-transmitted infection.

We are defining *relevant transfusion-transmitted infection* in proposed § 630.3(g)(1) to identify the currently recognized disease agents that are

associated with transmission from the donor to the recipient by transfusion, infusion, or injection of a blood component or blood derivative and for which there are appropriate screening and/or testing measures available. These are: HIV, types 1 and 2; HBV; HCV; human T-lymphotropic virus (HTLV), types I and II; *Treponema pallidum* (syphilis); Creuztfeldt-Jakob disease (CJD), variant Creutzfeldt-Jakob disease (vCJD); and *Plasmodium sp.* (malaria).

In the proposed rule entitled ''Requirements for Testing Human Blood Donors for Evidence of Infection Due to Communicable Disease Agents'' (64 FR 45340, August 19, 1999), we solicited comments, with supporting data, from the public in regard to the value of donor testing for syphilis as a marker of increased risk behavior, as a surrogate test for other infectious diseases, and in preventing the transmission of syphilis through blood transfusion. After reviewing the comments and submitted scientific data, we determined that the comments did not provide sufficient supporting data to justify eliminating the requirements for screening and testing the donor for syphilis. We continue to consider this issue, including any further studies that address the issues of transfusion-related syphilis infection or testing for syphilis as a surrogate marker for other communicable diseases; and we again request comments and data concerning whether establishments could discontinue syphilis testing without adversely affecting the safety of the blood supply. If we receive adequate data, we will eliminate or modify this testing requirement in the final rule.

The second part of the definition in § 630.3(g)(2), proposes criteria for identifying additional disease agents that present a risk of transmission from the donor to the recipient by transfusion of blood or blood components. This risk would include disease and disease agents with a known, presumptive, or theoretical risk of infection through transfusion, such as West Nile virus. (See ''Guidance for Industry: Assessing Donor Suitability and Blood and Blood Product Safety in Cases of Known or Suspected West Nile Virus Infection,'' dated June 2005.) To be a relevant transfusion-transmitted infection, a disease agent or disease must meet all of the following criteria:

- The disease agent or disease must present a significant health risk that could be fatal, life-threatening, cause permanent impairment of a body function or damage to body structure, or necessitate medical intervention to preclude such impairment or damage; and
- There must be appropriate screening and/or testing methods available; and
- The disease agent or disease must present a risk of transmission by the transfusion of the blood or blood component collected, or by the use of a blood derivative product manufactured from collected blood or blood components, to the potential recipient. The disease agent or disease must be potentially transmissible by that blood, blood component, or blood derivative product; and either have sufficient incidence and/or prevalence to affect the potential donor population; or have been accidentally or intentionally released in a manner that would place donors at risk of infection, such as a bioterrorism attack or laboratory accident that releases an agent, e.g., anthrax or smallpox, into the population.

We are also proposing in § 630.3(k) a definition for *transfusion-transmitted infection*. This definition would include any transfusion-transmitted disease not included under proposed § 630.3(g). The criteria for a transfusion-transmitted infection are as follows:

- The transfusion-transmitted infection must present a significant health risk that could be fatal, life-threatening, cause permanent impairment of a body function or damage to body structure, or necessitate medical intervention to preclude such impairment or damage; and
- The disease agent or disease may present a risk of transmission by the transfusion of the blood or blood component collected, or by the use of a blood derivative product manufactured from collected blood or blood components, to the potential recipient.

The definition of a transfusion-transmitted infection differs from a relevant transfusion-transmitted infection in that the existence of sufficient incidence and/or prevalence to affect the potential donor population is not a part of the definition. Available screening and testing methods may also be limited. One example of such a transfusion-transmitted infection is leishmania.

It is our intention to issue guidance following the good guidance practices in 21 CFR 10.115 to advise you when we believe that a new disease agent or disease meets the criteria for a relevant transfusion-transmitted infection, and that we recommend that you take steps to screen and/or test donors of all or certain blood components for that particular risk of transmission. The criteria expressed in this provision would support such a notification only when there is a significant concern. Moreover, good guidance practices provide the public with an opportunity to comment on guidance before its implementation, unless prior public participation is not feasible or appropriate, e.g., in a public health emergency. In addition, we intend to hold public meetings and/or consult with advisory committees where appropriate, to help us determine whether a disease agent or disease meets these criteria, and whether FDA should recommend that establishments perform donor screening and/or testing for it.

We believe that the issuance of such guidance will assist collecting establishments, especially small establishments that are not able to track emerging disease agents and diseases in a timely manner. By providing these notifications, we will perform an important communications function and assist collecting establishments in meeting their regulatory obligations to screen and test donors.

Donor, as used in the proposed regulation in § 630.3(c), is defined to include a person who is a potential candidate as well as a person who completes the act of donation.

We are defining *eligibility of a donor* in proposed § 630.3(d) and *suitability* of *the donation* in proposed § 630.3(i) so as to distinguish between the acceptability of a donor for donation and the acceptability of the donation for transfusion or for further manufacturing use.

We have defined *physician substitute* in proposed § 630.3(f), *responsible physician* in proposed § 630.3(h), and *trained personnel* in proposed § 630.3(j) according to the education and qualifications required to fulfill the position description.

You, in proposed § 630.3(l), is defined so as to establish who must comply with the requirements in proposed part 630.

G. Medical Supervision (Proposed § 630.5)

In § 630.5, we are proposing to include requirements prescribing the level of medical supervision at collecting establishments responsible for determining the eligibility of a donor, collecting blood and blood components, or performing other procedures with significant implications for both the continued health of donors and the safety of the blood supply. Proposed § 630.5 would:

- Apply to the collection of blood and blood components;
- Amend, combine, and redesignate certain regulations; and
- Codify certain recommendations currently in guidance documents.

Except as provided otherwise, proposed § 630.5(a) would require you to authorize a responsible physician, who is trained and qualified, to determine the eligibility of a donor of blood or blood components in accordance with part 630. We would require that each collecting establishment have a qualified physician on the premises when determining donor eligibility, immunizing donors for the purpose of producing high-titer plasma, collecting Whole Blood or blood components, and returning red blood cells to the donor.

Proposed § 630.5(b) would consolidate these requirements, and would require collecting establishments to have a responsible physician present during the determination of eligibility of a donor, the collection of blood and blood components, the collection of Source Plasma from ineligible donors in an approved program, the return of red blood cells to the donor, and the immunization of donors. The responsible physician would:

- Direct and control the physician substitutes and trained personnel; and
- Approve procedures concerning the determination of donor eligibility, the collection of blood and blood components, the immunization of a donor, and the return of red blood cells or other blood constituents to the donor during apheresis.

Proposed § 630.5(c) would permit a collecting establishment to authorize a physician substitute to perform the same functions of a responsible physician in the collection of Source Plasma, except the responsible physician would be required to be present for red blood cell immunizations. Many plasma collecting establishments currently have FDA approval under alternative procedures regulations in § 640.120 for the use of a physician substitute program for a variety of activities. These include supervising the collection of Source Plasma from donors who meet all normal donor suitability requirements, and for the scheduling and administration of the injection of a licensed vaccine for the production of high titer plasma. However, the responsible physician is required to be present during red blood cell immunization and high-risk collections. This proposed rule is consistent with these alternative procedures and with our recommendations issued in the August 15, 1988, memorandum to all plasma establishments entitled ''Physician Substitutes.'' We believe that the use of a physician substitute is adequate to help ensure the continued safety of Source Plasma donors and that the Source Plasma collected from these donors is safe, pure, and potent.

Proposed § 630.5(d) would permit collecting establishments to authorize trained personnel, including physician substitutes, to determine the donor's eligibility and collect blood and blood components in the absence of a responsible physician. Under § 606.100(b), we would require the collecting establishment to establish, maintain, and follow SOPs specifying criteria for determining donor eligibility, and for the collection of blood and blood components.

The collecting establishment would be required in proposed § 630.5(e) to have SOPs for providing emergency medical services to a donor within 15 minutes when necessary. Although we currently require the presence of appropriately trained medical personnel, our current regulations do not directly address the availability of emergency medical services, which a donor may require. We are interested in receiving comments on what would be considered as appropriate for available emergency medical services.

H. General Donor Eligibility Requirements (Proposed § 630.10)

We propose in § 630.10 to require certain steps for determining the eligibility of a donor to donate blood and blood components. In proposed § 630.10(a), a collecting establishment would be required to perform these prescribed steps, or assessments, to determine if the donation may adversely affect:

- The health of the donor or
- The safety, purity, or potency of blood or blood components.

We are proposing to combine and revise the donor suitability requirements in §§ 640.3 and 640.63 and to redesignate these requirements as § 630.10. Proposed § 630.10 would contain the requirements for determining the eligibility of the donor to donate blood and blood components, whether intended for transfusion or for further manufacturing use.

1. Educational Material

In § 630.10(b), we propose to require collecting establishments to provide to all donors, before donation, information about the relationship among behaviors that increase risks of relevant transfusion-transmitted infections, signs and symptoms of such infections, and the consequent risk to the safety of the blood and blood component. This information may be provided in oral, written, or multimedia form in a manner designed to be understood by the donor, in appropriate language and literacy level and taking into account any disabilities. When screening for behavioral risk factors is required for a relevant transfusion-transmitted infection (for example, HIV, HBV, or HCV), the material would instruct donors to self-defer if they determine that they have participated in an increased-risk behavior for, or show signs or symptoms of, that relevant transfusion-transmitted infection. Currently, we recommend that establishments provide educational material to inform potential donors of the risks of HIV transmission and the need to self-defer. The current recommendations for educational material are described in the memorandum entitled ''Revised Recommendation for the Prevention of Human Immunodeficiency Virus (HIV) Transmission by Blood and Blood Products,'' issued April 23, 1992. We intend to issue additional guidance on educational material in the future. The proposed rule would also require that educational material include behavioral risks and signs and symptoms for hepatitis and other relevant transfusion-transmitted infections determined to present a risk to the blood supply. We are soliciting comments on this provision, particularly on how comprehensive the educational material should be and the format or style in which it is presented.

2. Assessment of the Donor's Eligibility to Donate

Current § 640.3 requires that the donor be in good health and that the collecting establishment determine the donor's suitability for donation on the day of collection. The status of the donor's health is determined by performing a prescribed physical examination, and the donor may not serve as the source of Whole Blood more than once in 8 weeks.

Proposed § 630.10(c) would require that the collecting establishment perform an assessment of the donor's eligibility on the day of donation, and before collection. An exception would be allowed for the collection of blood components that cannot be stored for more than 24 hours, such as granulocytes for transfusion. For such components, the collecting establishment may perform a donor assessment and the testing required under § 610.40(a) and (b) 1 day before the collection of such products. Establishments would be required to have SOPs in place to identify such components.

In proposed § 630.10(d), determination of a donor's eligibility to

donate would consist of four assessments:

- Assessing the donor's deferral status;
- Assuring that the donation interval is appropriate, taking into account whether the donor is participating simultaneously in other blood or blood component collection programs;
- Assessing the donor's medical history; and
- Assessing the donor's health by performing a physical assessment of the donor.

Consistent with the good guidance practice regulations, we intend to issue guidance on determining the eligibility of a donor of blood and blood components. The guidance document would represent our current thinking on describing the assessment factors, signs, and symptoms, and recommended deferral periods to be included in a medical history questionnaire and a physical examination.

a. *Deferral status and donation history.*

After the donor has reviewed the educational material and does not self-defer, under proposed § 630.10(d)(1) the collecting establishment would check the donor deferral registry to determine whether the donor is deferred temporarily, indefinitely or permanently. (See section III.C of this document.) If the donor is deferred from allogeneic donation indefinitely, or permanently, or the temporary deferral period has not expired, the donor is ineligible to donate. Donor deferrals are based on the degree of risk to the donor's health, or the safety, purity, and potency of the donated blood or blood components. Under proposed § 630.10(d)(2), the collecting establishment would check the donor's most recent donation to assure that the donation interval is appropriate for the type of donation, as described in proposed § 630.15(a)(1) (Whole Blood), and § 640.22(b) (Platelets) and 640.65(b)(4) (Plasmapheresis) (§§ 640.22(b) and 640.65(b)(4)). In the interest of donor protection, we are proposing to include in proposed § 630.10(d)(2) the requirement that the establishment take into account whether the donor is participating in other blood or plasma collection programs, which could put the donor at risk by possible over-collection of a blood component. This is currently recommended in a blood memorandum dated March 10, 1995, to registered blood and Source Plasma establishments entitled ''Revision of FDA Memorandum of August 27, 1982: Requirements for Infrequent Plasmapheresis Donors.''

b. *The donor's medical history.*

Proposed § 630.10(e) would require the collecting establishment to establish that the donor is in good health. This is usually accomplished by administering an appropriate medical history questionnaire in oral, written, or multimedia form, and taking into account any disabilities using appropriate language and literacy level, to the donor on each day of donation. With frequent donation, e.g., frequent Source Plasma donations, an appropriate abbreviated questionnaire may be used if it adequately captures necessary donor medical history. The use of an abbreviated donor history questionnaire was discussed at the Blood Products Advisory Committee meeting held on December 11, 2003.

The questionnaire would enable the collecting establishment to do the following:

- Determine if the donor is in good health and if healthcare practitioners have advised the donor not to donate;
- Identify risk factors for relevant transfusion-transmitted infections;
- Determine the possibility of exposure to, or clinical evidence of, relevant transfusion-transmitted infections; and
- Determine whether there are other conditions that may adversely affect the donor or the safety, purity, or potency of the donated blood or blood component, such as by examining the phlebotomy site for infection or inflammation which may cause contamination of the unit being collected.

Proposed § 630.10(f) and (g) describe factors that make a donor ineligible to donate and that must be addressed in medical history questions.

Proposed § 630.10(f).—Proposed § 630.10(f) would require the collecting establishment to assess the donor for certain described factors, which may indicate that the donor is at increased risk for, or has evidence of, a relevant transfusion-transmitted infection; and to determine the donor ineligible to donate when the assessment indicates possible exposure to a relevant transfusion-transmitted infection that is still applicable at the time of donation. These factors are listed in proposed paragraphs (f)(1) through (f)(6). In addition to the following discussion of these factors, we refer you to the following current Memoranda to Blood Establishments and Blood Guidances, which discuss factors related to exposure to a relevant transfusion-transmitted infection. The draft guidances included in the following bulleted list, when finalized, will represent FDA's current thinking on those topics.

- ''Recommendations for the Management of Donor and Units that are Initially Reactive for Hepatitis B Surface Antigen (HBsAg),'' dated December 2, 1987;
- ''FDA Recommendations Concerning Testing for Antibody to Hepatitis B Core Antigen (Anti-HBc),'' dated September 10, 1991;
- ''Revised Recommendations for the Prevention of Human Immunodeficiency Virus (HIV) Transmission by Blood and Blood Products,'' dated April 23, 1992;
- ''Revised Recommendations for Testing Whole Blood, Blood Components, Source Plasma and Source Leukocytes for Antibody to Hepatitis C Virus Encoded Antigen (Anti–HCV),'' dated April 23, 1992;
- ''Draft Guidance for Industry: Revised Recommendations for Donor and Product Management Based on Screening Tests for Syphilis,'' dated June 2003;
- ''Recommendations for the Deferral of Current and Recent Inmates of Correctional Institutions as Donors of Whole Blood, Blood Components, Source Leukocytes, and Source Plasma,'' dated June 8, 1995;
- ''Guidance for Industry: Revised Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Blood and Blood Products,'' dated January 2002;
- Draft ''Guidance for Industry: Recommendations for Donor Questioning Regarding Possible Exposure to Malaria,'' dated June 2000;
- ''Guidance for Industry: Recommendations for Assessment of Donor Suitability and Blood and Blood Product Safety in Cases of Possible Exposure to Anthrax,'' dated October 2001;
- ''Guidance for Industry: Assessing Donor Suitability and Blood and Blood Product Safety in Cases of Known or Suspected West Nile Virus Infection,'' dated June 2005;
- ''Guidance for Industry: Recommendations for Deferral of Donors and Quarantine and Retrieval of Blood and Blood Products in Recent Recipients of Smallpox Vaccine (Vaccinia Virus) and Certain Contacts of Smallpox Vaccine Recipients,'' dated December 2002; and
- ''Guidance for Industry: Revised Recommendations for the Assessment of Donor Suitability and Blood Product Safety in Cases of Suspected Severe Acute Respiratory Syndrome (SARS) or Exposure to SARS,'' dated September 2003.

These memoranda and guidance documents further discuss the applicability of these factors in donor screening. All current memoranda and guidance documents referenced in this rulemaking may be found at *http://www.fda.gov/cber/reading.htm*.

Social behaviors (Proposed § 630.10(f)(1)).—Under proposed § 630.10(f)(1), establishments must determine whether a donor has engaged in social behaviors associated with increased risk of infection with relevant transfusion-transmitted infections. Some examples of social behaviors associated with increased risk of exposure to HIV and viral hepatitis identified in current guidance are men who have had sex with another man even one time since 1977; exchanging sex for drugs or money; or intravenous drug use. Participation in social behaviors associated with relevant transfusion-transmitted infections would cause the donor to be ineligible to donate and to be deferred. We have issued guidance on such deferrals and we will continue to do so, pursuant to our good guidance practices. We include assessment of certain social behaviors because of the risk that testing alone would not detect infection due to testing error, the early stage of the donor's infection (the window period), or the donor's low antibody level or intermittent viremia.

To assist us in developing such guidance documents, we intend to hold workshops and public meetings on social behaviors associated with increased risk of infection with a relevant transfusion-transmitted infection. The public will have the opportunity to submit comments on specific issues as they are presented.

Medical treatment and procedures (Proposed § 630.10 (f)(2)).—We are proposing that you assess donors to determine whether they have received medical treatment or undergone a medical procedure that would put the individual at risk for potential exposure to a relevant transfusion-transmitted infection. Such donors would be ineligible to donate. Some examples of treatments or procedures that may transmit a disease or disease agent are receipt of dura mater graft, transfusion with blood or blood components within the previous 12 months, or the receipt of human-derived clotting factor within the previous 12 months.

Signs and symptoms of relevant transfusion-transmitted infections (Proposed § 630.10(f)(3)).—We would require blood establishments to assess donors for signs or symptoms of relevant transfusion-transmitted infections; donors exhibiting such signs or symptoms would be ineligible to donate blood and blood components. This provision is intended to help ensure that an individual who exhibits one or more of the signs and symptoms of HIV infection or viral hepatitis, or any other relevant transfusion-transmitted infection that would be applicable under proposed § 630.3(g), and who is, therefore, a potential source of transmitting a relevant transfusion-transmitted infection, does not donate blood or blood components.

Institutionalization (Proposed § 630.10(f)(4)).—A collecting establishment would determine whether a donor is currently an inmate of a correctional institution or has been incarcerated within the last 12 months, and if so, whether the risk of exposure related to that incarceration is still applicable at the time of donation. Current guidance recommends that a donor not be eligible to donate if incarcerated in a correctional institution for more than 3 consecutive days during the past 12 months.

Intimate contact (Proposed § 630.10(f)(5)). We would require collecting establishments to determine whether a donor is or was an intimate contact of a person who is at an increased risk for exposure to, or is known to be infected with, a relevant transfusion-transmitted infection that is spread by intimate contact and, is thus, ineligible to donate. One example is a heterosexual partner of an injection drug user. Such individuals are at increased risk for contracting relevant transfusion-transmitted infections due to the exchange of bodily fluids, including blood or saliva.

Percutaneous exposure (Proposed § 630.10(f)(6)).—We would require collecting establishments to assess whether a donor had a nonsterile percutaneous inoculation within the past year. A piercing of the skin with an instrument used previously on another person with a relevant transfusion-transmitted infection could expose the donor to such infections. Under this provision, establishments would defer donors who, within the last 12 months, experienced any piercing of the skin by a nonsterile instrument, such as may be used in tattoos, body or ear piercing, or intentional or accidental needlestick (percutaneous exposure). FDA understands that certain establishments are licensed by a State or credentialed by a responsible certifying body to perform such procedures with sterile needles. FDA does not intend for such a procedure performed by a state-licensed or responsibly certified establishment to be a reason to defer the donor.

Proposed § 630.10(g).—There are other factors that make a donor ineligible because of the risk they present to the health of the donor before, during, and after the donation process, or because they could adversely affect the safety, purity, and potency of the blood and blood component. Proposed paragraph (g) would require the collecting establishment to determine the donor ineligible to donate if the following factors existed and the collecting establishment decided that donation by the donor would present a risk to the health of the donor, or to the safety, purity, and potency of the blood and blood component. In addition to the following discussion, we refer you to the following current Memoranda to Blood Establishments and Guidances, which discuss factors related to donor risk or product safety. The draft guidance documents included in the following bulleted list, when finalized, will represent FDA's current thinking on that topic.

- ''Deferral of Blood and Plasma Donors Based on Medications,'' dated July 28, 1993;
- ''Deferral of Blood Donors Who Have Received the Drug Accutane,'' dated February 28, 1984;
- ''Deferral of Donors Who Have Received Human Pituitary-Derived Growth Hormone,'' dated November 25, 1987;
- Draft ''Guidance for Industry: Precautionary Measures to Reduce the Possible Risk of Transmission of Zoonoses by Blood and Blood Products from Xenotransplantation Product Recipients and Their Intimate Contacts,'' dated February 2002.

Medical or dental treatment, or symptoms of a recent or current illness (Proposed § 630.10(g)(1).—Under proposed paragraph (g)(1), the collecting establishment must assess the health of the donor based on medical or dental treatments. The collecting establishment must also assess the health of the donor for symptoms of recent or current illnesses. The establishment must determine whether the donor is ineligible to donate temporarily, indefinitely, or permanently, depending on the illness or treatment, if that assessment reveals a factor that may adversely affect the safety, purity, or potency of the blood or blood component, or that the donation may adversely affect the health of the donor. For example, if the donor recently was diagnosed with pneumonia, the interviewer would further assess the donor to assure that the donor is in good health at the time of donation and that the donor's health would not be adversely affected by the donation. If

the donor had a recent tooth extraction or oral surgery, the collecting establishment would temporarily defer the donor due to concern for possible contamination of blood or blood components due to transient bacteremia caused by the performance of dental procedures.

Medications (Proposed § 630.10(g)(2)).—We would require collecting establishments to assess the effects of medication taken by the donor and to defer that donor if the medication could have an adverse effect on the blood and blood components, the recipient, or on the developing fetus of a pregnant recipient. The proposed regulation is consistent with current industry practice to screen prospective donors to identify such medications, and evaluate the potential for each medication to have an adverse effect on the safety of the blood supply. For example, following current industry practice and FDA recommendations, collecting establishments would defer from donation, either temporarily or permanently, a donor who had taken certain medications (e.g., Accutane and Tegison). We further discuss the use of certain medications that adversely affect platelet function in section III.O of this document.

Major surgical procedure (Proposed § 630.10(g)(3)).—We would require establishments to defer donors who have experienced major surgery within the past 12 months. This deferral is to protect the donor whose health may be compromised by the donation and to address the possibility that the donor may have unknowingly received blood or blood components during surgery.

Travel to endemic areas for transfusion-transmitted infections (Proposed § 630.10(g)(4)).—It is known that several transfusion-transmitted infections exist for which the risk is closely associated with a geographic area, e.g., leishmania. Typically, such infections would not be ''relevant transfusion-transmitted infections'' requiring broader screening and testing because they do not have sufficient incidence or prevalence in the potential donor population. This provision is designed to identify donors who may be at risk for additional transfusion-transmitted infections. Because donors harboring such infections may be asymptomatic, or the signs and symptoms may be mild enough to go undetected at the time of donation, we would require the collecting establishment to assess whether the donor has visited or is a former resident of endemic areas known to harbor the disease agent or disease, whether the risk of exposure is still applicable at the time of donation, and, if so, determine the donor ineligible to donate.

Xenotransplantation product recipient and intimate contact (Proposed § 630.10(g)(5)).—The potential for infectious disease transmission and public health risks associated with xenotransplantation products has become an increasing concern. Because xenotransplantation disrupts the recipient's usual protective physical and immunologic barriers, receipt of a xenotransplantation product may facilitate transmission of infectious agents to humans. Additionally, transmission of such an infectious agent to an intimate contact of a xenotransplantation product recipient may be possible. Therefore, a xenotransplantation product recipient and an intimate contact of a xenotransplantation product recipient would be determined to be ineligible and deferred from donating.

Exposure to a released disease agent or disease (Proposed § 630.10(g)(6)).—Recent events have made us aware that donors may be affected by a released disease agent or disease. The release may occur accidentally, such as in a laboratory accident, or intentionally, such as in a bioterrorist attack. An example is the exposure in 2001 of individuals to Bacillus anthracis through the U.S. mail. Proposed § 630.10(g)(4) would require the collecting establishment to assess the donor for exposure or possible exposure to a released disease agent or disease with a potential for transmission by transfusion, when the establishment becomes aware that such a release of a disease agent or disease may have occurred in the community. The collecting establishment would find donors ineligible when the disease agent or disease may affect the health of the donor, or the safety, purity, or potency of the blood and blood components.

Pregnancy (Proposed § 630.10(g)(7)).—In order to prevent any adverse effect on the donor or her fetus, collecting establishments would determine a pregnant woman ineligible to donate. A woman who is up to 6 weeks postpartum would also be determined ineligible so as not to jeopardize her health by donating.

Unreliable answers (Proposed § 630.10(g)(8)).—Section § 640.63(d) requires plasma establishments to defer a Source Plasma donor from donating if, in the opinion of the interviewer, the individual appears to be under the influence of drugs or alcohol or does not appear to be providing credible answers to medical history questions. In proposed § 630.10(g)(8), this requirement would apply to all donors of blood and blood components as well as Source Plasma. The establishment would assess the donor for impairment due to the influence of drugs or alcohol, or for providing unreliable answers to the medical history interview. One example of an unreliable answer is when a donor states that he or she is donating for the purpose of getting tested for a relevant transfusion-transmitted infection. Such action would indicate that the donor has reason to believe there is a possibility of infection due to participation in high-risk activities.

c. Physical assessment.

Sections 640.3(b) and 640.63(c) currently require collecting establishments to determine that a donor is in good health on the day of donation, indicated in part by a normal temperature, a blood pressure within normal limits, and a hemoglobin level of no less than 12.5 grams per 100 milliliters (mL) of blood or no less than a hematocrit value of 38 percent. We are moving these requirements to proposed § 630.10(h)(1) through (h)(6) as criteria for determining that a donor is in good health to protect the health of the donor and to ensure the safety, purity, and potency of the blood and blood components.

Temperature (Proposed § 630.10(h)(1)).—We would require the collecting establishment to determine that the donor has a normal body temperature. An elevated temperature could indicate a possible infection. We are proposing that the maximum acceptable temperature not exceed 37.5 °C (99.5 °F) when taken orally, or the equivalent if the temperature is taken at an alternative body site. These acceptable values are consistent with good medical judgment and current industry practice. Collecting establishments determining body temperatures using a device that measures body temperature other than orally, such as by a probe placed in the ear, would list in their SOP the maximum acceptable temperature adjusted according to the method used.

Blood pressure (Proposed § 630.10(h)(2)).—For the purpose of this rulemaking, we would require under proposed paragraph (h)(2) that the collecting establishment determine not to be eligible a donor whose blood pressure measures above 180 mm of mercury or below 90 mm of mercury for the systolic value, and above 100 mm of mercury or below 50 mm of mercury for the diastolic value. These limits are currently an industry standard in use by many blood establishments. We are soliciting comments with supporting

scientific data on the need for such limits on systolic and diastolic values, on the limits we have proposed, and on adverse events associated with donation that have been attributed to blood pressure. In particular, we are seeking comments with supporting scientific data on the necessity, or lack of necessity, of specific upper or lower blood pressure limits in blood donation, and any adverse events attributed to blood pressure and associated with donation. If the record supports the need for different limits on systolic and diastolic values, for example, a lower systolic limit of 90 mm of mercury and a lower diastolic limit of 50 mm of mercury, we will make appropriate changes in the final rule. We are also soliciting comments on whether an abnormal blood pressure may be an indication that the donor has an undetected illness, such as cardiovascular or renal disease, may not be in good physical health and, therefore, may be harmed by the act of donating.

We are also seeking comments on the accuracy and interpretation of blood pressure measurements taken in the setting of blood and plasma donation. Although the occluding cuff technique is simple and easy to learn, errors can still be made. A single blood pressure measurement taken at the time of donation may not represent the donor's true baseline due to variations in the donor's blood pressure throughout the day or under different situations. There are also many other causes of error and inaccuracy in the measurement of blood pressure. There is no uniform standard methodology for day-to-day use by all donor room personnel (Ref. 2).

Both aneroid and electronic instruments have some advantages of portability and ease of use, but few of these instruments have had adequate validation. Still fewer of these instruments are calibrated regularly and most of the instruments have not been validated over a wide range of blood pressures and ages (Ref. 3). Therefore, an isolated measurement of blood pressure may not reliably assess eligibility for blood donation.

Hemoglobin or hematocrit determination (Proposed § 630.10(h)(3)).—The current regulations in § 640.3(b)(3) require that an allogeneic donor have a minimum hemoglobin level of 12.5 grams per deciliter of blood or a hematocrit value of 38 percent to participate in a collection program; and that an autologous donor have a minimum hemoglobin level of 11.0 grams per deciliter of blood or a hematocrit value of 33 percent. In proposed § 630.10(h)(3), we are proposing to continue requiring these minimal hemoglobin levels or hematocrit values for allogeneic donors, including Source Plasma donors, and autologous donors. The collecting establishment would be permitted to obtain the blood sample by fingerstick or venipuncture or by another method providing equivalent results. However, the earlobe would not be an acceptable site for the collection of a blood sample to measure the hemoglobin level or hematocrit value. We propose this restriction based on evidence that a blood sample collected from the earlobe does not accurately reflect the donor's true venous hemoglobin level or hematocrit value (Ref. 4).

We are specifically soliciting comments and supporting data on the following:

- Changing the minimum acceptable hemoglobin level to 12.0 grams per deciliter of blood or a hematocrit value of 36 percent as acceptable minimal values for female allogeneic donors;
- The possibility of adverse effects caused by the collection of blood and blood components from allogeneic donors with such minimum hemoglobin level of 12.5 grams per deciliter of blood or a hematocrit value of 38 percent for males, and hemoglobin level of 12.0 grams per deciliter of blood or a hematocrit value of 36 percent for females, which are considered below normal by medical criteria; or if such decisions should be left to the discretion of the medical director of the collecting establishment on a case-by-case basis;
- Establishing a more stringent inter-donation interval; and
- The use of copper sulfate solution based methods as an appropriate method to determine acceptable hemoglobin levels.

Pulse (Proposed § 630.10(h)(4).—We would require the collecting establishment to take the donor's pulse rate, which is an indicator of the donor's cardiovascular health. We would consider as acceptable a regular pulse rate and any value between 50 and 100 beats per minute. Any irregular pulse, or any value below 50 beats per minute or above 100 beats per minute would be cause to determine the donor ineligible to donate, unless the responsible physician examines the donor and determines that the health of the donor would not be adversely affected.

Weight (Proposed § 630.10(h)(5)).—Proposed § 630.10(h)(5). This paragraph would require that a donor weigh a minimum of 50 kilograms (110 pounds) and not have any unexplained loss of greater than 10 percent of body weight within the past 6 months. Except as stated in proposed § 630.15(b)(2) for donors of Source Plasma, the proposed regulation would not require collecting establishments to physically weigh individuals at each donation, but § 606.160(b)(1)(i) would require the collecting establishments to retain documentation of the donor's responses when asked if the donor weighs more than 110 pounds, and if the donor experienced an unexplained loss of greater than 10 percent of body weight within the past 6 months, which may be a sign or symptom of a relevant transfusion-transmitted infection.

We recognize that some collecting establishments believe it acceptable and safe to collect a reduced volume of blood and blood components from a donor weighing less that 110 pounds. We are requesting comments and supporting scientific data regarding both the volume of blood that can be safely collected from a donor in relation to the donor's body mass, and the criteria to define a standard unit of blood. We are also seeking comments on the feasibility and impact of determining that a donor has experienced a significant recent and unexplained loss of weight, and, if so, whether an unexplained loss of 10 percent of the donor's weight is an appropriate marker of possible underlying illness, and whether loss of weight in the 6 month time period prior to donation is an appropriate time frame to indicate that such weight loss is an appropriate marker for such potential illness.

Collecting establishments routinely weigh donors of Source Plasma so that they may apply the nomograms for volume limits as recommended in the Memorandum to All Licensed Source Plasma Establishments issued November 4, 1992, entitled ''Volume Limits for Automated Collection of Source Plasma.'' Under proposed § 630.15(b)(2), we would require collecting establishments to weigh a donor of Source Plasma at each donation. For donors of Source Plasma, records of donor weight should be examined for unexplained weight loss at the time of the donor's annual medical examination. (See also section III.I.2.b of this document.)

Skin examination (Proposed § 630.10(h)(6)).—We would require that the collecting establishment examine: (1) The phlebotomy site for evidence of infection, inflammation, lesions, or pitted skin (to eliminate contaminating the donation and possibly putting the recipient at risk for sepsis) and (2) the donor's arms and forearms for punctures and scars indicative of injected drugs of abuse. Use of injected drugs not prescribed for medical reasons (drug

abuse), regardless of the site of injection, would place the donor at increased risk for exposure to a relevant transfusion-transmitted infection.

3. Additional Requirements for Determining Donor Eligibility

Proof of identity and mailing address (Proposed § 630.10(i)(1)).—Proposed § 630.10(i)(1) would require the collecting establishment to obtain, before donation, donor identification, such as a photograph identification and an address as required under § 606.160(b)(1)(x). Collecting establishments are required under § 630.6 (proposed redesignation to § 630.40) to notify donors that they are deferred from further donation based on the results of tests for evidence of infection with a communicable disease agent(s). Having a current address will assist the collecting establishment in the notification process when necessary.

Donor's written statement of understanding (Proposed § 630.10(i)(2)).—In order to ensure that the donor has been informed of and understands the collection procedure and the educational material, the collecting establishments would be required to provide a written statement to the donor, using appropriate language and literacy level and taking into account any donor disabilities, to read and sign before phlebotomy is performed. This statement would be written in a clear and understandable terminology and not include language that would waive any of the donor's legal rights. The document would provide the following information as described in proposed § 630.10(i)(2)(i) through (i)(2)(vii):

- The donor reviewed the provided educational material regarding the relevant transfusion-transmitted infections, including HIV, HBV, and HCV, and understands that such infections present potential risks to the safety of the blood supply;
- The donor agrees not to donate if the donation could result in a potential risk to the safety of the blood supply as described by the educational material;
- The donor understands that, a sample of the donor's blood taken at the time of phlebotomy will be tested for specified relevant transfusion-transmitted infections;
- The donor understands that, if any of the tests for the relevant transfusion-transmitted infections required under § 610.40(a) are reactive, the blood sample will be tested further as necessary and appropriate to determine the donor's infection status;
- The donor understands that, if a basis for deferral is discovered, the donor will be deferred from further donation temporarily, indefinitely, or permanently, and notified of the basis of the deferral;
- The donor understands the hazards and risks of the procedure; and
- The donor has the opportunity to ask questions and refuse to donate at any time.
- The collecting establishment must not proceed with the phlebotomy until the donor signs the statement.

•We also note that some blood components may be stored indefinitely before they are used. During that time, we may become aware of new infectious agents, which may be identified only through the use of investigational tests. An establishment may want to test stored blood components using the investigational test, but face obstacles due to the lack of donor consent to the use of an investigational test. An establishment may seek to address this problem, in advance, by obtaining adequate informed consent to investigational tests at the time of donation. We note that consent to authorize investigational testing subject to investigational new drug or investigational device exemption requirements must meet the requirements of 21 CFR part 50.

I. Donor Eligibility Requirements Specific to Whole Blood and Plasma Collected by Plasmapheresis (Proposed § 630.15)

The donor eligibility requirements under proposed § 630.10 would apply to all donors of Whole Blood and blood components, including Plasma collected by plasmapheresis. In addition to these proposed requirements, other requirements specific to Whole Blood or Plasma collected by plasmapheresis are proposed in § 630.15.

1. Whole Blood

The following two sections are specific to Whole Blood donation.

a. *Donation frequency.*

With the establishment of double Red Blood Cells unit collection programs by some establishments, we are proposing to adjust the donation frequency requirements currently in § 640.3(f). Proposed § 630.15(a)(1) would continue the requirement in § 640.3(b) that collecting establishments collect a single unit of Whole Blood from a donor no more than once in 8 weeks. We also are proposing that if a donor is participating in a double Red Blood Cells unit collection program, i.e., where two units of Red Blood Cells are collected by an automated blood cell separator on the same occasion, then the collecting establishment would be required to defer the donor for 16 weeks before allowing the donor to participate in a Whole Blood collection program, in any apheresis program, or in a double Red Blood Cells unit collection program again. This is currently recommended in the January 2001 guidance entitled ''Guidance for Industry: Recommendations for Collecting Red Blood Cells by Automated Apheresis Methods.'' This proposed requirement protects the donor's health. We also are proposing that a donor may donate sooner than the proposed required time period if the collecting establishment's responsible physician examines the donor and certifies the donor to be in good health and one of the following three conditions exist:

- The donor presents a physician's prescription for a therapeutic phlebotomy; or
- The donation is an autologous donation; or
- The donation is dedicated to a specific recipient based on documented medical need.

The responsible physician would explain to the donor in the written statement of understanding (proposed § 630.10(i)(2)(vi)) the hazards or risks from more frequent donations.

b. *Therapeutic phlebotomy.*

Currently, under § 640.3(d), we require that blood drawn to promote the health of the donor not be used as a source of Whole Blood unless the container label conspicuously indicates the donor's disease that necessitated the phlebotomy. Under the new proposed § 630.15(a)(2), we would continue to require that the container label state the donor's disease that necessitated the phlebotomy, but would permit an exception to this provision. In August 2001, we issued ''Guidance for Industry: Variances for Blood Collection from Individuals with Hereditary Hemochromatosis,'' which provides guidance for requesting a variance from the labeling requirement for individuals with hereditary hemochromatosis (HH). This proposed rule would codify those recommendations, eliminate the need for a variance request, and permit all collecting establishments to use a donation from an individual with HH as a source of Whole Blood and not affix a disease label for HH, if the following conditions are met:

- The donor with HH otherwise meets the same eligibility requirements under proposed § 630.10 as for other allogeneic donors whose blood would be used for transfusion or further manufacturing use; and
- The collecting establishment does not charge a fee for any phlebotomies performed on individuals with HH,

including those who do not meet the eligibility requirements proposed under § 630.10. As explained in the August 2001 guidance, if a blood establishment charged a fee for therapeutic phlebotomy, but not for a collection of blood for transfusion, the HH donor would have an incentive to deny risk conditions that might preclude cost-free donation. Accordingly, this provision removes that incentive. Blood and blood components collected from persons undergoing therapeutic phlebotomies who are ineligible to donate would be discarded unless other arrangements are in place to permit the practice, such as license amendments, requests for variance, or short supply agreements (for example, if certain rare antibodies are present, or for manufacture into an in vitro reagent) (§§ 601.12, 610.40(h)(2) and § 640.120).

2. Plasma Collected by Plasmapheresis

a. *Examination by a responsible physician.*

In addition to the eligibility requirements proposed in § 630.10, proposed § 630.15(b)(1) would require the responsible physician to examine the donor initially and annually for medical conditions that would place the donor at risk during the process of plasmapheresis and explain the hazards of the procedure so that the donor may choose not to donate. The initial examination would occur no more than 1 week before the first donation. In addition, under proposed § 630.15(b)(4), if the donor is participating in an immunization program for the collection of high-titer plasma, then the examination must occur no more than 1 week before the first immunization injection. It is not necessary to repeat the physical examination if the immunized donor's plasma is collected within 3 weeks of the first immunization injection. These provisions are currently required under § 640.63(b)(1), (b)(2)(i), and (b)(2)(ii).

b. *Weight.*

In proposed § 630.15(b)(2), we would require that establishments determine a donor's weight at each donation. This information allows you to determine the appropriate amount of plasma that can be safely removed. We note that, although unexplained weight loss can be a sign or symptom of a relevant transfusion-transmitted infection, the proposed rule does not require establishments to measure donor weight at the time of apheresis as an indicator of underlying disease. FDA is soliciting comments with supporting data on the usefulness of measuring weight loss at the time of donation by apheresis as an indicator to identify health problems in the donor.

c. *Total protein.*

Under existing § 640.63(c), we require collecting establishments to test the donor's blood sample for total protein on the day of and before plasmapheresis. We would continue to require under proposed § 630.15(b)(3) that collecting establishments test the donor's sample for a total plasma or serum protein and have a value of no less than 6.0 grams per deciliter or no more than 9.0 grams per deciliter, the minimum and maximum normal values, for the donor to donate. If the value is less than 6.0 grams per deciliter or more than 9.0 grams per deciliter, the collecting establishment would be required to defer the donor until the donor's total protein level is at an acceptable value.

d. *Deferral due to red blood cell loss.*

Under proposed § 630.15(b)(5), in order to protect the donor's health, we would require the collecting establishment to defer a donor from donating plasma for 8 weeks after one of the following events:

- The donor experienced a red blood cell loss of 200 mL or more of red blood cells during a single automated or manual plasmapheresis procedure; or
- The donor experienced an unexpected red blood cell loss of any volume in an automated apheresis procedure on two occasions within the last 8 week period;
- The donor experienced a red blood cell loss equivalent to or greater than 200 mL of red blood cells as a result of failure to return red blood cells during a manual plasmapheresis procedure; or
- The donor donated a unit of Whole Blood.

However, if a donor participates at any time in a double Red Blood Cells unit collection program, then the collecting establishment would be required to defer the donor for 16 weeks after the last double red blood cell donation under proposed § 630.15(a)(1).

Under proposed § 630.15(b)(6), we would allow exceptions to the deferral for red blood cell loss if all of the following criteria are met.

- The donor is examined at the time of donation and certified by the responsible physician to be in good health and the donor's health permits the plasmapheresis; and
- The donor possesses an antibody that is transitory, of a highly unusual or infrequent specificity, or of an unusually high titer; and
- The collecting establishment documents the special characteristics of the antibody and the need for plasmapheresis under proposed § 630.20(c)(2).

e. *Exception to the donor eligibility requirements for Plasma collected by plasmapheresis.*

Under § 640.63(c)(9), a Source Plasma donor must be free from any disease transmissible by blood transfusion, other than malaria, insofar as the disease can be identified by history and examinations. In ''Memorandum to Registered Blood Establishments—Recommendations for Deferral of Donors for Malaria Risk'' issued in July 1994, and a draft guidance issued for public comment in June 2000, entitled ''Guidance for Industry: Recommendations for Donor Questioning Regarding Possible Exposure to Malaria,'' we make recommendations for assessing donors for malaria risk. These apply only to donations containing intact red blood cells or platelets, where the protozoa are found. Donors of Source Plasma collected by plasmapheresis are excluded from the malaria risk assessment since plasma does not contain intact red blood cells, which harbor the infectious agent. Moreover, Source Plasma undergoes further manufacturing to remove or inactivate pathogens. We maintain this exception in proposed § 630.15(b)(7). However, we are interested in receiving comments with supporting data on the following: (1) Whether Fresh Frozen Plasma collected by plasmapheresis can be safely manufactured from donors with risk of malaria and (2) whether this exception should be expanded to apply to other parasitic diseases.

J. General Exceptions from the Donor Eligibility Requirements (Proposed § 630.20)

Proposed § 630.20 would permit, under certain circumstances and under the supervision of the responsible physician, the collection of blood and blood components from individuals who do not meet one or more of the eligibility requirements proposed in §§ 630.10(d), 630.15, and 610.41. We would require that the responsible physician examine the donor and certify that the donor's health permits the collection procedure, and that the collection be performed under the supervision of the responsible physician, who is aware of the donor's health status. We would only allow this exception in the following situations.

- The donation is for autologous use as prescribed by the donor's physician and is not intended for allogeneic transfusion or for further manufacturing use; or

• The donor is participating in a plasmapheresis program that collects plasma for further manufacturing use into products for which there are no alternative sources, and the program has received prior approval from the Director, Center for Biologics Evaluation and Research, consistent with § 606.110. For example, the donor may serve as a source of antibody to hepatitis B surface antigen for the preparation of Hepatitis B Immune Globulin (Human) or as a component of a medical device. Other examples are discussed in the ''Guideline for Collection of Blood or Blood Products from Donors with Positive Tests for Infectious Disease Markers (High Risk Donors),'' dated September 1989; or

• The donation is for the sole use of a specified recipient based on documented medical need, and the responsible physician determines that the donation presents no undue medical risk to the recipient. The donation must test negative in all tests required under § 610.40, unless an exception in § 610.40(h)(2) applies. However, for deferrals under § 610.41, we are soliciting comments on permitting, in the case of documented medical need, the use of donations testing reactive for antibody to hepatitis B core antigen. For example, we are considering whether, when the recipient has a rare red blood cell antibody and the donor is lacking the red blood cell antigen for the antibody, to permit the use of a donation that is reactive when tested for hepatitis B core antibody by a screening test.

K. Exceptions from Certain Donor Eligibility Requirements for Infrequent Plasmapheresis (Proposed § 630.25)

Under proposed § 630.25, we intend to reduce the medical examination and laboratory testing burden on collecting establishments when donors are participating in plasma collection programs at intervals of 4 weeks or more. Consistent with existing guidance in memoranda issued March 10, 1995, entitled ''Memorandum to Registered Blood and Source Plasma Establishments, Revision of FDA Memorandum of August 27, 1982: Requirements for Infrequent Plasmapheresis Donors'' and November 4, 1992, entitled ''Volume Limits for Automated Collection of Source Plasma,'' we would except the collecting establishment from the requirements for frequency of examination in proposed § 630.15(b)(1) and (b)(3), and current § 640.65(b)(1) and (b)(2), if the following occurs:

• The donor has not donated Whole Blood in the preceding 8 weeks or plasma by apheresis in the preceding 4 weeks, or participated in a double Red Blood Cells unit collection program within the preceding 16 weeks;

• The donor has not donated more than 12.0 liters of plasma in the past year (14.4 liters of plasma for donors weighing more than 175 lbs.);

• The donor is determined by the responsible physician to be in good health under proposed § 630.10(d); and

• The donor is not participating in an immunization program for the production of high-titer plasma.

L. Donation Suitability Requirements (Proposed § 630.30)

The collecting establishment would determine a donation as suitable when the following occurs:

• The donor is not currently deferred from donation;

• The results of the medical history and physical examination indicate that the donor is in good health and donating would not adversely affect the health of the donor;

• The donor is free from risk factors for, or evidence of, transfusion-transmitted infections;

• The donor's tests for relevant transfusion-transmitted infections are negative or nonreactive;

For platelet components, the test for bacterial contamination is negative; and

The donor or donation meets other requirements in 21 CFR subchapter F.

When one or more of the criteria in proposed § 630.30 for determining a donation as suitable are not met, the collecting establishment would determine that the donation is not suitable, would defer the donor until the basis of deferral is resolved, and must notify the donor of the reason for the deferral under § 630.6 (redesignated as § 630.40 in this proposed rule). Under § 610.40(h), the collecting establishment must not ship or use donations that test reactive for tests required under § 610.40(a) and (i), unless one of the limited exceptions apply. Under proposed § 606.160(e)(2), we also would require that the collecting establishment provide to appropriate personnel of the establishment a list of those donors who are not eligible to donate under proposed § 630.10(f)(1) through (f)(6) and (g)(1) through (g)(6).

M. Requalification of Previously Deferred Donors (Proposed § 630.35)

We would permit the requalification of a previously deferred donor into the donor pool (commonly referred to as donor re-entry) under proposed § 630.35. If a donor had been deferred from donation because the donor did not meet the requirements in part 630, then the otherwise eligible donor may be determined to be eligible to donate if the basis for the previous deferral is no longer applicable. To requalify a donor deferred under § 610.41(a), because the donor tested reactive by a screening test for evidence of infection due to a relevant transfusion-transmitted infection, the collecting establishment would determine the donor to be eligible for donation by a requalification method found acceptable for such purpose by FDA under § 610.41(b). For example, FDA issued draft guidance on a requalification method or process for reentry of donors deferred because of a reactive screening test for HIV or HCV entitled ''Guidance for Industry: Nucleic Acid Testing (NAT) for Human Immunodeficiency Virus Type 1 (HIV–1) and Hepatitis C Virus (HCV): Testing, Product Disposition, and Donor Deferral and Reentry,'' dated July 2005. Donor screening tests may yield a number of false positive test results. For a donor deferred under such a test, an establishment could retest the donor, following the recommendations for donor re-entry in the guidance, when finalized. If results of the retesting meet the reentry criteria found acceptable for such purposes by FDA, the donor would be requalified under § 610.41(b) and no longer would be deferred. Of course, the donor would be required to meet the eligibility criteria at each subsequent donation.

N. Requirements for Notifying Deferred Donors (Proposed Newly Redesignated § 630.40)

On June 11, 2001, we published a final rule entitled ''General Requirements for Blood, Blood Components, and Blood Derivatives; Donor Notification'' (June 2001 final rule) in the **Federal Register** (66 FR 31165), codified at § 630.6. The June 2001 final rule requires blood and plasma establishments to notify donors, including autologous donors, whenever the donors are deferred or determined not to be eligible for current or future donations of blood and blood components. Blood and plasma establishments also are required to notify the referring physician for an autologous donor when the autologous donor is deferred based on the results of tests for evidence of infection due to communicable disease agent(s). This proposed rule would amend part 630, redesignate current § 630.6 as § 630.40, and revise all references to § 630.6 accordingly. We also are proposing to revise all references to donor eligibility by replacing §§ 640.3 and 640.63 with §§ 630.10 and 630.15. Consistent with proposed § 630.30(b)(4), proposed

newly redesignated § 630.40(a) would require a collecting establishment to notify a donor whose platelet component tests positive for an endogenous bacteremia.

O. Eligibility Requirements Specific for Platelet Donors (Proposed § 640.21)

We are proposing to amend § 640.21 by revising the subject heading and paragraphs (a) through (c), and by adding paragraphs (d) and (e) for consistency with other parts of this rulemaking.

In addition to meeting the proposed requirements in §§ 630.10 and 630.15, under proposed § 640.21(a)(2), the donor's written statement of understanding in proposed § 630.10(i)(2)(vi) would require a statement that the long-term effects of frequent apheresis are unknown.

Proposed § 640.21(b) for plateletpheresis donors, would require that a donor not serve as a source of platelets for transfusion after the donor has ingested drugs that adversely affect platelet function. At a BPAC meeting held in March 2006, we discussed the deferral of donors who had recently ingested aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs). BPAC provided advice on deferral periods for ingestion of these products. Based on the information received at this meeting, we intend to issue for public comment a draft guidance on deferrals for ingestion of drugs that adversely affect platelet function. The draft guidance document, when finalized, will assist blood collecting establishments in appropriately deferring donors as a result of ingestion of aspirin, NSAIDs, and other drugs that may adversely impact platelet function.

We would permit, under proposed § 640.21(c), plateletpheresis donations at intervals shorter than 8 weeks provided:

- The collecting establishment performs a platelet count before the initial procedure and before each subsequent procedure; and
- The pre-donation count is greater than 150,000/µL; and the donor's post-donation count is no less than 100,000/µL; and
- The donor undergoes no more than a total of 24 plateletpheresis collections within 12 months (e.g., either 24 single, double, or triple platelet component collection procedures);
- For single component collection procedures, there are no more than 2 plateletpheresis procedures within 7 calendar days; and there is a minimum of 2 calendar days between procedures;
- For double or triple component collection procedures, there is no more than one plateletpheresis procedure within 7 calendar days.

At the BPAC meeting held in March 2006, we also discussed the frequency of platelet collection and the impact on the donor's safety. Blood establishments commented by providing data on the safety of collecting more than 24 platelet components per year, including 24 triple platelet component collection procedures per year. BPAC advised that the data supported continuation of up to 24 platelet collections of triple components per year. The BPAC also recommended that the donor's post-donation targeted platelet count not fall below 100,000/µL.

Under proposed § 640.21(d), we would permit a donor to serve as a dedicated plateletpheresis donor as often as necessary during a 30-day period if the donor is in good health and the donor's platelet count is greater than 150,000/µL. The collecting establishment must follow the requirements in § 610.40(c)(1) for testing and labeling for dedicated donors.

Under proposed § 640.21(e), if, over an 8-week period, a donor cumulatively loses 450 mL or more of whole blood or 200 mL or more of red blood cells, or donates a unit of Whole Blood, the collecting establishment must defer the donor for 8 weeks; or, if the donor participates in a double Red Blood Cells unit collection program, the collecting establishment must defer the donor for 16 weeks. An exception to this proposed requirement would be permitted when:

- The donor waits 2 calendar days for plateletpheresis after donating Whole Blood or sustaining a blood loss and
- The extracorporeal red blood cell volume during the plateletpheresis procedure is 100 mL or less.

P. Eligibility Requirements Specific for Source Plasma Donors (Proposed §§ 640.65(b) and 640.69)

In addition to proposed technical amendments to § 640.65(b)(1)(i) and (b)(2)(i), proposed § 640.65(b)(2)(i) would add an upper value of 9.0 grams per deciliter of plasma sample for acceptable total protein and a comparable level for a serum sample and would require the responsible physician to review the laboratory data, the calculated values of each component, and the collection records within 14 calendar days after the sample is drawn to determine if the donor should be deferred from further donation. If the review is not completed within 14 calendar days, we would require the collecting establishment to defer the donor pending the review. We have reduced the time period for record review from 21 to 14 calendar days because results are typically transmitted and recorded electronically, permitting faster access.

We are proposing to add to § 640.69 paragraphs (e) and (f). Proposed § 640.69(e) would require collecting establishments to ensure that Source Plasma donated by paid donors not be used for further manufacturing into injectable products unless the paid donor has a record of two suitable donations within the last 6 months at the plasma establishment where the donations occurred. Proposed paragraph § 640.69(f) would require collecting establishments to ensure that Source Plasma donated by paid donors determined to be suitable for further manufacturing into injectable products be held in quarantine for a minimum of 60 days to permit the retrieval of a Source Plasma donation in the event it is later determined to be unsuitable. Any Source Plasma shipped prior to 60 days after the date of collection must be labeled to indicate that the Source Plasma is in quarantine. These proposed requirements would support product safety. In a report entitled ''Blood Plasma Safety: Plasma Product Risks Are Low if Good Manufacturing Practices Are Followed'' (September 9, 1998), the GAO identified certain voluntary industry initiatives as greatly reducing the chances of reactive units being used in manufacturing pools. These voluntary initiatives included the use of repeat donors only and a 60-day inventory hold on all units to allow manufacturers to retrieve units from donors who subsequently test positive or are otherwise deferred. We are proposing to require these practices in the proposed rulemaking. However, we are soliciting comments and supporting data on whether other requirements would achieve the same goal. We are also soliciting comments on whether these provisions should also apply to Source Plasma from paid donors collected for manufacture into non-injectable products.

Q. Reporting of Donor Reactions (Proposed § 640.73)

Section 640.73 requires establishments collecting Source Plasma to report to us any donor fatality associated with plasmapheresis. We are proposing to retain this requirement in proposed § 640.73(a) and to add § 640.73(b), which would require establishments collecting Source Plasma to report to us any donor adverse experience as described in § 600.80(a) related to the administration of an immunizing agent, such as red blood cells or a vaccine.

If the adverse experience is serious or life threatening as described in § 600.80(a), then we would require the establishment to report to us as soon as possible by telephone or other rapid means of communication, and submit a written followup report of the investigation within 7 days of learning of the donor's adverse experience; if the adverse experience is neither serious nor life threatening, the establishment would submit the report in an annual report on the anniversary of FDA's approval of the immunization program.

Because manufacturers of blood and blood components are currently exempt from the safety reporting requirements under § 600.80, we do not receive adequate information to monitor and assess safety-related information (other than fatalities) concerning donors enrolled in immunization programs and the collection of Source Plasma by plasmapheresis. Such information is essential for evaluating our scientific and regulatory policies and for monitoring industry practices and their implications on donor and blood safety.

R. Alternative Procedures (Proposed § 640.120)

We are proposing an amendment which would separate and revise § 640.120(a) into proposed paragraphs (a) and (b), and revise and redesignate current paragraph (b) as paragraph (c).

Under proposed § 640.120(a), a manufacturer could initiate agency review of a proposed alternative procedure. The manufacturer would submit the request either as a written request, which would include a facsimile or e-mail, or as an oral request. This is consistent with § 640.120. We are adding proposed paragraph (b) to permit the Director of the Center for Biologics Evaluation and Research to issue an exception or alternative to the regulations in the event of a public health emergency. This procedure would be initiated only when a variance is necessary to assure the availability of blood, blood components, and blood products, in a specific location and in response to an unanticipated immediate need for blood, blood components, and blood products, as in situations involving large numbers of casualties.

Proposed § 640.120(c) states that FDA periodically would list approved alternative procedures and exceptions on the Center for Biologics Evaluation and Research home page on the Internet.

S. Reagent Red Blood Cells (Proposed § 660.31)

In § 660.31, we are proposing to remove ''§ 640.3'' and ''except in paragraphs (b)(5) and (b)(6), (d), and (e) of § 640.3,'' and add in its place ''§ 630.10 and 630.15.'' This proposed revision would require donor eligibility determination requirements for donations intended as a source material or component of a medical device, including Reagent Red Blood Cells. We would eliminate the current exceptions to be consistent with the applicability of donor eligibility determination requirements for blood and blood components collected for use in the manufacture of other in vitro diagnostic products. We are interested in receiving comments on limiting donor eligibility determination requirements to donations collected in the United States for use in the manufacture of Reagent Red Blood Cells.

T. Quality Systems Regulations (Proposed § 820.1(a)(1))

In part 820, we have issued current good manufacturing practice (CGMP) requirements applicable to manufacturers of all finished devices intended for human use. Section 820.1(a)(1) states that manufacturers of blood and blood components are not subject to part 820, but are subject to part 606. We are proposing in this rule to clarify the applicability of the requirements in 21 CFR Chapter I, subchapter F to donors of human blood or blood components used in the manufacture of a medical device as well as for transfusion.

U. Technical Amendments

We also propose technical changes to existing regulations, for consistency with this proposed rulemaking. We propose to remove §§ 640.3, 640.61, 640.62, and 640.63. We propose to revise § 606.3(a) and (c), and 1270.3(b) for consistency with proposed § 630.3(a) and (b). We propose to revise §§ 606.100(b)(20), 606.110(b), 606.160(b)(1)(ix) and (b)(1)(xi), 640.4, 640.12, 640.22, 640.31, 640.32, 640.51, 640.52, 640.65(b), and 640.72(a)(2), (a)(3), and (a)(4) by changing headings or references to CFR cites, and redesignating paragraphs.

IV. Proposed Effective Date

We propose that any final rule that may issue based on this proposal become effective 180 days after the date of its publication in the **Federal Register**.

V. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this proposed rule is not a significant regulatory action as defined by the Executive order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because this proposed rule incorporates industry's usual and customary business practices, the agency certifies that the proposed rule will not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing ''any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year.'' The current threshold after adjustment for inflation is $122 million, using the most current (2005) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this proposed rule to result in any 1-year expenditure that would meet or exceed this amount.

A. Objectives and Basis of the Action

As discussed previously, we are proposing this action to help protect donor health and to help ensure the safety, purity, and potency of the national blood supply. The safety, purity, and potency of the national blood supply is enhanced when blood donors are assessed for eligibility and blood donations are assessed for suitability. The health of the donor is protected through certain physical assessments, such as those regarding blood pressure and hemoglobin levels.

This action is taken under the authority of sections 351 and 361 of the PHS Act to prevent the introduction, transmission, and spread of communicable disease. Since blood and blood components are also drugs and devices, the provisions of the act (21 U.S.C. *et seq.*) also generally apply. In particular, section 501 of the act provides authority to ensure that methods used in manufacturing conform with CGMP. See section II.A of

this document for further details. We have reviewed related Federal rules and have not identified any rules that duplicate, overlap, or conflict with the rule.

B. Nature of the Impact

The proposed rule requires that for each donation of blood or blood component, blood establishments maintain minimum standards for donor eligibility (proposed §§ 630.10 and 630.15), and blood and blood component suitability (proposed § 630.30). A blood establishment must also establish, maintain, and follow SOPs for the determination of donor eligibility (proposed § 606.100(b)).

C. Type and Number of Entities Affected

This proposed rule would affect all blood establishments that collect blood and blood components, including Source Plasma and Source Leukocytes. Our registration database for blood and plasma establishments has records of approximately 1,709 establishments: 81 licensed Source Plasma establishments with multiple locations and 1,628 registered blood establishments. The DHHS estimates that approximately 15 million blood donations are collected annually (Ref. 5). According to a 2002 report by the Government Accountability Office (at that time, the General Accounting Office), 13 million donations of Source Plasma are collected annually by plasma centers (Ref. 6).

D. Estimated Impact of Requirements for Assessment of Donor Eligibility

The rule provides for the establishment of minimum criteria for the assessment of donor eligibility, and the suitability of the donation of blood and blood components. The rule is expected to have a minor net impact on blood establishments because it is already usual and customary business practice in the blood industry to assess donors for eligibility, and donations for suitability. We believe the primary impact of the rule will be the one-time review of current SOPs that the proposed rule would require each blood collecting establishment to conduct.

The burden imposed by this one-time effort to review and, if necessary, modify current SOPs will vary among the 1,709 establishments, depending on an establishment's existing procedures. For establishments that have already established procedures that conform to the proposed rule, we estimate that it would take approximately 40 hours of staff time to review the establishment's current SOPs to confirm that the SOPs comply with the regulation. A technical specialist who acts as a regulatory reviewer or manager of quality assurance could perform this process. Based on the total average hourly compensation (including benefits) of $37.03 for management, professional and related occupations in private industry healthcare and social assistance workers, as reported by the Bureau of Labor Statistics, the cost would be approximately $1,481 ($37.03 per hour x 40 hours) per establishment (Ref. 7).

For establishments that do not already conform to the proposed rule, we estimate that approximately 60 hours of staff time would be required to align current inadequate SOPs with the provisions of the rule. As we believe most establishments have SOPs that are consistent with the rule, the extent that staff would need to be notified of these updated SOPs would not result in extensive formal training. The cost in this case would be $2,222 ($37.03 x 60) per establishment. Assuming a minimal review is needed at two-thirds of the 1,709 currently operating establishments and a more extensive review is conducted by the other one-third, the total one-time cost for the blood and plasma industries is estimated to be $2,953,000 ((2/3 x 1,709) x $1,481)) + ((1/3 x 1,709) x $2,222)).

Our cost estimate assumes that the assessment of donors for eligibility and donations for suitability are already usual and customary business practices. We believe that most establishments already conform to this proposed rule and others nearly conform to this proposed rule and assume a two-thirds one-third division between the two groups of establishments. Nevertheless, because we lack information on the characteristics or fraction of establishments not currently in compliance, we welcome comment on our assumption. Also, while we assume the costs are limited to a review of SOPs, if these reviews were to uncover deficiencies requiring complex operational changes, the impact of this proposed rule could exceed our estimate. We request comment from blood establishments on our assumption.

E. Expected Benefits of the Rule

This proposed rule would help ensure the continued safety of the blood supply. As described in the preamble to this rule, the assessment of eligibility of donors and the suitability of donations will help prevent unsafe units of blood or blood components from entering the blood supply. This will protect the health of donors and will preserve the safety, purity, and potency of blood and blood components. The rule is intended to increase the safety of all blood and blood components by providing recipients with increased protection against communicable disease transmission.

The gravity of the disease risks associated with blood and blood components is widely recognized. Transfusion transmission of HIV, the virus that causes AIDS, continues to cause great concern. Human T-lymphotropic viruses types I and II were identified in the early 1980s. Infection with these viruses is associated with tropical spastic paraparesis, adult T-cell leukemia/ lymphoma, and some inflammatory disorders (Ref. 8). These viruses are known to be transmitted by transfusion.

HBV is a major cause of acute and chronic hepatitis, cirrhosis, and hepatocellular carcinoma worldwide. The Centers for Disease Control and Prevention (CDC) estimates that 1.25 million Americans are chronically infected with HBV, 15 to 25 percent of whom will die of chronic liver disease, and that there are an additional 60,000 new infections each year (Ref. 9). Approximately 5,000 individuals in the United States die each year from disease caused by HBV (Ref. 10). Prior to the development of hepatitis screening tests, transfusion-related risks were significant.

While recipients of blood products prior to 1992 are at risk for infection with HCV, blood donor screening for HCV has reduced transfusion-associated transmission to less than one in 1.6 million transfused units of blood (Ref. 11). Persons currently at increased risk for HCV infection include parenteral drug users and health care workers with occupational exposure to blood. CDC estimates approximately 26,000 new HCV infections occur annually in the United States and that 4.1 million Americans have been infected with HCV (Ref. 12). Despite advances in treatment with interferon and ribavirin, HCV infection remains a leading indication for liver transplant and up to five percent of those infected will die from the consequences of long-term infection (Ref. 10).

The requirement that, for each donation of blood or blood component, blood establishments maintain standards for donor eligibility and blood and blood component donation suitability significantly reduces the public risk of exposure to the morbidity and mortality risks associated with diseases such as HIV types 1 and 2, HBV, HCV, HTLV types I and II, and syphilis. Such standards also reduce the attendant costs of these diseases.

F. Small Entity Impact

The Regulatory Flexibility Act requires agencies to assess whether a rule may have a significant economic impact on a substantial number of small entities. This rule is not expected to have a significant impact on a substantial number of such entities.

According to size standards established by the Small Business Administration (SBA), a small blood or plasma establishment (NAICS code 621991, Blood and Organ Banks) has annual receipts of less than $9 million (Refs. 13 and 14). The number of blood and plasma collecting establishments that qualify as small entities is uncertain, but is not expected to be substantial. For such small entities, the cost of performing a review of SOPs is expected to be no more than $2,222. We believe a small independent establishment, not associated with a hospital, might collect as few as 200 units per week. A small processing fee for blood and blood components can be between $150 and $300 per unit, depending on the component and the region of the country. Assuming this small independent establishment collects a processing fee for two blood components for every unit collected, and the processing fee is at the lower end of the fee scale for blood components, the annual revenues for such an establishment would be $3.12 million (200 x 2 x 52 x $150). Even for the smallest establishment, the cost of performing a review of SOPs would be less than one tenth of one percent of revenues. For establishments associated with hospitals or establishments with multiple locations, we believe parent company revenues to be much greater than $2.22 million, putting the impact of this rule at less than one tenth of one percent of revenues for those firms, as well. We believe blood establishment employees already have the skills required to perform the tasks specified in the rule, and that the rule does not require establishments to seek out employees with new expertise.

Although the proposed rule would impose some costs on small entities involved in the collection of blood and blood components, including Source Plasma and Source Leukocytes, we believe that the proposed rule represents an effective means of protecting donor health and helping to ensure the safety, purity, and potency of blood and blood components. We considered, as a less burdensome alternative to the proposed rule, continuing with the use of trade organization standards by industry and FDA guidance. We found this approach would be inadequate to assure uniform or consistent compliance and would preclude our ability to effectively monitor the safety, purity, and potency of blood and blood components, including Source Plasma and Source Leukocytes. This proposed rule would enhance both public health and public confidence in the safety and quality of blood and blood components, while imposing only a minimum burden on the affected industry.

VI. The Paperwork Reduction Act of 1995

This proposed rule contains information collection provisions that are subject to review by OMB under the Paperwork Reduction Act of 1995 (the PRA) (44 U.S.C. 3501–3520). A description of these provisions is given in the following paragraphs with an estimate of the annual reporting and recordkeeping burden. Included in the estimate is the time for reviewing the instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

FDA invites comments on these topics: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Title: Requirements for Human Blood and Blood Components Intended for Transfusion or for Further Manufacturing Use

Description: FDA proposes to revise and update the regulations applicable to blood and blood components, including Source Plasma and Source Leukocytes, and to add donor eligibility requirements for consistency with current practices in the blood industry. This proposed rule's information collection provisions are for recordkeeping and reporting.

Proposed § 606.100(b)—Current § 606.100(b) requires collecting establishments to establish and maintain written SOPs for all steps in the collection, processing, compatibility testing, storage, and distribution of blood and blood components for transfusion and for further manufacturing use. We are proposing to revise § 606.100(b) by adding that the collecting establishment would not only establish and maintain the SOPs, but also would follow the SOPs. We are proposing to require establishments to establish, maintain, and follow SOPs for investigating product deviations (§ 606.171), and for recordkeeping related to CGMP (part 606) and biological product standards (part 610), which would include all recordkeeping requirements not listed in § 606.100(b)(1) through (b)(20).

Proposed § 606.160(e)—We are proposing to revise current § 606.160(e). Paragraph (e) would require collecting establishments to maintain a list identifying ineligible donors (otherwise known as a deferral list or donor deferral registry) and to provide this list to appropriate personnel to prevent the collection of blood and blood components from such individuals.

Proposed § 630.10(b)—We are proposing to require that collecting establishments provide to the donor educational material containing useful and current information concerning the relevant transfusion-transmitted infections so that the donor may self-defer from donation if necessary.

Proposed § 630.10(c)—Proposed § 630.10(c) would permit the collecting establishment to determine a donor's eligibility and collect a sample for testing one day before collection, when the donor is donating blood components that cannot be stored more than 24 hours. We would require the collecting establishment to identify such blood components in an SOP.

Proposed § 630.10(i)(2)—In proposed § 630.10(i)(2), we would require the collecting establishment to provide the donor with information concerning the donation procedure, and to permit the donor to ask questions and at any time to withdraw consent to donate.

Proposed § 630.15(b)(6)(iii)—We would redesignate current § 640.63(e)(3) as proposed § 630.15(b)(6)(iii). Consistent with the current regulation, we would require plasma collecting establishments to document the special characteristics of the donor's antibody and the need for plasmapheresis, i.e., there is no alternative source.

Proposed § 630.20(c)(3)—Under proposed § 630.20(c)(3), we would require the collecting establishment to document the recipient's medical need, which necessitates the collection of blood or blood components from a donor who is determined to be ineligible to donate.

Proposed § 640.72(a)(2)(i), (a)(3), and (a)(4)—We are proposing to revise

current § 640.72(a)(2), (a)(3), and (a)(4). Proposed § 640.72(a)(2)(i) would require the collecting establishment to maintain for each donor records of initial and periodic examinations, tests, laboratory data, and interviews as required in proposed §§ 630.10, 630.15, and current §§ 640.65, 640.66, and 640.67. Proposed § 640.72(a)(3) and (a)(4) would require the collecting establishment to maintain a record of the donor's written statement of understanding and documentation of the donor's good health, respectively.

Proposed § 640.73—Under proposed § 640.73, we would require establishments collecting Source Plasma to report adverse reactions experienced by donors. Proposed § 640.73(a) would require the reporting of fatal donor reactions associated with plasmapheresis, and proposed § 640.73(b) would require the reporting of adverse experiences related to the administration of an immunizing agent. Proposed § 640.73(c) would require the submission to FDA of a written followup report within 7 days of learning of the fatality or the serious or life threatening donor adverse experience related to immunization of the donor.

Description of respondents: Establishments that collect blood and blood components, including Source Plasma and Source Leukocytes

According to our registration database, there are currently about 1,709 establishments affected by this rule: (1) Approximately 81 licensed plasma establishments with multiple locations that collect Source Plasma and (2) approximately 1,628 registered blood establishments that collect blood and blood components. Based on estimates provided by HHS and GAO, these establishments collect annually approximately 15 million units of Whole Blood, and approximately 13 million donations of Source Plasma. FDA estimates the information collection burden as follows:

TABLE 1.—ESTIMATED ANNUAL RECORDKEEPING BURDEN[1]

21 CFR Section	No. of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Record	Total Hours
606.100(b) (Maintenance of SOPs)	1,709	1	1,709	24	41,016
606.160(e)	1,628	52	84,656	8	677,248
630.15(b)(6)(iii)	81	1	81	0.17	13.8
640.72(a)(2)(i), (a)(3), and (a)(4)	81	18,518.5	1,500,000	0.08	120,000
Total					838,277.8

[1]There are no capital costs or operating and maintenance costs associated with this collection of information.

TABLE 2.—ESTIMATED ONE-TIME RECORDKEEPING BURDEN[1]

21 CFR Section	No. of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Record	Total Hours
606.100(b) (Creation of SOPs)	1,139	1	1,139	40	45,560
606.100(b) (Creation of SOPs)	570	1	570	56	31,920
630.10(c)	1,628	1	1,628	16	26,048
Total					103,528

[1]There are no capital costs or operating and maintenance costs associated with this collection of information.

TABLE 3.—ESTIMATED ANNUAL REPORTING BURDEN[1]

21 CFR Section	No. of Responses	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
630.10(i)(2)	81	18,518.5	1,500,000	0.17	255,000
640.73(a) and (c)	81	.037	3	20	60
640.73(b)	81	.037	3	1	3
Total					255,063

[1]There are no capital costs or operating and maintenance costs associated with this collection of information.

Recordkeeping

As shown in table 1 of this document, for each of the 1,709 collecting establishments, we estimate that it will take approximately 24 hours annually to maintain the SOPs. As discussed in section V.C of this document, we estimate in table 2 of this document that two-thirds of 1,709 collecting establishments (1,139) will each expend, as a one-time burden, an average of 40 hours to reconcile their SOPs with the requirements, and the remaining one-third of the collecting establishments (570) would expend as a one-time burden an average of 56 hours to reconcile their SOPs with the requirements.

Also, as part of a one-time burden in table 2 of this document, 1,628 blood collecting establishments would create a

new SOP under proposed § 630.10(c), which we estimate will take 16 hours to create.

In table 1 of this document, under proposed § 606.160(e), Source Plasma collecting establishments are already providing to personnel a list identifying unsuitable donors as usual and customary business practice. Under proposed § 606.160(e), we estimate that it would take each blood-collecting establishment an average of 8 hours per week to update and provide their list (1,628 x 52 x 8 = 677,248). This estimated burden of 8 hours per week may appear to be lower or higher than the burden experienced by individual establishments. Since there is no available data, the burden is an estimated burden, taking into account the range of impact on each establishment. Some establishments may have the ability to generate the lists by computer; others may rely on manual preparation.

For proposed § 630.15(b)(6)(iii), Source Plasma collecting establishments would be permitted to collect plasma from a donor who is deferred due to red blood cell loss if the establishment documents the special characteristics of the antibody and the need for the plasmapheresis. Although we do not have data available, we believe that such a situation would occur infrequently. Consequently, we are estimating that each Source Plasma collecting establishment would have one occurrence per year and that it would take approximately 10 minutes (0.17 hours) to document the health of the donor and the special characteristics of the antibody and the need for the plasmapheresis.

Under proposed § 630.20(c)(3), donors who do not meet criteria under §§ 630.10, 630.15, or 610.41 would be permitted to donate under this proposed provision. Such donations, used solely by a specified recipient based on documented medical need, would occur rarely. Consequently, the burden to collecting establishments is negligible.

In proposed § 640.72(a)(2)(i), (a)(3), and (a)(4), we would require that Source Plasma collecting establishments maintain records for each donor of all examinations, tests, laboratory data, interviews, the donor's written statement of understanding and the donor's good health respectively. In table 1 of this document, we use GAO's estimate of approximately 1,500,000 donors that annually donate Source Plasma. We also estimate that the establishment would expend approximately 5 minutes (0.08 hours) for each donor.

Reporting

Proposed § 630.10(b), would require the collecting establishments to provide the donor with educational material. There is no calculated burden for this proposed requirement since establishments collecting blood and blood components perform this activity as a usual and customary business practice.

The burden for proposed § 630.10(i)(2) in table 3 of this document is only calculated for Source Plasma collecting establishments since the blood collecting establishments already provide the donor with a statement of understanding as a usual and customary business practice. We estimate that approximately 81 Source Plasma collecting establishments would take an estimated 10 minutes (0.17) to perform this activity. Based on the GAO estimate of approximately 1,500,000 donors that annually donate Source Plasma, the total annual burden would be 255,000 hours (1,500,000 x 0.17).

Proposed § 640.73(a) would require 81 Source Plasma collecting establishments to report fatalities associated with plasmapheresis. We estimate that approximately 3 fatalities would be reported annually. A written followup report would also be required under § 640.73(c). Approximately 20 hours is estimated for both the initial and followup report.

Proposed § 640.73(b) would require Source Plasma collecting establishments to report any serious or life threatening adverse reaction experienced by a donor after administration with an immunization agent. Although we do not have access to data regarding such reports, we estimate that approximately 3 serious or life-threatening adverse reactions would occur annually, and that the establishment would expend approximately 1 hour to complete the initial and followup reports.

In this rulemaking, we are redesignating current § 630.6 as proposed § 630.40, which requires the collecting establishment to notify a donor when the donor is deferred from donation. Current § 630.6 is approved under OMB control number 0910–0116. This approval expires December 31, 2008.

We are not calculating information collection burden for § 640.120, because by permitting industry to use alternatives in complying with certain regulations for blood and blood components, we believe that this provision reduces burden on industry.

In compliance with the Paperwork Reduction Act of 1995 (44 U.S.C. 3507(d)), the agency has submitted the information collection provisions of this proposed rule to OMB for review. Interested persons are requested to send comments regarding information collection to OMB (see **DATES** and **ADDRESSES**).

VII. Environmental Impact

The agency has determined under 21 CFR 25.30(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VIII. Federalism

FDA has analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the proposed rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the agency has concluded that the rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement is not required.

IX. Request for Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments on this proposed rule. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

X. References

The following references have been placed on display in the Division of Dockets Management (see **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday. (FDA has verified the Web site addresses, but FDA is not responsible for any subsequent changes to the Web site after this document publishes in the **Federal Register**.)

1. Yomtovian R., ''Bacterial Contamination of Blood: Lessons From the Past and Road Map For the Future,'' *Transfusion*, March 2004; 44:450–460.

2. Boulton F., ''Determination of Blood Pressure of Blood Donors at Blood Collection Sessions,'' presented at the 26th meeting of the Select Committee of Experts on Quality

Assurance in Blood Transfusion Services, February 2003.

3. Perloff D., et al., ''Human Blood Pressure Determination by Sphygmomanometry,'' *Circulation*, November 1993; 88(5 Pt 1):2460–70.

4. Wood, E.M., D.M. Kim, J.P. Miller, ''Accuracy of Predonation Hct Sampling Affects Donor Safety, Eligibility, and Deferral Rates,'' *Transfusion*, March 2001; 41:353–359.

5. HHS, ''The 2005 Nationwide Blood Collection and Utilization Survey Report,'' p.14, 2005, *http://www.aabb.org/apps/docs/05nbcusrpt.pdf*.

6. U.S. General Accounting Office, ''Blood Supply Generally Adequate Despite New Donor Restrictions,'' p. 5 note 7, July 2002, *http://www.gao.gov/new.items/d02754.pdf*.

7. U. S. Bureau of Labor Statistics, ''Employer Costs for Employee Compensation,'' table 14, September 2006.

8. Lapane, K. L., et al., ''Hepatitis C Infection Risk Analysis: Who Should Be Screened? Comparison of Multiple Screening Strategies Based on the National Hepatitis Surveillance Program,'' *The American Journal of Gastroenterology*, April 1998; 93:591–596.

9. U.S. Centers for Disease Control and Prevention, ''Viral Hepatitis B Fact Sheet,'' July 27, 2007, *http://www.cdc.gov/ncidod/diseases/hepatitis/b/bfact.pdf*.

10. U.S. Centers for Disease Control and Prevention, ''Viral Hepatitis B Frequently Asked Questions,'' *http://www.cdc.gov/ncidod/diseases/hepatitis/b/faqb.htm#gen*.

11. Stramer, S.L. ''US NAT yield: Where Are We After 2 Years?'' *Transfusion Medicine*, August 2002; 12:243–53.

12. U.S. Centers for Disease Control and Prevention, ''Viral Hepatitis C Fact Sheet,'' May 24, 2005, *http://www.cdc.gov/ncidod/diseases/hepatitis/c/cfact.pdf*.

13. North American Industry Classification System (NAICS), available online at *http://www.naics.com/sba_sizestandards.htm*.

14. U.S. Small Business Administration, Office of Size Standards, ''Table of Small Business Size Standards,'' 2007, *http://www.sba.gov/size/sizetable2007.pdf*.

List of Subjects

21 CFR Part 606

Blood, Labeling, Laboratories, Reporting and recordkeeping requirements.

21 CFR Parts 610 and 660

Biologics, Labeling, Reporting and recordkeeping requirements.

21 CFR Part 630

Blood, Reporting and recordkeeping requirements.

21 CFR Part 640

Blood, Labeling, Reporting and recordkeeping requirements.

21 CFR Part 820

Medical devices, Reporting and recordkeeping requirements.

21 CFR Part 1270

Communicable diseases, HIV/AIDS, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, and under the authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR Chapter I be amended as follows:

PART 606—CURRENT GOOD MANUFACTURING PRACTICE FOR BLOOD AND BLOOD COMPONENTS

1. The authority citation for 21 CFR part 606 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 355, 360, 360j, 371, 374; 42 U.S.C. 216, 262, 263a, 264.

2. Section 606.3 is amended by revising paragraphs (a) and (c) to read as follows:

§ 606.3 Definitions.

* * * * *

(a) *Blood* means a product that is the fluid containing dissolved and suspended elements, which circulates in the vascular system of a human.

* * * * *

(c) *Blood component* means a product containing a part of human blood separated by physical or mechanical means.

* * * * *

3. Section 606.100 is amended by revising the introductory text in paragraph (b); by revising paragraph (b)(20); and by adding paragraph (b)(21) to read as follows:

§ 606.100 Standard operating procedures.

* * * * *

(b) Establishments must establish, maintain, and follow written standard operating procedures for all steps in the collection, processing, compatibility testing, storage, and distribution of blood and blood components for allogeneic transfusion, autologous transfusion, and further manufacturing purposes; for all steps in the investigation of product deviations related to § 606.171; and for all steps in recordkeeping related to current good manufacturing practice and biological product standards. Such procedures must be available to the personnel for use in the areas where the procedures are performed. The written standard operating procedures must include, but are not limited to, descriptions of the following, when applicable:

* * * * *

(20) Procedures for donor deferral as prescribed in § 610.41 of this chapter; and

(21) Procedures for donor notification and autologous donor referring physician notification, including procedures for the appropriate followup if the initial attempt at notification fails, as prescribed in § 630.40 of this chapter.

* * * * *

§ 606.110 [Amended]

4. Section 606.110(b) is amended by removing ''640.63'' and by adding in its place ''630.10, 630.15''.

5. Section 606.160 is amended by revising paragraphs (b)(1)(ix), (b)(1)(xi), and (e) to read as follows:

§ 606.160 Records.

* * * * *

(b) * * *

(1) * * *

(ix) Records of notification of donors deferred or determined not to be eligible for donation, including appropriate followup if the initial attempt at notification fails, performed under § 630.40 of this chapter.

* * * * *

(xi) Records of notification of the referring physician of a deferred autologous donor, including appropriate followup if the initial attempt at notification fails, performed under § 630.40 of this chapter.

* * * * *

(e)(1) Establishments must maintain a record of all ineligible donors so that blood and blood components are not collected from such individuals while they are ineligible or deferred; and

(2) Establishments must provide, to appropriate personnel at all locations operating under the same license or under common management, a collective list of ineligible donors with sufficient information to prevent the collection of blood and blood components from any donors currently identified at each location as not eligible to donate under § 630.10(f) and (g)(1) through (g)(6) of this chapter, or deferred based on test results under § 610.41 of this chapter.

PART 610—GENERAL BIOLOGICAL PRODUCTS STANDARDS

6. The authority citation for 21 CFR part 610 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 360, 360c, 360d, 360h, 360i, 371, 372, 374, 381; 42 U.S.C. 216, 262, 263, 263a, 264.

Subpart E [Amended]

7. Subpart E is amended by removing ''communicable disease agents'' and by adding in its place ''relevant transfusion-transmitted infections'' in

the subpart heading and everywhere it appears throughout the subpart.

8. Section 610.40 is amended by revising paragraph (a) and (e) introductory text to read as follows:

§ 610.40 Test requirements.

(a) *Human blood and blood components.* Except as specified in paragraphs (c) and (d) of this section, and except for syphilis, which must be tested under § 610.40(i), for each donation of blood and blood components intended for use in preparing a product, including donations intended as a component of, or used to prepare a medical device, you, an establishment that collects blood and blood components, must test:

(1) For evidence of infection due to the following relevant transfusion-transmitted infections described in § 630.3(g)(1)(i) through (g)(1)(iv) of this chapter:

(i) Human immunodeficiency virus, types 1 and 2;

(ii) Hepatitis B virus;

(iii) Hepatitis C virus; and

(iv) Human T-lymphotropic virus, types I and II;

(2) In addition, for evidence of infection due to relevant transfusion-transmitted infections described in § 630.3(g)(1)(vi) through (g)(1)(viii) and 630.3(g)(2) of this chapter, provided that testing for the disease agent or disease is available and necessary to reduce the risk of transmission of the relevant transfusion-transmitted infection by the blood or blood component.

* * * * *

(e) *Further testing.* You must further test each donation, including autologous donations, found to be reactive by a screening test performed under paragraphs (a) and (b) of this section using one or more FDA-approved supplemental (additional, more specific) test(s), or other appropriate, additional tests. You must perform such further testing as necessary and appropriate to determine the deferred donor's infection status for the purpose of donor notification required under § 630.40 of this chapter, except:

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PART 630—REQUIREMENTS FOR HUMAN BLOOD AND BLOOD COMPONENTS INTENDED FOR TRANSFUSION OR FOR FURTHER MANUFACTURING USE

9. The authority citation for part 630 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 355, 360, 371; 42 U.S.C. 216, 262, 264.

10. Revise the heading for part 630 to read as set forth above.

11. Add a heading for new subpart C to read as follows:

Subpart C—Donor Notification

12. Redesignate § 630.6 as § 630.40, and transfer newly designated § 630.40 to subpart C.

13. Amend § 630.40 as follows:

a. Revise the section heading.

b. Remove ''suitable'' wherever it appears and add ''eligible'' in its place; and remove ''suitability'' wherever it appears and add ''eligibility'' in its place.

c. Revise the first sentence in paragraph (a).

The revisions read as follows:

§ 630.40 Requirements for notifying deferred donors.

(a) *Notification of donors.* You must make reasonable attempts to notify any donor, including an autologous donor, who has been deferred based on the results of tests for evidence of infection with a relevant transfusion-transmitted infection(s) as required by § 610.41 of this chapter; who has been determined not to be eligible as a donor based on eligibility criteria under §§ 630.10 and 630.15 of this chapter; or whose platelet component has tested positive for an endogenous bacterial contamination. * * *

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14. Add subparts A and B to part 630 to read as follows:

Subpart A—General Provisions

Subpart B—Donor Eligibility Requirements

Subpart A—General Provisions

§ 630.1 Purpose and scope.

(a) *Purpose. What is the purpose of subparts A, B, and C of this part?* The purpose of these subparts, together with §§ 610.40 and 610.41 of this chapter, is to provide certain minimum criteria for each donation of blood and blood components, for:

(1) Determining the eligibility of a donor of blood and blood components;

(2) Determining the suitability of the donation of blood and blood components; and

(3) Notifying a donor who is deferred from donation.

(b) *Scope. Who must comply with subparts A, B, and C of this part?* You, as defined in § 630.3(l), must comply with subparts A, B, and C of this part.

§ 630.3 Definitions.

As used in this part and 21 CFR part 640 of this chapter:

(a) *Blood* means a product that is the fluid containing dissolved and suspended elements, which circulates in the vascular system of a human.

(b) *Blood component* means a product containing a part of blood separated by physical or mechanical means.

(c) *Donor* means a person who:

(1) Donates blood or blood components for transfusion or for further manufacturing use or

(2) Presents as a potential candidate for such donation.

(d) *Eligibility of a donor* means the determination that the donor is qualified to donate blood and blood components.

(e) *Intimate contact* means an activity that could result in an exchange of body fluids, including blood or saliva, with another individual.

(f) *Physician substitute* means a trained and qualified person(s) who is:

(1) A graduate of an education program for health care workers that includes clinical training;

(2) Currently licensed or certified as a health care worker in the jurisdiction where the collecting establishment is located;

(3) Currently certified in cardiopulmonary resuscitation; and

(4) Trained and authorized to perform specified functions under the direction of the responsible physician.

(g) *Relevant transfusion-transmitted infection* means:

(1) Any of the following transfusion-transmitted infections:

(i) Human immunodeficiency virus, types 1 and 2 (HIV);

(ii) Hepatitis B virus (HBV);

(iii) Hepatitis C virus (HCV);

(iv) Human T-lymphotropic virus, types I and II (HTLV);

(v) *Treponema pallidum* (syphilis);

(vi) Creutzfeldt-Jakob disease (CJD);

(vii) Variant Creutzfeldt-Jakob disease (vCJD); and

(viii) *Plasmodium sp.* (malaria).

(2) Other transfusion-transmitted infections not listed in paragraph (g)(1) of this section:

(i) For which appropriate screening measures are developed and/or an appropriate screening test for donor

specimens is licensed, approved, or cleared for such use by FDA and is available; and

(ii) That:

(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 donors at risk of infection.

(h) *Responsible physician* means an individual who is:

(1) Licensed to practice medicine in the jurisdiction where the collecting establishment is located;

(2) Adequately trained and qualified to direct and control personnel and relevant procedures concerning the determination of donor eligibility; collection of blood and blood components; the immunization of a donor; and the return of red blood cells or other blood components to the donor during collection of blood component(s) by apheresis; and

(3) Designated by the collecting establishment to direct and control personnel, and to approve relevant procedures specifying decision-making criteria for determining donor eligibility, the collection of blood or blood components, the immunization of a donor, and the return of red blood cells or other blood components to a donor during collection of blood component(s) by apheresis.

(i) *Suitability of the donation* means a determination of whether the donation is acceptable for transfusion or for further manufacturing use.

(j) *Trained personnel* means authorized individuals, including physician substitutes, who are adequately instructed and qualified to perform specified functions under the direction of the responsible physician.

(k) *Transfusion-transmitted infection* means a disease or disease agent:

(1) That could be fatal or life-threatening, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of body function or permanent damage to a body structure; and

(2) For which there may be a risk of transmission by the blood and blood components collected, or by a blood derivative product manufactured from the collected blood or blood components, because the disease agent or disease is potentially transmissible by that blood, blood component, or blood derivative product.

(l) *You* means an establishment that collects blood and blood components as described in paragraphs (a) and (b) of this section.

Subpart B—Donor Eligibility Requirements

§ 630.5 Medical supervision.

(a) *Who must determine the eligibility of a donor?* The responsible physician authorized by you, as described in § 630.3(l), must determine the eligibility of a donor of blood or blood components in accordance with this part.

(b) *Must the responsible physician be present at the collecting establishment at all times?* Except as provided in paragraphs (c) and (d) of this section and § 630.15(b)(1) and (b)(4), you must assure that the responsible physician is in attendance when any of the following activities are performed at the collecting establishment:

(1) Determining the eligibility of a donor;

(2) Collecting blood or blood components;

(3) Collecting Source Plasma in an approved collection program from donors who are otherwise determined to be unsuitable;

(4) Returning red blood cells to the donor during plasmapheresis; or

(5) Immunizing a donor in an approved hyperimmunization program.

(c) *What specified functions of the responsible physician in the collection of Source Plasma may be performed by a physician substitute?* You may authorize a physician substitute to perform any specified function listed in paragraph (b) of this section in the collection of Source Plasma except for red blood cell immunizations performed under paragraph (b)(5) of this section.

(d) *What specified functions of the responsible physician in the collection of blood and blood components may be performed by a physician substitute or trained personnel?* In the absence of the responsible physician, you may authorize a physician substitute or trained personnel to determine donor eligibility and collect blood and blood components.

(e) *Must emergency medical services be available?* Yes, you must establish, maintain, and follow standard operating procedures for providing within 15 minutes emergency medical services for donors when medically necessary.

§ 630.10 General donor eligibility requirements.

(a) *What factors determine the eligibility of a donor?* You must not collect blood and blood components before you determine that the donor is eligible to donate. A donor is not eligible if the donor is not in good health or if you identify factors that may adversely affect:

(1) The health of the donor or

(2) The safety, purity, or potency of the blood or blood components collected from the donor.

(b) *What educational material must you provide to the donor before determining eligibility?* Before determining eligibility, you must provide the donor with educational material containing useful and current information concerning the relevant transfusion-transmitted infections defined in § 630.3(g). The educational material must include an explanation of the signs and symptoms of and the readily identifiable risk factors closely associated with exposure to the relevant transfusion-transmitted infections. You must present educational material in an appropriate form, e.g., in oral, written or multimedia, and in a manner designed to be understood by the donor. The educational material must state that the donor may not donate blood and blood components when such signs and symptoms or risk factors are present.

(c) *When must you determine the eligibility of a donor?* You must determine donor eligibility on the day of donation, and before collection. When a donor is donating blood components that cannot be stored for more than 24 hours, you may determine the donor's eligibility and collect a sample for testing required under § 610.40 and § 640.5 of this chapter, 1 day before the donation. You must have standard operating procedures in place for identifying such components.

(d) *How must you determine the eligibility of a donor?* Before collection, you must determine the donor's eligibility by the following procedures:

(1) Assessing the donor's deferral status by checking the collective list of ineligible donors required under § 606.160(e)(2) of this chapter;

(2) Assuring that the interval since the donor's last donation is appropriate, taking into account the donor's participation, if any, in other blood or blood component collection programs;

(3) Assessing the donor's medical history; and

(4) Performing a physical assessment of the donor.

(e) *How do you assess the donor's medical history?* Before collection, you must take a medical history designed to determine if the donor is in good health and if health care practitioners have ever advised the donor not to donate; to identify risk factors closely associated with exposure to, or clinical evidence of, infection due to a relevant transfusion-transmitted infection; and to

determine if there are other conditions that may adversely affect the donor or the safety, purity, or potency of the blood or blood components or any product produced from the blood or blood components.

(f) *What factors make the donor ineligible because of an increased risk for, or evidence of, a relevant transfusion-transmitted infection?* The donor is ineligible to donate when information provided by the donor or other reliable evidence indicates possible exposure to a relevant transfusion-transmitted infection. Information that a donor has participated in any of the following renders the donor ineligible if that risk of exposure is still applicable at the time of donation:

(1) Social behaviors associated with relevant transfusion-transmitted infections;

(2) Medical treatments and procedures associated with exposure to relevant transfusion-transmitted infections;

(3) Signs and symptoms of relevant transfusion-transmitted infections;

(4) Institutionalization in a correctional institution;

(5) Intimate contact with an individual who is at an increased risk for exposure to, or is known to be infected with, a relevant transfusion-transmitted infection that is spread by such type of intimate contact; and

(6) Nonsterile percutaneous inoculation.

(g) *What other factors make the donor ineligible to donate because of risk to the health of the donor, or to the safety, purity, or potency of the blood or blood component?* You must assess the donor for each of the following factors to determine whether donating could adversely affect the health of the donor, or whether the safety, purity, or potency of the blood or blood component could be affected, and if so, you must determine the donor to be ineligible:

(1) Medical or dental treatment, or symptoms of a recent or current illness;

(2) Medication;

(3) Major surgical procedure;

(4) Travel to, or residence in, an area endemic for a transfusion-transmitted infection;

(5) Xenotransplantation product recipient or intimate contact of a xenotransplantation product recipient;

(6) Exposure or possible exposure to a released disease agent or disease relating to a transfusion-transmitted infection, if you know or suspect that such a release has occurred;

(7) Pregnancy at the time of, or 6 weeks before, donation; and

(8) Unreliable answers to medical history questions due to the apparent influence of drugs or alcohol, or due to another reason affecting the reliability of the donor's answers.

(h) *How do you perform a physical assessment of the donor?* You must determine that the donor is in good health based on the following, at a minimum:

(1) *Temperature.* The donor's oral body temperature must not exceed 37.5 °C (99.5 °F), or the equivalent if measured at another body site;

(2) *Blood pressure.* The donor's systolic blood pressure must not measure above 180 millimeters of mercury or below 90 millimeters of mercury, and the diastolic blood pressure must not measure above 100 millimeters of mercury or below 50 millimeters of mercury. A donor with measurements outside these limits may be permitted to donate only when the responsible physician has examined the donor and determined that the health of the donor would not be adversely affected by donating.

(3) *Hemoglobin or hematocrit determination for allogeneic donation.* (i) You must determine the donor's hemoglobin level or hematocrit value by using a sample of blood obtained by fingerstick, venipuncture, or by a method that provides equivalent results. Blood obtained from the earlobe is not acceptable; and

(ii) An allogeneic donor must have a hemoglobin level no less than 12.5 grams per deciliter of blood, or a hematocrit value no less than 38 percent. An autologous donor must have a hemoglobin level no less than 11.0 grams per deciliter of blood, or a hematocrit value no less than 33 percent.

(4) *Pulse.* The donor's pulse rate must be regular and between 50 and 100 beats per minute. A donor with an irregular pulse rate or measurements outside these limits may be permitted to donate only when the responsible physician has examined the donor and determines that the health of the donor would not be adversely affected.

(5) *Weight.* The donor must weigh a minimum of 50 kilograms (110 pounds) and must not have had an unexplained loss of greater than 10 percent of body weight within the past 6 months; and

(6) *Skin examination.* (i) The donor's phlebotomy site must be free of infection, inflammation, lesions, and pitted skin; and

(ii) The donor's arms and forearms must be free of punctures and scars indicative of injected drugs of abuse.

(i) *What additional requirements must you complete before determining the eligibility of the donor?* Immediately before donation, you must obtain the following:

(1) *Proof of identity and mailing address.* You must obtain proof of identity of the donor and an address where the donor may be contacted for 8 weeks after donation; and

(2) *Donor's written statement of understanding.* You must provide a written statement of understanding to be read and signed by the donor. You must establish procedures in accordance with § 606.100 of this chapter to provide assistance to those unable to read the written statement of understanding. You must design those procedures to assure that the donor understands fully the material in the donor's written statement of understanding, and provide for a signature or acceptable substitute for a signature to indicate that understanding. The written statement of understanding must not include any exculpatory language through which the donor is made to waive or appear to waive any of the donor's legal rights. The statement must clearly state the following:

(i) The donor has reviewed the provided educational material required by § 630.10(b) regarding relevant transfusion-transmitted infections, including the fact that relevant transfusion-transmitted infections present potential risks to the safety, purity, or potency of the blood supply;

(ii) The donor agrees not to donate if the donation could result in a potential risk to the safety, purity, or potency of the blood supply as described in the educational material;

(iii) A sample of the donor's blood will be tested for specified relevant transfusion-transmitted infections required in § 610.40(a) of this chapter and for syphilis.

(iv) If any of the tests required in § 610.40(a) of this chapter are reactive, the sample of blood will be tested further, as required in § 610.40(e) of this chapter;

(v) If the donation is determined to be not suitable under § 630.30(a) or if the donor is deferred from donation under § 610.41 of this chapter, the donor's record must identify the donor as ineligible to donate and the donor must be notified under § 630.40 of the basis for the deferral and the period of deferral;

(vi) The hazards and risks of the donation procedure or of hyperimmunization, if applicable; and

(vii) the donor has the opportunity to ask questions and withdraw consent at any time.

§ 630.15 Donor eligibility requirements specific to Whole Blood and to Plasma collected by plasmapheresis.

(a) *What additional donor eligibility requirements are specific to Whole Blood?*—(1) *Donation frequency.* Whole Blood must not be collected from a donor more than once in 8 weeks if the donor participates in a single unit collection program; or more than once in 16 weeks if the donor participates in a double unit collection program, unless the donor is examined and certified to be in good health by a responsible physician at the time of donation and one of the following three conditions exist:

(i) An individual presents a physician's prescription for therapeutic phlebotomy for medical reasons; or

(ii) The donation is for autologous use; or

(iii) The donation is a dedicated donation based on the intended recipient's documented medical need.

(2) *Therapeutic phlebotomy.* When a donor who is determined to be eligible under § 630.10(d) undergoes a therapeutic phlebotomy to promote the health of the donor, the container label must conspicuously state the disease of the donor that necessitated phlebotomy. However, no disease labeling is required under this section for a donation collected from a donor who meets all eligibility criteria and undergoes a therapeutic phlebotomy as ordered by a physician treating the donor for Hereditary Hemochromatosis, provided that you perform without charge therapeutic phlebotomies for all individuals with Hereditary Hemochromatosis.

(b) *What additional donor eligibility requirements are specific to Plasma collected by plasmapheresis?*—(1) *Physical examination and informed consent.* (i) In addition to the physical assessment required in § 630.10(d), the responsible physician must examine the donor for medical conditions that would place the donor at risk during plasmapheresis. If the donor is determined to be at risk, you must defer the donor from donating. In a program of repeat plasmapheresis, i.e., collections occur more than once every 28 days, the donor must be examined on the day of the first donation or no more than 1 week before the first donation and at subsequent intervals of no more than 1 year.

(ii) When conducting the physical examination, the responsible physician must explain the hazards of the procedure to the donor. The explanation must include the risks of a hemolytic transfusion reaction if the donor is given the cells of another donor, and the hazards involved if the donor is hyperimmunized. The explanation must be made in such a manner that the donor may give informed consent and has a clear opportunity to refuse the procedure as required under § 630.10(i)(2).

(2) *Weight.* You must weigh a donor at each donation.

(3) *Total protein level.* Before each plasmapheresis procedure, a donor must have a total plasma protein level of no less than 6.0 grams per deciliter and no more than 9.0 grams per deciliter of plasma sample or the comparable level for a serum sample.

(4) *Examination before immunization.* (i) In addition to the determination of donor eligibility required in § 630.10(d), the responsible physician must perform the physical examination no more than 1 week before the first immunization injection for the production of high-titer plasma. It is not necessary to repeat the physical examination requirement in paragraph (b)(1) of this section, if the immunized donor's plasma is collected within 3 weeks of the first immunization injection; and

(ii) A donor determined to be eligible under § 630.10(d) and currently participating in a plasmapheresis program, does not need to be re-examined before immunization for the production of high-titer antibody plasma.

(5) *Deferral due to red blood cell loss.* You must defer a donor from donating plasma for a period of 8 weeks after any of the following events:

(i) The donor experienced a red blood cell loss of equal to or greater than 200 milliliters of red blood cells during a single automated plasmapheresis procedure; or

(ii) The donor experienced an unexpected red blood cell loss of any volume in an automated apheresis procedure on two occasions within the last 8-week period; or

(iii) The donor experienced a red blood cell loss equivalent to or greater than 200 milliliters of red blood cells as a result of failure to return red blood cells during a manual plasmapheresis procedure; or

(iv) The donor donated a unit of Whole Blood.

(6) *Exceptions to deferral due to red blood cell loss.* You are not required to defer a donor from participation in a plasmapheresis program due to red blood cell loss if the following occurs:

(i) The donor is examined at the time of the current donation and certified by the responsible physician to be in good health under § 630.10(h) and the donor's health permits the plasmapheresis; and

(ii) The donor possesses an antibody that is transitory, of a highly unusual or infrequent specificity, or of an unusually high titer, and

(iii) The special characteristics of the antibody and the need for plasmapheresis of the donor under § 630.20(c)(2) are documented at your establishment.

(7) *Malaria.* Freedom from risk of malaria is not required for a donor of Source Plasma.

§ 630.20 General exceptions from donor eligibility requirements.

You may collect blood and blood components from a donor who is determined to be not eligible to donate under §§ 630.10(d) and 630.15, or deferred under § 610.41 of this chapter only if:

(a) The responsible physician examines the donor and certifies in writing that the donor's health permits the collection procedure;

(b) The collection is performed under the supervision of the responsible physician who is aware of the donor's health status; and

(c) At least one of the following is met:

(1) The donation is for autologous use as prescribed by the donor's physician, and is not for allogeneic transfusion or for further manufacturing use;

(2) The donor is participating in a plasmapheresis program that collects plasma for further manufacturing use into products for which there are no alternative sources, and the collection program has received prior approval from the Director, Center for Biologics Evaluation and Research; or

(3) The donation is restricted for use solely by a specific recipient based on documented medical need and the responsible physician determines that the donation presents no undue medical risk to the recipient.

§ 630.25 Exceptions from certain donor eligibility requirements for infrequent plasmapheresis.

You are not required to perform a physical examination of the donor for medical conditions under § 630.15(b)(1), to perform a test for total protein under § 630.15(b)(3), to determine the immunoglobulin composition of the serum or plasma under § 640.65(b)(1)(i) of this chapter, or to review the laboratory data as required in § 640.65(b)(2)(i) of this chapter, if:

(a) The donor has not donated Whole Blood in the preceding 8 weeks, Plasma by plasmapheresis in the preceding 4 weeks, or participated in a double Red Blood Cells unit collection program within the preceding 16 weeks;

(b) The donor has not donated more than 12.0 liters of plasma (14.4 liters of plasma for donors weighing more than 175 lbs.) in the past year;

(c) The donor is determined by the responsible physician to be in good health under § 630.10(d); and

(d) The donor is not participating in an immunization program for the production of high-titer plasma.

§ 630.30 Donation suitability requirements.

(a) *When is a donation suitable?* A donation is suitable when:

(1) The donor is not currently deferred from donation;

(2) The results in accordance with §§ 630.10 through 630.25 indicate that the donor is in good health and that the donation would not adversely affect the health of the donor;

(3) The donor is free from risk factors for, or evidence of transfusion-transmitted infections under § 630.10(f) and (g);

(4) The donor's blood is tested in accordance with § 610.40 of this chapter, and is negative or nonreactive, unless an exception applies under § 610.40(h) of this chapter;

(5) For platelet components, you have taken adequate steps to assure that the donation is tested for bacterial contamination and found negative; and

(6) The donation meets other requirements in this subchapter.

(b) *What must you do when the donation is not suitable?* (1) When the donation does not meet the criteria in paragraphs (a)(1) through (a)(3) and (a)(5) of this section, the donation is not suitable and you must defer the donor from donation;

(2) When the donation does not meet the criteria in paragraph (a)(4) of this section, defer the donor from donation in accordance with § 610.41(a) of this chapter;

(3) Identify a donor not eligible under § 630.10(f)(1) through (f)(6) and § 630.10(g)(1) through (g)(6) as not eligible to donate under § 606.160(e) of this chapter; and

(4) Notify a donor found not eligible to donate under § 610.41 of this chapter, and §§ 630.10 through 630.25, or 630.30(a)(5) of the deferral, the deferral period, and the reason for the deferral, in accordance with the notification requirements in § 630.40.

§ 630.35 Requalification of previously deferred donors.

(a) A deferred donor identified under § 630.30(b)(1) may be determined eligible as a donor of blood and blood components if, at the time of the current collection, except for the record of previous deferral, the donor meets the eligibility criteria in this part; and the criteria, which were the basis for the previous deferral, are determined to be no longer applicable.

(b) A deferred donor identified under § 630.30(b)(2) may be determined eligible as a donor of blood and blood components if, at the time of the current collection except for the record of the previous deferral, the donor meets the eligibility criteria in this part; and the criteria which were the basis for the previous deferral are determined to be no longer applicable under § 610.41(b) of this chapter.

PART 640—ADDITIONAL STANDARDS FOR HUMAN BLOOD AND BLOOD PRODUCTS

15. The authority citation for 21 CFR part 640 continues to read as follows:

Authority: 21 U.S.C. 321, 351, 352, 353, 355, 360, 371; 42 U.S.C. 216, 262, 263, 263a, 264.

§ 640.3 [Removed]

16. Section 640.3 is removed.

§ 640.4 [Amended]

17. Section 640.4 is amended by removing paragraph (a) and by redesignating paragraphs (b) through (h) as paragraphs (a) through (g).

18. Section 640.12 is revised to read as follows:

§ 640.12 Eligibility of donor.

Collecting establishments must determine the eligibility of donors of the source blood for Red Blood Cells in accordance with §§ 630.10 and 630.15 of this chapter.

19. Section 640.21 is revised to read as follows.

§ 640.21 Eligibility of donors.

(a)(1) Collecting establishments must determine the eligibility of Whole Blood donors and plateletpheresis donors in accordance with §§ 630.10 and 630.15 of this chapter, except as expressly modified in paragraph (e) of this section.

(2) Under § 630.10(i)(2)(vi) of this chapter, the statement of understanding must include a statement that the long-term effects of frequent apheresis are unknown.

(b) A donor must not serve as a source of platelets for transfusion if the donor has recently ingested drugs that adversely affect platelet function.

(c) A plateletpheresis donor may donate at intervals shorter than 8 weeks provided:

(1) The establishment performs a platelet count before starting the initial plateletpheresis procedure and before each subsequent procedure;

(2) The platelet count required in paragraph (c)(1) of this section is greater than 150,000/μL;

(3) The donor's post-donation platelet count is no less than 100,000 platelets/μL; and

(4) The donor donates the following:

(i) No more than a total of 24 plateletpheresis collections during a 12-month period;

(ii) For single component collection procedures, no more than 2 plateletpheresis procedures within a 7 calendar day period with a minimum of 2 calendar days between procedures;

(iii) For a double or triple component collection procedure, no more than one procedure within a 7 calendar day period.

(d) For a period not to exceed 30 days, a donor may serve as a dedicated plateletpheresis donor for a single recipient, in accordance with § 610.40(c)(1) of this chapter, as often as is medically necessary, provided that the donor is in good health, as determined by a physician, and the donor's platelet count is greater than 150,000/μL, measured at the conclusion of the previous donation or before initiating apheresis for the current donation.

(e) Except as provided in paragraphs (e)(1) and (e)(2) of this section, a plateletpheresis donor must be deferred for a period of 8 weeks after donating a unit of Whole Blood or after losing a volume of whole blood equal to or greater than 450 mL, or red blood cells equal to or greater than 200 mL, cumulatively over an 8 week period; or be deferred for a period of 16 weeks after donating a double Red Blood Cells unit collection. In exception, the plateletpheresis donor may donate if all of the following criteria are met:

(1) The donor waits 2 calendar days after donating Whole Blood or after experiencing the blood loss; and

(2) The extracorporeal red blood cell volume during the apheresis procedure is equal to or less than 100 mL.

§ 640.22 [Amended]

20. Section 640.22(b) is amended by removing ''640.62'' and by adding in its place ''630.5''.

21. Section 640.31 is revised to read as follows:

§ 640.31 Eligibility of donors.

(a) Whole Blood donors must meet the criteria for donor eligibility prescribed in §§ 630.10 and 630.15 of this chapter.

(b) Collecting establishments must determine the eligibility of plasmapheresis donors in accordance with §§ 630.10 and 630.15 of this chapter.

§ 640.32 [Amended]

22. Section 640.32(b) is amended by removing ''640.62'' and by adding in its place ''630.5''.

23. Section 640.51 is revised to read as follows:

§ 640.51 Eligibility of donors.

(a) Whole blood donors must meet the criteria for eligibility prescribed in §§ 630.10 and 630.15 of this chapter.

(b) Collecting establishments must determine the eligibility of plasmapheresis donors in accordance with §§ 630.10 and 630.15 of this chapter.

§ 640.52 [Amended]

24. Section 640.52(b) is amended by removing ''640.62'' and by adding in its place ''630.5''.

§ 640.61 [Removed]

25. Section 640.61 is removed.

§ 640.62 [Removed]

26. Section 640.62 is removed.

§ 640.63 [Removed]

27. Section 640.63 is removed.

28. Section 640.65 is amended by revising paragraphs (b)(1)(i) and (b)(2)(i) to read as follows:

§ 640.65 Plasmapheresis.

* * * * *

(b) * * *

(1)(i) Except as provided under § 630.25 of this chapter, a sample of blood must be drawn from each donor on the day of the initial physical examination or plasmapheresis, whichever comes first, and at least every 4 months thereafter. A serological test for syphilis, a total plasma or serum protein determination, and electrophoresis or quantitative immunodiffusion test or an equivalent test to determine immunoglobulin composition of the plasma or serum, must be performed on the sample.

* * * * *

(2)(i) Except as provided under § 630.25 of this chapter, the accumulated laboratory data, including tracings of the plasma or serum protein electrophoresis pattern, if any, the calculated values of each component, and the collection records must be reviewed by the responsible physician as required in § 630.5 of this chapter within 14 calendar days after the sample is drawn to determine whether or not the donor should be deferred from further donation. If a determination is not made within 14 calendar days, the donor must be deferred pending such a determination. The responsible physician must sign the review. If the protein composition is not within normal limits established by the testing laboratory, or if the total protein is less than 6.0 grams per deciliter of plasma sample or more than 9.0 grams per deciliter of plasma sample, or the comparable level for a serum sample, the donor must be deferred from donation until the protein composition returns to acceptable levels. Reinstatement of the donor into the plasmapheresis program when the donor's values have returned to acceptable levels must first be approved by the responsible physician.

* * * * *

29. Section 640.69 is amended by adding paragraphs (e) and (f) to read as follows:

§ 640.69 General requirements.

* * * * *

(e) *Restrictions on distribution.* Establishments must ensure that Source Plasma donated by paid donors not be used for further manufacturing into injectable products until the donor has a record of two suitable donations within the last 6 months.

(f) *Hold.* Source Plasma donated by paid donors determined to be suitable for further manufacturing into injectable products must be held in quarantine for a minimum of 60 days before it is released for further manufacturing.

30. Section 640.72 is amended by revising paragraphs (a)(2), (a)(3), and (a)(4) to read as follows:

§ 640.72 Records.

(a) * * *

(2)(i) For each donor, a separate and complete record of initial and periodic examinations, tests, laboratory data, and interviews as required in §§ 630.10 and 630.15 of this chapter and §§ 640.65, 640.66, and 640.67, except as provided in paragraph (a)(2)(ii) of this section.

(ii) Negative results for testing for evidence of infection due to relevant transfusion-transmitted infections required in § 610.40 of this chapter, and the volume or weight of plasma withdrawn from a donor need not be recorded on the individual donor record if such information is maintained on the premises of the plasmapheresis center where the donor's plasma has been collected.

(3) The original or a clear copy of the donor's written statement of understanding for participation in the plasmapheresis program or for immunization.

(4) Documentation by the responsible physician that the donor is in good health under §§ 630.10 and 630.15 of this chapter on the day of examination; such documentation must address the eligibility of the donor as a plasmapheresis donor and, when applicable, an immunized donor.

* * * * *

31. Section 640.73 is revised to read as follows:

§ 640.73 Reporting of donor reactions.

(a) If a donor has a fatal reaction which, in any way, may be associated with plasmapheresis, you must notify the Director of the Center for Biologics Evaluation and Research by telephone as soon as possible.

(b) If a donor enrolled in an immunization program for the collection of Source Plasma under this subpart has an adverse experience related to your administration of the immunizing agent, you must report the event to FDA:

(1) By telephone, facsimile, express mail, or electronic mail as soon as possible, if the adverse experience is a serious or life threatening adverse experience, as described in § 600.80(a) of this chapter; or

(2) In an annual report, if the adverse experience is neither serious nor life threatening. Such a report is due to FDA on the anniversary of FDA's approval of your immunization program.

(c) You must follow up the initial report required under paragraphs (a) and (b)(1) of this section by submitting a written report of the investigation to the Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research, within 7 days of your first learning of the donor's reaction. (See § 600.2 of this chapter.)

32. Section 640.120 is revised to read as follows:

§ 640.120 Alternative procedures.

(a) The Director, Center for Biologics Evaluation and Research, may approve an exception or alternative to any requirement in subchapters C and F of chapter I of title 21 of the Code of Federal Regulations regarding blood, blood components, or blood products. If the Director issues such approval orally, the Director will follow up that oral approval by issuing a written approval. If approval is appropriate, the Director may issue such an approval in response to:

(1) A written request from an establishment. Licensed establishments must submit such requests in accordance with § 601.12 of this chapter;

(2) An oral request from an establishment, if there are difficult circumstances and submission of a written request is not feasible. Establishments must follow up such oral request by submitting written

requests under paragraph (a)(1) of this section within 5 working days.

(b) In a public health emergency, the Director may issue an exception or alternative to any requirement in subchapters C and F of chapter I of title 21 of the Code of Federal Regulations regarding blood, blood components, or blood products, if a variance under this section is necessary to assure that blood, blood components, or blood products will be available in a specified location to respond to an unanticipated immediate need for blood, blood components, or blood products.

(c) Periodically, FDA will provide a list of approved alternative procedures and exceptions at *www.fda.gov/cber*.

PART 660—ADDITIONAL STANDARDS FOR DIAGNOSTIC SUBSTANCES FOR LABORATORY TESTS

33. The authority citation for 21 CFR part 660 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 360, 360c, 360d, 360h, 360i, 371, 372; 42 U.S.C. 216, 262, 263, 263a, 264.

34. Section 660.31 is revised to read as follows:

§ 660.31 Eligibility of donor.

Donors of peripheral blood for Reagent Red Blood Cells must meet all the criteria for donor eligibility under §§ 630.10 and 630.15 of this chapter.

PART 820—QUALITY SYSTEM REGULATION

35. The authority citation for 21 CFR part 820 continues to read as follows:

Authority: 21 U.S.C. 351, 352, 360, 360c, 360d, 360e, 360h, 360i, 360j, 360l, 371, 374, 381, 383; 42 U.S.C. 216, 262, 263a, 264.

36. Section 820.1(a)(1) is amended by revising the last sentence to read as follows:

§ 820.1 Scope.

(a) *Applicability.* (1) * * * Manufacturers of blood and blood components used for transfusion or for further manufacturing are not subject to this part, but are subject to subchapter F of this chapter.

* * * * *

PART 1270—HUMAN TISSUE INTENDED FOR TRANSPLANTATION

37. The authority citation for 21 CFR part 1270 continues to read as follows:

Authority: 42 U.S.C. 216, 243, 264, 271.

38. Section 1270.3 is amended by revising paragraph (b) to read as follows:

§ 1270.3 Definitions.

* * * * *

(b) *Blood component* means a product containing a part of human blood separated by physical or mechanical means.

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Dated: October 25, 2007.

Jeffrey Shuren,

Assistant Commissioner for Policy.

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