

reference this action with the Unified Agenda.

Unfunded Mandates Reform Act

The Department will analyze any action that might be proposed for the purpose of the Unfunded Mandates Reform Act of 1995 to assess whether a rulemaking would impose unfunded mandates.

National Environmental Policy Act

The Department will analyze any action that might be proposed for the purpose of the National Environmental Policy Act of 1969 (42 U.S.C. 4321–4347) to determine whether there would be any effect on the quality of the environment.

(Authority: 49 U.S.C. Chapters 401, 411, 417; 14 CFR Part 204.)

Dated: July 24, 2003.

Michael W. Reynolds,

Acting Assistant Secretary for Aviation and International Affairs.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 600, 606, 610, and 640

[Docket No. 2003N–0211]

Revisions to Labeling and Storage Requirements for Blood and Blood Components, Including Source Plasma

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to revise the labeling and storage requirements for certain human blood and blood components, including Source Plasma, by combining, simplifying, and updating specific regulations applicable to container labeling and instruction circulars, and the shipping and storage temperatures for frozen noncellular blood components. This proposed rule would facilitate the use of a labeling system using machine-readable information that would be acceptable as a replacement for the “ABC Codabar” system for labeling blood and blood components. FDA is taking this action as part of its “Blood Initiative” to comprehensively review and, as necessary, revise its regulations, policies, guidances, and procedures related to the licensing and regulation of

blood products. This proposed rule is intended to help ensure the continued safety of the blood supply, and to help ensure consistency in container labeling and storage temperatures.

DATES: Submit written or electronic comments on the proposed rule by October 28, 2003. See section VIII of this document for the proposed effective date of a final rule based on this document.

ADDRESSES: Submit written comments to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>.

FOR FURTHER INFORMATION CONTACT: Sharon A. Carayiannis, Center for Biologics Evaluation and Research (HFM–17), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448, 301–827–6210.

SUPPLEMENTARY INFORMATION:

I. Background

A. Development of the International Society for Blood Transfusion (ISBT) 128

In the *Federal Register* of August 30, 1985 (50 FR 35472), FDA published a notice of availability entitled “Guideline for the Uniform Labeling of Blood and Blood Components,” which described the uniform container label for blood and blood components. The standard labels for blood and blood components recommended in the guideline incorporated barcode symbology known as “ABC Codabar.”

In August 1989, the ISBT, an organization established to promote and maintain a high level of ethical, medical, and scientific standards in blood transfusion medicine and science throughout the world, recognized that “ABC Codabar,” the first barcoding system adopted by the health care industry, was becoming outdated and initiated the design of a new system using the barcode symbology known as Code 128 (identified hereafter as ISBT 128).

Currently, under § 606.121(c)(13) (21 CFR 606.121(c)(13)), the container label for blood and blood components may bear encoded information in the form of machine-readable symbols approved for use by the Director, Center for Biologics Evaluation and Research (CBER). On March 23, 1995, FDA asked the Blood Products Advisory Committee (BPAC) whether FDA should support conversion from the “ABC Codabar” system to the ISBT 128 system. BPAC

voted in favor of FDA supporting the transition to the new barcoding system. The change to ISBT 128 was also supported by the Department of Defense (DoD), and by the blood industry including America’s Blood Centers (ABC), American Association of Blood Banks (AABB), and American National Red Cross (ARC). In December 1996, the International Council for Commonality in Blood Bank Automation (ICCBBA) held an ISBT 128 Consensus Conference in Washington, DC, to provide an opportunity for dialogue among the affected industry groups and FDA. Although consensus was obtained for use of ISBT 128, some participants expressed concerns regarding implementation timeframes and costs of implementation to hospital transfusion services. However, the updated symbology used in ISBT 128 has numerous advantages over the “ABC Codabar.” In addition to other reasons, the conversion to ISBT 128 was supported because ISBT 128 is more secure, allows more flexibility in coding highly variable information, uses double-density coding to allow more information to be encoded in a limited space, and can be interpreted by some of the barcode readers used with “ABC Codabar.”

The ICCBBA, including representatives from ABC, AABB, ARC, and DoD, developed and submitted to FDA a draft document that recommended that ISBT 128 replace the “ABC” Codabar system used on blood and blood component labels in the United States. ICCBBA recommended that the document entitled “United States Industry Consensus Standard for the Uniform Labeling of Blood and Blood Components Using ISBT 128,” Version 1.2.0 (draft standard), serve as the basis for FDA guidance on blood and blood component labeling. On November 21, 1998, FDA made a copy of the draft standard available on its Web site for public comment. In the *Federal Register* of November 27, 1998 (63 FR 65600), FDA announced the availability of the draft standard and requested public comment on both the use of ISBT 128 and timeframes for implementation. The ICCBBA revised the draft standard in response to public comment and submitted to FDA the revised document, “United States Industry Consensus Standard for the Uniform Labeling of Blood and Blood Components Using ISBT 128,” Version 1.2.0, dated November 1999 (the “Version 1.2.0 Standard”).

FDA reviewed the draft standard, the comments received in response to the *Federal Register* notice of November 27, 1998, and the “Version 1.2.0 Standard,”

and concluded that conformance to the "Version 1.2.0 Standard," prepared and revised by ICCBBA, would help facilitate the use of a uniform container label for blood and blood components. In the **Federal Register** of June 6, 2000 (65 FR 35944), FDA announced the availability of a final guidance entitled "Guidance for Industry: Recognition and Use of a Standard for the Uniform Labeling of Blood and Blood Components" dated June 2000, which recognizes as acceptable, except where inconsistent with the regulations, use of the "Version 1.2.0 Standard" prepared by ICCBBA, and the implementation of the ISBT 128 uniform labeling system. Although FDA finds the system acceptable, FDA has identified two inconsistencies between the "Version 1.2.0 Standard" and the current requirements of § 606.121(c)(2) and (e)(1)(ii). This proposed rule would delete the current requirement of § 606.121(c)(2) to include the FDA assigned registration number on blood and blood component labels. This revision is intended to provide establishments flexibility in using the registration number or other recognized donation facility identification numbers, such as the ISBT facility code (which includes machine-readable information), as the unique facility identifier. Additionally, this proposed rule would delete the current requirement of § 606.121(e)(1)(ii) that the anticoagulant precede the proper name. However, until the date a final rule resulting from this proposal becomes effective, if a manufacturer intends to follow the "Version 1.2.0 Standard" in lieu of current § 606.121(c)(2) or (e)(1)(ii), a manufacturer would seek an approval for exceptions or alternatives under § 640.120 (21 CFR 640.120). Once the application for an alternative is approved, a manufacturer may use the "Version 1.2.0 Standard" to produce labels that meet FDA's labeling requirements.

B. Changes to Storage and Shipping Temperatures

FDA has reviewed data concerning the storage and shipping temperatures of frozen noncellular blood components, e.g., Cryoprecipitated Antihemophilic Factor and Fresh Frozen Plasma. We have determined that the current requirements for storage and shipping temperatures should be updated to ensure potency of the blood components over time and to provide more flexibility in inventory management. Therefore, we are proposing to revise the current storage and shipping temperatures for frozen noncellular blood components, both for transfusion and for further manufacturing use, to guard against degradation of the heat labile clotting factors. The proposed changes in shipping and storage temperatures are consistent with published data and current industry practice (Ref. 1).

II. Highlights of the Proposed Rule

FDA is proposing to remove, simplify, or update specific labeling regulations applicable to blood and blood components to be more consistent with current practices and to remove any unnecessary or outdated requirements. FDA is proposing to consolidate the labeling requirements for blood and blood components intended for transfusion and for blood and blood components intended for further manufacturing use. FDA is proposing to revise specific regulations to facilitate the use of a uniform container label for blood and blood components in the United States and internationally and to remove any inconsistency between the "Version 1.2.0 Standard" and the Federal regulations at § 606.121. The proposed rule would facilitate the use of a labeling system using the ISBT 128 machine-readable data. In addition, the proposal would facilitate the use of new labeling systems that may be developed in the future.

The proposed changes would also simplify the regulations by consolidating the regulations for labeling blood and blood components,

including Source Plasma, into one section, making it unnecessary for blood establishments to refer to several sections of the regulations to find applicable labeling standards.

In addition to moving certain regulations to § 606.121, FDA is also proposing to revise some of the labeling provisions regarding storage and shipping temperatures for frozen noncellular blood components in proposed § 640.70(a)(3) and (b). FDA is proposing to revise storage and shipping temperatures in current §§ 600.15, 610.53, 640.34, 640.54, 640.69, and 640.76, (21 CFR 600.15, 610.53, 640.34, 640.54, 640.69, and 640.76) to help ensure the potency of the frozen noncellular blood components and for consistency between the labeling regulations and the regulations concerning shipping and storage temperatures of frozen noncellular blood components. As part of this rulemaking, FDA is proposing to update the temperature requirements and address as many labeling changes as possible at one time, thereby limiting the number of times establishments must revise container labels. Also, we have replaced "shall" with "must" in all places wherever it appears in the regulations.

A. Summary of Consolidation of Regulations in § 606.121

FDA is proposing to consolidate regulations so blood establishments may find all applicable labeling standards under one section of regulations. The regulations for labeling all blood and blood components would be moved from other sections of the regulations to § 606.121. The following table summarizes the regulations that would be revised, consolidated, and redesignated under the proposal. The table is intended to serve as a convenient reference for the consolidation of regulations; all revisions to the regulations are discussed later in this preamble. A current regulation listed in the table remaining unchanged may not be discussed further in the preamble.

Current Section:	Would be Revised, and/or Redesignated as:	Revisions Discussed in Section II of this document:
§ 606.121(a)	The Introductory paragraph of § 606.121, paragraph (a) is reserved	B
§ 606.121(b)	Revised only	B
§ 606.121(c)(1)	Revised only	B
§ 606.121(c)(2)	Revised only	C
§ 606.121(c)(3)	Revised only	B

Current Section:	Would be Revised, and/or Redesignated as:	Revisions Discussed in Section II of this document:
§ 606.121(c)(4)	Revised only	B
§ 606.121(c)(5)	§ 606.121(c)(8)(v)	B
§ 606.121(c)(6)	§ 606.121(c)(5)	B
§ 606.121(c)(7)	Unchanged	B
§ 606.121(c)(8)	Revised only	B
§ 606.121(c)(9)	§ 606.121(c)(8)(iv)	B
§ 606.121(c)(10)	§ 606.121(c)(6)	B
§ 606.121(c)(11)	§ 606.121(c)(10)	B
§ 606.121(c)(12)	§ 606.121(c)(9)	B
§ 606.121(c)(13)	Unchanged	C
§ 606.121(d)(1) to (d)(3)	Revised only	B
§ 606.121(d)(4)	Deleted	B
§ 606.121(d)(5)	§ 606.121(d)(4)	B
§ 606.121(e)(1)(i)	§ 606.121(e)(1)(ii)	B
§ 606.121(e)(1)(ii)	§ 606.121(e)(1)(i)	C
§ 606.121(e)(1)(iii)	Revised only	B
§ 606.121(e)(2)	Unchanged	B
§ 606.121(e)(3)	Deleted, see 606.121(c)(4)	B
§ 606.121(e)(4)	§ 606.121(e)(3)	B
§ 606.121(e)(5)(i)	§ 606.121(e)(4)(i)	B
§ 606.121(e)(5)(ii)	Deleted, see 606.121(e)(5)(i)	B
§ 606.121(e)(5)(iii)	§ 606.121(e)(4)(ii)	B
§ 606.121(f)	Revised only	B
§ 606.121(g)	Unchanged	B
§ 606.121(h)	Revised only	B
§ 606.121(i)(1) to (3)	Revised only, paragraph (i)(4) added	E
§ 606.121(i)(4)	§ 606.121(i)(5)	E
§ 606.121(i)(5)	§ 606.121(i)(6)	E
§ 606.121(j)	Revised only	B
§ 606.122(e), (f), and (m)	Revised only	E
§ 640.70(a), the introductory sentence	§ 606.121(e)(5)	B
§ 640.70(a)(1)	Deleted, see § 606.121(c)(1)	B
§ 640.70(a)(2)	§ 606.121(c)(10) and § 606.121(e)(5)(i)	B
§ 640.70(a)(3)	§ 606.121(e)(5)(ii)	D
§ 640.70(a)(4)	§ 606.121(e)(5)(iii)	B
§ 640.70(a)(5)	Deleted, see § 606.121(c)(3)	B
§ 640.70(a)(6)	The second sentence of § 606.121(c)(4)	B

Current Section:	Would be Revised, and/or Redesignated as:	Revisions Discussed in Section II of this document:
§ 640.70(a)(7)	§ 606.121(e)(5)(vi)	B
§ 640.70(a)(8)	§ 606.121(c)(11)	E
§ 640.70(a)(9)	§ 606.121(e)(5)(iv)	B
§ 640.70(a)(10) Deleted	see § 606.121(c)(2)	C
§ 640.70(a)(11)	§ 606.121(c)(11)	E
§ 640.70(b)	§ 606.121(e)(5)(v)	D

B. Proposed Revisions to Clarify and Consolidate Regulations, Including Source Plasma Regulations

The following proposed revisions are intended to consolidate the existing labeling regulations in § 640.70 into § 606.121. As part of the consolidation, labeling regulations in § 640.70 would be moved to § 606.121, and § 640.70 would be removed from the Code of Federal Regulations (CFR). This change would enable blood establishments to find all the labeling requirements for blood and blood components, including Source Plasma, in one section of the CFR rather than having to consult different sections of the CFR when manufacturing several products. Any redundant regulations have been eliminated. FDA is proposing minor edits for clarity.

1. Proposed Revisions to § 606.121(a)

FDA is proposing to amend § 606.121(a), which describes the container label requirements for blood and blood components, by redesignating current paragraph (a) to create an introductory paragraph under § 606.121 and reserving paragraph (a). Under the proposal, the first sentence of the introductory paragraph (current § 606.121(a)) would be revised by deleting the phrase “except Source Plasma” to provide that proposed § 606.121 applies to all blood and blood components, including Source Plasma.

2. Proposed Revisions to § 606.121(b)

FDA is proposing to amend § 606.121(b) by adding the phrase “with any appropriate modifiers and attributes” to clarify that the label may be altered under specific circumstances to adequately identify the contents of a container. Examples of appropriate modifiers include “washed,” “frozen,” and “liquid.” Examples of attributes include “irradiated,” and “divided” which indicate a process change. For consistency, FDA is proposing conforming amendments to § 606.121(c)(1) and (d)(2).

3. Proposed Revisions to § 606.121(c)

Because proposed § 606.121(c)(1) applies to the container label of all blood and blood components, including Source Plasma, FDA is proposing to delete current § 640.70(a)(1). The proposed revisions to § 606.121(c)(2) are discussed in section III.C.1 of this document.

FDA is proposing to revise § 606.121(c)(3) to require that labels include all the donor numbers or a pool number that would enable establishments to trace each individual unit in the pool to the donor. Proposed § 606.121(c)(3) includes the same requirements for container labels for pooled products found in § 640.70(a)(5); therefore, FDA is proposing to delete § 640.70(a)(5).

FDA is proposing to amend § 606.121(c)(4) to clarify the expiration date of pooled plasma and to delete § 606.121(e)(3) because it would be redundant with revised § 606.121(c)(4). Under the proposal, § 640.70(a)(6) would be revised and redesignated as the second sentence of § 606.121(c)(4). If Source Plasma intended for further manufacturing into noninjectable products is pooled, the expiration date is determined from the collection date of the oldest unit in the pool, and the pooling records must show the collection date for each unit in the pool. The proposed changes would simplify the regulations by moving the requirements for determining the expiration date of Source Plasma to the section that specifies requirements for an expiration date on the container label for blood and blood components.

Current § 606.121(c)(5) is redesignated and revised, as discussed in the following paragraph. FDA is proposing that current § 606.121(c)(6) remain unchanged and be redesignated as § 606.121(c)(5). Under the proposal, current § 606.121(c)(7) remains unchanged.

FDA is proposing to simplify the wording of § 606.121(c)(8)(i). Paragraphs 606.121(c)(8)(ii) and (c)(8)(iii) remain

unchanged. FDA is proposing to redesignate § 606.121(c)(9) as § 606.121(c)(8)(iv) and to revise redesignated § 606.121(c)(8)(iv) by deleting the redundant phrase “The statement.” FDA is proposing to redesignate § 606.121(c)(5) as § 606.121(c)(8)(v) and to revise redesignated § 606.121(c)(8)(v) by deleting the redundant phrase “If the product is intended for transfusion.”

FDA is proposing to redesignate current § 606.121(c)(12) as § 606.121(c)(9). FDA is proposing to revise redesignated § 606.121(c)(9) by adding a phrase to clarify that the labeling requirements would apply to products intended for manufacturing use when an ABO and/or Rh designation is appropriate. In addition, FDA is proposing to update redesignated §§ 606.121(c)(9)(ii) and (c)(9)(iii) by using current terminology for a weak expression of the D antigen on red blood cells. The revised section would read “If the test using Anti-D Blood Grouping Reagent is negative but the test for weak D (formerly DU) is * * *”

Under the proposal, current § 606.121(c)(10) is redesignated as § 606.121(c)(6).

FDA is proposing to combine current § 606.121(c)(11) and part of current § 640.70(a)(2) and redesignate the combined regulations as proposed § 606.121(c)(10). FDA is proposing to revise redesignated § 606.121(c)(10) by adding a phrase to the first sentence to clarify that blood and blood components intended for further manufacturing use, and Source Plasma are subject to these requirements. Additionally, FDA is proposing to revise redesignated § 606.121(c)(10) by adding an alternative warning statement and provide for the use of “other cautionary statements as approved by CBER.” These proposed changes and the alternative warning statement reflect current industry practice. FDA is proposing to delete current § 606.121(e)(5)(ii) because it

would be redundant with redesignated § 606.121(c)(10).

4. Proposed Revisions to § 606.121(d)

FDA is proposing to amend § 606.121(d) by deleting the phrase "Except for recovered plasma intended for manufacturing use or" and revise the regulation to clarify that this paragraph applies to the container labels for all blood and blood components. Additionally, § 606.121(d) is revised to remove an obsolete mail code and to provide for the use of labels printed on materials other than paper. FDA is proposing to amend § 606.121(d)(1) to clarify the labeling requirements that apply to the ABO and Rh blood grouping label. The revised regulation remains consistent with current blood establishment practice and the proposed changes are intended only to make the regulations more descriptive and precise. In addition to the conforming amendment previously discussed, proposed § 606.121(d)(2) and (d)(3) are revised to clarify the labeling requirements, as well as provide for use of a variety of labeling color schemes.

FDA is proposing to delete current § 606.121(d)(4) requiring the use of ink colors that are a visual match to the specific color samples designated by the Director, CBER, and to redesignate current § 606.121(d)(5) as § 606.121(d)(4). As proposed, redesignated § 606.121(d)(4) (current § 606.121(d)(5)) would also be revised to update the regulations consistent with current industry practice, to provide a consistent label appearance, and to facilitate the use of black and white labels produced by on-demand printers while still allowing for the use of color coded labels if blood establishments wish to continue their use. FDA believes, consistent with current industry practice, that the use of color coded labels with strict adherence to specific color samples does not increase product safety, and that the use of black and white or color coded labels without specific color samples would not have an adverse affect on identification of the ABO blood group.

5. Proposed Revisions to § 606.121(e)

FDA is proposing to redesignate current § 606.121(e)(1)(i) as § 606.121(e)(1)(ii). FDA is proposing to redesignate current § 606.121(e)(1)(ii) as § 606.121(e)(1)(i) and to amend redesignated § 606.121(e)(1)(i) as discussed in section II.C.2 of this document. FDA is proposing to revise § 606.121(e)(1)(iii) by changing "shall" to "must." Section 606.121(e)(2) remains unchanged.

FDA is proposing to delete current § 606.121(e)(3) because it is redundant with proposed § 606.121(c)(4) and redesignate current § 606.121(e)(4) as § 606.121(e)(3) and current § 606.121(e)(5) as § 606.121(e)(4). Additionally, a conforming amendment is proposed to current § 606.121(j) because it refers to the current § 606.121(e)(4). FDA is proposing to update redesignated § 606.121(e)(3) (current § 606.121(e)(4)) by changing "shall" to "must."

As proposed, redesignated § 606.121(e)(4)(i) and (e)(4)(ii) (current §§ 606.121(e)(5)(i) and (e)(5)(iii), respectively) remain unchanged. Consistent with current industry practice, FDA is proposing to add § 606.121(e)(4)(iii) to require establishments to state on the container label the type of anticoagulant from which the recovered plasma was prepared.

FDA is proposing to add new § 606.121(e)(5) to include the provisions in the introductory sentence of current § 640.70(a), part of § 640.70(a)(2), and §§ 640.70(a)(3), (a)(4), (a)(7), (a)(9), and (b). Proposed § 606.121(e)(5) would clarify and consolidate in § 606.121 labeling requirements specific for Source Plasma. As proposed, redesignated § 606.121(e)(5)(i) (part of current § 640.70(a)(2)) would be updated, consistent with proposed § 606.121(c)(10), to provide flexibility in the use of upper and lowercase types in cautionary statements. Additional revisions to redesignated §§ 606.121(e)(5)(ii) (current § 640.70(a)(3)) and 606.121(e)(5)(v) (current §§ 640.70(a)(3) and (b), respectively) are discussed in section II.D of this document. FDA is proposing to redesignate current § 640.70(a)(7) as § 606.121(e)(5)(vi). Under the proposal, FDA would update redesignated § 606.121(e)(5)(vi) (current § 640.70(a)(7)) to broaden the labeling requirements to include collections from donors who are not immunized but are in specific collection programs, such as disease associated collections from donors who have antibodies to cytomegalovirus. FDA is proposing to redesignate current § 640.70(a)(4) as § 606.121(e)(5)(iii) and current § 640.70(a)(9) as § 606.121(e)(5)(iv).

6. Proposed Revisions to §§ 606.121(f) and (h)

FDA is proposing to amend § 606.121(f) by revising the last sentence. The proposed change would clarify that all blood and blood components intended solely for further manufacturing, including recovered plasma and Source Plasma, do not need

to be labeled "NOT FOR TRANSFUSION" because their intended use for further manufacturing is clearly stated on the label. Section 606.121(g) remains unchanged. Under the proposal, § 606.121(h) would be revised by changing "shall" to "must", and "640.2(f)" to read "§ 610.40(g)".

7. Summary of Consolidation of Regulations in § 640.70 into § 606.121

As previously discussed in this section, FDA is proposing to consolidate the existing labeling regulations in § 640.70 into § 606.121. As part of the consolidation, regulations that currently exist in both sections would be found only in § 606.121 as follows:

- § 640.70(a)(1) is deleted because it is redundant with proposed § 606.121(c)(1).
- § 640.70(a)(2) is revised and redesignated as proposed § 606.121(c)(10) and as proposed § 606.121(e)(5)(i).
- § 640.70(a)(4) is revised and redesignated as § 606.121(e)(5)(iii).
- § 640.70(a)(5) is removed because it is redundant with proposed § 606.121(c)(3).
- § 640.70(a)(6) is revised and redesignated as the second sentence of proposed § 606.121(c)(4).
- § 640.70(a)(7) is revised and redesignated as § 606.121(e)(5)(vi).
- § 640.70(a)(9) is revised and redesignated as § 606.121(e)(5)(iv).

C. Proposed Revisions to Clarify and Consolidate Regulations Related to Use of a Labeling System Using Machine-Readable Information

The proposed revisions discussed in this section of this document are primarily intended to allow for the use of a machine-readable encoded information system, such as ISBT 128. Those changes would allow manufacturers of blood, blood components, and Source Plasma to submit product specific labeling that is consistent with approved labeling formats, such as ISBT 128, to the Director, CBER, for approval without requesting a variance under § 640.120. Under this proposal, § 606.121(c)(13) would remain unchanged. In the **Federal Register** of March 14, 2003 (68 FR 12499) FDA issued a proposed rule entitled "Bar Code Label Requirements for Human Drug Products and Blood" (proposed Bar Code Rule), that would amend § 606.121(c)(13) to require certain human drug and biological product labels to bear bar codes and also would require the use of machine-readable information on container labels for blood and blood components intended for transfusion. The proposed

Bar Code Rule specifically invites comment on whether FDA should require the use of ISBT 128, or require "machine-readable information" as approved by the Director, CBER, or some other standard or symbology. If you are interested in commenting on the use of bar codes on container labels for blood and blood components for transfusion, please refer to the proposed Bar Code Rule and submit your comments (see 68 FR 12499).

1. Proposed revisions to § 606.121(c)(2)

FDA is proposing to amend § 606.121(c)(2) by replacing "registration number" with "unique facility identifier." This change would remove the requirement to include the FDA assigned registration number on blood and blood component labels. Although the FDA assigned registration number is acceptable as a "unique facility identifier," the proposal would also provide for the use of other recognized donation facility identification numbers, such as the ISBT facility code (which includes machine-readable information). Consistent with the general provisions for licensing in 21 CFR part 601, establishments collecting Source Plasma may use their registration number or other recognized donation facility identification number as the unique facility identifier which would aid in identifying the location where the product was collected. Under the proposal, current § 640.70(a)(10) would be removed because the requirements of § 640.70(a)(10) for "name, address, and license number" on the Source Plasma label are included in proposed § 606.121(c)(2).

2. Proposed Revisions to § 606.121(e)(1)(i)

As previously discussed in section II.B of this document, FDA is proposing to amend redesignated § 606.121(e)(1)(i) (current § 606.121(e)(1)(ii)). This revision is intended to facilitate the use of a labeling system using machine-readable information, such as ISBT 128, by providing more flexibility in labeling. Specifically, this revision would remove the labeling requirements regarding the placement and prominence of the anticoagulant.

D. Proposed Revisions Related to Temperature Requirements

FDA is proposing revisions to update temperature requirements for storage and shipment of blood and blood components. The proposed changes described in this section are intended to provide consistency with data published in Europe and to help ensure

the potency of blood and blood components by guarding against the degradation of heat labile clotting factors during storage and shipment (Ref. 1). Because these storage and shipping temperatures may be reflected in the product labeling, FDA is proposing to update the temperature requirements in this rulemaking to address as many labeling changes as possible as part of this rulemaking and enable establishments to make a number of revisions to labels for blood products at one time. This revision would simplify labeling of blood and blood components. Additionally, this approach is intended to reduce the burden on industry by minimizing the number of times blood container labels must be revised and reordered.

1. Proposed Revisions to §§ 610.53, 640.34, and 640.54

FDA is proposing to revise §§ 610.53, and 640.34(b) by changing "shall" to "must", and by changing the storage and shipping temperatures for Cryoprecipitated Antihemophilic Factor (AHF) and for Fresh Frozen Plasma to -25 °C or colder if stored for 24 months after the date of collection, and -18 to -25 °C if stored for 3 months after the date of collection. FDA is proposing changes to § 640.54 for consistency with the proposed changes in shipping and storage temperatures for Cryoprecipitated AHF.

2. Proposed Revisions to §§ 640.69, 640.70, and 640.76

As previously mentioned, FDA is proposing to redesignate current § 640.70(a)(3) as § 606.121(e)(5)(ii). FDA is proposing to revise redesignated § 606.121(e)(5)(ii) (current §§ 640.70(a)(3)), 640.69(c), and 640.76(a) and (b) by changing the storage and shipping temperatures for Source Plasma to -30 °C and -15 °C, respectively, or colder. FDA is proposing to redesignate current § 640.70(b) as § 606.121(e)(5)(v), and to revise redesignated § 606.121(e)(5)(v) by changing the storage and shipping temperatures for Source Plasma diverted for Source Plasma Salvaged to -30 °C and -15 °C, respectively, or colder.

3. Proposed Revisions to § 640.34

FDA is proposing to revise § 640.34(g)(2) to clarify that frozen plasma must be stored at appropriate temperatures to ensure product potency.

E. Proposed Changes to Clarify and Consolidate Regulations Related to Communicable Disease Testing, and Autologous Donations

The proposed revisions discussed in this section of this document would require labels for blood, blood components, and Source Plasma to include the results of the communicable disease tests performed on a sample of the donor's blood obtained at the time of the blood donation. The proposed regulations would require establishments to include on product labels the results of all communicable disease testing performed as required in § 610.40. Currently in §§ 606.121 and 640.70, only the results of tests for Hepatitis B surface antigen (HBsAg) and antibody to Human Immunodeficiency Virus (anti-HIV) are required on the label. In the **Federal Register** of June 11, 2001 (66 FR 31146), FDA published a related rulemaking entitled "Requirements for Testing Human Blood Donors for Evidence of Infection Due to Communicable Disease Agents" (the testing final rule). The proposed revisions are consistent with the requirements of the testing final rule.

1. Proposed Revisions to Redesignated § 606.121(c)(11)

FDA is proposing to redesignate current §§ 640.70(a)(8) and (a)(11) as § 606.121(c)(11) and to revise redesignated § 606.121(c)(11) to require labeling statements based on communicable disease test results. The proposed change provides that the labeling requirements apply to Source Plasma and would require establishments to label products for further manufacture with the results of all required communicable disease testing performed in accordance with § 610.40.

2. Proposed Addition to § 606.121(c)(12)

As previously described in this section, FDA is proposing to redesignate current § 606.121(c)(12) as § 606.121(c)(9), and to add new § 606.121(c)(12). Proposed § 606.121(c)(12) is intended to clarify that blood establishments would be permitted under certain circumstances to use blood or blood components which test repeatedly reactive for communicable disease agents, provided the units are appropriately labeled to indicate all test results. This labeling change is consistent with the labeling requirements of § 610.40 of the testing final rule described in the previous paragraph.

3. Proposed Revisions to § 606.121(i)

FDA is proposing to revise § 606.121(i) by using more descriptive and precise terms, by replacing the word “shall” with “must” and by replacing “Whole Blood or Red Blood Cells” with “blood or blood components.” Section 606.121(i)(1) would be revised consistent with industry practice by adding “date of birth” to the list of examples of information that may be used to help ensure correct identification of the autologous transfusion recipient. In addition, FDA is proposing to delete the words “blood group” from the list of information that may identify an autologous transfusion recipient in § 606.121(i)(1). No revision is proposed for § 606.121(i)(2). FDA is proposing to revise § 606.121(i)(3) to simplify the requirements and to provide consistency with current industry practice and with the requirements for appropriate donor classification proposed in redesignated § 606.121(c)(8)(v). FDA is proposing to add new paragraph (i)(4) to clarify and update the existing requirements. Accordingly, FDA is proposing to redesignate current §§ 606.121(i)(4) and (i)(5) as § 606.121(i)(5) and (i)(6), respectively.

FDA is proposing to revise redesignated § 606.121(i)(5) (current § 606.121(i)(4)) to provide that the label for blood or blood components intended for autologous transfusion must be labeled as “FOR AUTOLOGOUS USE ONLY” if obtained from a donor who is reactive to one or more tests for evidence of infection due to communicable disease agents. Current § 606.121(i)(4) is specific for the tests currently required in the regulations. Consistent with the testing final rule, the proposed revision to redesignated § 606.121(i)(5) (current § 606.121(i)(4)) would provide for appropriate labeling regardless of how testing standards may change in the future. FDA is proposing to update redesignated § 606.121(i)(6) (current § 606.121(i)(5)), revising it by replacing “homologous” with “allogeneic.”

4. Proposed Revisions to § 606.122

FDA is proposing to amend § 606.122 *Instruction circular* by revising the introductory paragraph and paragraphs (e), (f), and (m). Section 606.122 requires that an instruction circular must be available for distribution if the product is intended for transfusion. The introductory paragraph would be revised to replace “shall” with “must”. Current § 606.122(e) requires that the instruction circular contain statements

that the product was prepared from blood that was negative when tested for antibody to human immunodeficiency virus (HIV), was nonreactive for hepatitis B surface antigen by FDA required tests and nonreactive when tested by a serological test for syphilis. Proposed § 606.122(e) would clarify that the instruction circular must contain statements regarding the results of all required infectious agent testing. By making this change, it would become unnecessary to revise the labeling regulations as testing requirements may be revised in the future. FDA is proposing to amend § 606.122(f) by updating the warning statement, which currently refers only to the hazard of transmitting hepatitis, to reflect the risk associated with the communicable disease agents for which testing is currently performed.

Note that the terms “infectious agent testing” and “communicable disease testing” (used interchangeably in this proposed rule and in guidance documents) refer to the same testing performed in accordance with § 610.40. The term “infectious agent” is used rather than “communicable disease agent” for consistency with the “Version 1.2.0 Standard.”

FDA is proposing to amend the introductory phrase in § 606.122(m), and paragraphs (m)(2), (m)(3), and (m)(5) to update the information required in the instruction circular for plasma. In the introductory sentence of § 606.122(m), FDA is proposing to update the regulations by replacing the word “shall” with “must.” Section 606.122(m)(1) would remain unchanged. FDA is proposing to revise § 606.122(m)(2) and (m)(3) to clarify that the instruction circular must contain instructions to thaw the frozen product at a temperature “appropriate for the product” and, when applicable, instructions to begin administration of the product within “a specified time” after thawing, respectively. The proposed changes would provide greater flexibility in the instruction circular, and would provide for various new thawing methods and procedures for administration that might be used in the future without requiring additional changes to the regulation.

FDA is proposing to amend § 606.122(m)(5), consistent with the changes in proposed redesignated § 606.122(e), to update the information in the instruction circular regarding the transfusion of plasma to warn of the risk of transmission of many communicable disease agents, rather than refer only to the hazard of transmitting hepatitis.

III. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866 and 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). Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement of anticipated costs and benefits before proposing any rule that may result in an expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100 million in any one year (adjusted annually for inflation). Under the Regulatory Flexibility Act, unless an agency certifies that a rule will not have a significant economic impact on a substantial number of small entities, the agency must analyze regulatory options that would minimize any significant impact of a rule on small entities.

The agency has reviewed this proposed rule and believes that it is consistent with the regulatory philosophy and principles identified in the Executive order and these two statutes. The proposed rule is not a significant regulatory action as defined by the Executive order and so is not subject to review under the Executive order. No further analysis is required under the Regulatory Flexibility Act because the agency has determined that these proposed rule amendments have no compliance costs and will not have a significant effect on a substantial number of small entities. This proposed rule also does not trigger the requirements for a written statement under section 202(a) of the Unfunded Mandates Reform Act because it does not impose a mandate that results in expenditure of \$100 million or more by State, local, and tribal governments in the aggregate, or by the private sector in any one year.

The purpose of the proposed rule amendments is to simplify and unify the existing labeling standards. Labeling standards are currently found in multiple sections of the regulations and these amendments would move these standards to one section of the regulations. By revising, consolidating, and redesignating these regulations, parties wishing to understand the labeling requirements will be able to

refer to a single source. The proposed rule amendments also include provisions that add flexibility to the regulations that should lower the cost of compliance.

Some aspects of the proposed rule amendments do establish new label requirements and provisions. One such requirement is that the label must reflect updated testing requirements. The agency believes these requirements, including the requirement for the label to reflect updated testing requirements, conform to current industry practice and do not impose an additional burden.

The proposed rule requires a change in the instruction circular to reflect current testing practices. Existing labeling regulations do not allow the circular to reflect current required testing or to adjust to future changes in required testing or plasma thawing procedures. The agency believes the instruction circular would already be in compliance with the proposed rule amendments and reflect current requirements and practices if compliance were permitted by existing regulations. By adding flexibility to the rules regarding the instruction circular, the proposed rule lowers the overall cost of compliance. Moreover, as the instruction circular is updated regularly, the agency believes any required changes can be made in the ordinary revision cycle and that this rule will not impose an additional burden.

The proposed rule amendments also update the temperature requirements for storage and shipping of blood and blood components. The agency believes that these requirements reflect current industry practice and do not impose an additional burden.

In general, the agency believes the proposed rule will have no compliance costs, because any requirements are either industry practice or would be industry practice absent existing prohibitions. Because the agency believes these proposed rule amendments have no compliance costs, the agency certifies they will not have a significant economic impact on a substantial number of small entities.

IV. The Paperwork Reduction Act of 1995

This proposed rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under

the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). As previously described, FDA is proposing to consolidate regulations so blood establishments may find all applicable labeling standards under one section of regulations. The regulations for labeling of all blood and blood components would be moved from other sections of the regulations to § 606.121. Since the agency believes the proposed rule amendments conform to current industry practice, FDA is not estimating the burden of the proposed rule. The information collection requirements under §§ 606.121 and 606.122 are approved under OMB control number 0910–0116.

V. Environmental Impact

The agency has determined under 21 CFR 25.30(j) 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.

VI. Federalism

FDA has analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the 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.

VII. Request for Comments

Interested persons may submit to the Division of Dockets Management (see ADDRESSES) written or electronic comments regarding 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.

VIII. Proposed Effective Date

The agency is proposing that any final rule that may issue based upon this proposed rule become effective 180 days after its date of publication in the Federal Register.

IX. Reference

The following reference has 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.

1. Krotitschke, R., “Stability of Fresh Frozen Plasma: Results of 36-Month Storage at -20 °C, -25 °C, -30 °C, and -40 °C,” *Infusion Therapy and Transfusion Medicine*, 27:174–180, 2000.

List of Subjects

21 CFR Part 600

Biologics, Reporting and recordkeeping requirements.

21 CFR Part 606

Blood, Labeling, Laboratories, Reporting and recordkeeping requirements.

21 CFR Part 610

Biologics, Labeling, Reporting and recordkeeping requirements.

21 CFR Part 640

Blood, Labeling, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act, and the Public Health Service Act, and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR parts 600, 610, 606, and 640 be amended as follows:

PART 600—BIOLOGICAL PRODUCTS: GENERAL

1. The authority citation for 21 CFR part 600 continues to read as follows:

Authority: 21 U.S.C. 321, 351, 352, 353, 355, 360, 360i, 371, 374; 42 U.S.C. 216, 262, 263, 263a, 264, 300aa–25.

2. Section 600.15 is amended in the table in paragraph (a) by revising the entries for Cryoprecipitated AHF, Fresh Frozen Plasma, and Source Plasma to read as follows:

§ 600.15 Temperatures during shipment.

* * * * *

(a) *Products.*

Product	Temperature
Cryoprecipitated AHF	-25 °C or colder if expiration is 24 months or -18 to -25 °C if expiration is 3 months.
* * * * *	

Product	Temperature
Fresh Frozen Plasma	-25 °C or colder if expiration is 24 months or -18 to -25 °C if expiration is 3 months.
* * * * *	
Source Plasma	-15 °C or colder.
* * * * *	

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

3. 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.

4. Section 606.121 is revised to read as follows:

§ 606.121 Container label.

The container label requirements are designed to facilitate the use of a uniform container label for blood and blood components, including Source Plasma, by all blood establishments.

(a) [Reserved]

(b) The label provided by the collecting facility and the initial processing facility must not be removed, altered, or obscured, except that the label may be altered to indicate the proper name, with any appropriate modifiers and attributes, and other information required to identify accurately the contents of a container after blood components have been prepared.

(c) The container label must include the following information, as well as other specialized information as required in this section for specific products:

(1) The proper name of the product in a prominent position, with any appropriate modifiers and attributes;

(2) The name, address, unique facility identifier, and, if a licensed product, the license number of each manufacturer;

(3) The donor or lot number relating the unit to the donor. If pooled, all donor numbers, all donation numbers, or a pool number that is traceable to each individual unit comprising the pool;

(4) The expiration date, including the day, month, and year, and, if the dating period for the product is 72 hours or less, including any product prepared in a system that might compromise sterility, the hour of expiration. If Source Plasma intended for manufacturing into noninjectable products is pooled, the expiration date is determined from the collection date of the oldest unit in the pool, and the

pooling records must show the collection date for each unit in the pool.

(5) For Whole Blood, Plasma, Platelets, and partial units of Red Blood Cells, the volume of the product, accurate to within ±10 percent; or optionally for Platelets, the volume range within reasonable limits.

(6) Where applicable, the name and volume of source material.

(7) The recommended storage temperature (in degrees Celsius).

(8) If the product is intended for transfusion, the statements:

(i) "Rx only."

(ii) "See Circular of Information for indications, contraindications, cautions, and methods of infusion."

(iii) "Properly identify intended recipient."

(iv) "This product may transmit infectious agents."

(v) The appropriate donor classification statement, i.e., "paid donor" or "volunteer donor," in no less prominence than the proper name of the product.

(A) A paid donor is a person who receives monetary payment for a blood donation.

(B) A volunteer donor is a person who does not receive monetary payment for a blood donation.

(C) Benefits, such as time off from work, membership in blood assurance programs, and cancellation of nonreplacement fees that are not readily convertible to cash, do not constitute monetary payment within the meaning of this paragraph.

(9) If the product is intended for transfusion or as is otherwise appropriate, the ABO group and Rh type of the donor must be designated conspicuously. For Cryoprecipitated Antihemophilic Factor (AHF), the Rh type may be omitted. The Rh type must be designated as follows:

(i) If the test using Anti-D Blood Grouping Reagent is positive, the product must be labeled: "Rh positive."

(ii) If the test using Anti-D Blood Grouping Reagent is negative but the test for weak D (formerly Du) is positive, the product must be labeled: "Rh positive."

(iii) If the test using Anti-D Blood Grouping Reagent is negative and the test for weak D (formerly Du) is negative, the product must be labeled: "Rh negative."

(10) If the product is not intended for transfusion, a statement as applicable: "Caution: For Manufacturing Use Only," or "Caution: For Use in Manufacturing Noninjectable Products Only," or other cautionary statement as approved by the Director, Center for Biologics Evaluation and Research (CBER).

(11) If the product is intended for further manufacturing use, a statement listing the names and results of all the tests for communicable disease agents for which the donation has been tested and found negative.

(12) The blood and blood components must be labeled in accordance with § 610.40, when the donation is tested and demonstrates evidence of infection due to a communicable disease agent(s).

(13) The container label may bear encoded information in the form of machine-readable symbols approved for use by the Director, Center for Biologics Evaluation and Research (HFB-1).

(d) Unless otherwise approved by the Director, CBER, the container label must be white and print must be solid black, with the following additional exceptions:

(1) The ABO and Rh blood groups must be printed as follows:

(i) Rh positive: Use black print on white background and use solid black or other solid color for ABO.

(ii) Rh negative: Use white print on black background for Rh and use black outline for ABO.

(2) The proper name of the product, with any appropriate modifiers and attributes, the donor classification statement, and the statement "properly identify intended recipient" may be printed in solid red or in solid black.

(3) The following color scheme may be used for differentiating ABO Blood groups:

Blood group	Color of label
O	Blue
A	Yellow
B	Pink
AB	White

(4) Special labels, such as those described in paragraphs (h) and (i) of this section, may be color coded.

(e) Container label requirements for particular products or groups of products.

(1) Whole Blood labels must include:

(i) The name of the applicable anticoagulant approved for use by the Director, CBER.

(ii) The volume of anticoagulant.

(iii) If tests for unexpected antibodies are positive, blood intended for transfusion must be labeled: "Contains (name of antibody)."

(2) Except for frozen, deglycerolized, or washed Red Blood Cell products, red blood cell labels must include:

(i) The volume of Whole Blood, and the type of anticoagulant with which the product was prepared.

(ii) If tests for unexpected antibodies are positive and the product is intended for transfusion, the statement: "Contains (name of antibody)."

(3) If tests for unexpected antibodies are positive, Plasma intended for transfusion must be labeled: "Contains (name of antibody)."

(4) Recovered plasma labels must include:

(i) In lieu of an expiration date, the date of collection of the oldest material in the container.

(ii) For recovered plasma not meeting the requirements for manufacture into licensable products, the statement: "Not for Use in Products Subject to License Under Section 351 of the Public Health Service Act."

(iii) The type of anticoagulant with which the product was prepared.

(5) Source Plasma labels must include the following information:

(i) The cautionary statement, as specified in § 606.121(c)(10), must follow the proper name with any appropriate modifiers and attributes and be of similar prominence as the proper name.

(ii) The statement "Store at -30 °C or colder": Provided, That where plasma is intended for manufacturing into noninjectable products, this statement may be replaced by a statement of the temperature appropriate for manufacture of the final product to be prepared from the plasma.

(iii) The total volume or weight of plasma and total quantity and type of anticoagulant used.

(iv) When plasma collected from a donor is reactive for a serologic test for syphilis, a statement that the plasma is reactive and must be used only for the manufacturing of positive control reagents for the serologic test for syphilis.

(v) Source Plasma diverted for Source Plasma Salvaged must be relabeled "Source Plasma Salvaged" as prescribed in § 640.76 of this chapter. Immediately

following the proper name of the product, with any appropriate modifiers and attributes, the labeling must conspicuously state as applicable, "STORAGE TEMPERATURE EXCEEDED -30 °C" or "SHIPPING TEMPERATURE EXCEEDED -15 °C".

(vi) A statement as to whether the plasma was collected from nonimmunized donors, or from donors in specific collection programs approved by the Director, CBER. In the case of specific collection programs the label must state the defining characteristics of the plasma.

(f) Blood and blood components determined to be unsuitable for transfusion must be prominently labeled: "NOT FOR TRANSFUSION," and the label must state the reason the unit is considered unsuitable. The provision does not apply to blood and blood components intended solely for further manufacturing.

(g) [Reserved]

(h) The following additional information must appear on the label for blood or blood components shipped in an emergency prior to completion of required tests, in accordance with § 610.40(g) of this chapter:

(1) The statement: "FOR EMERGENCY USE ONLY BY _____."

(2) Results of any tests prescribed under §§ 610.40 and 640.5(a), (b), or (c) of this chapter completed before shipment.

(3) Indication of any tests prescribed under §§ 610.40 and 640.5(a), (b), or (c) of this chapter not completed before shipment.

(i) The following additional information must appear on the label for blood or blood components intended for autologous transfusion:

(1) Information adequately identifying the patient e.g., name, date of birth, hospital, and identification number.

(2) Date of donation.

(3) The statement: "AUTOLOGOUS DONOR."

(4) The ABO and Rh blood group and type, unless exempt under § 606.121(c)(9).

(5) In place of the allogeneic blood group label, each container of blood intended for autologous use and obtained from a donor who fails to meet any of the donor suitability requirements under § 640.3 of this chapter or who is reactive to or positive for one or more tests for evidence of infection due to communicable disease agents must be prominently and permanently labeled: "FOR AUTOLOGOUS USE ONLY."

(6) Units of blood originally intended for autologous use, except those labeled as prescribed under paragraph (i)(5) of

this section, may be issued for allogeneic transfusion provided the container label complies with all applicable provisions of paragraphs (b) through (e) of this section. In such case, the special label required under paragraphs (i)(1), (i)(2), and (i)(3) of this section must be removed or otherwise obscured.

(j) A tie-tag attached to the container may be used for providing the information required by paragraphs (e)(1)(iii), (e)(2)(ii), and (e)(3), (h), or (i)(1), (i)(2), and (i)(3) of this section.

5. Section 606.122 is amended by revising the introductory paragraph, and paragraphs (e), (f), (m)(2), (m)(3), and (m)(5) to read as follows:

§ 606.122 Instruction circular.

An instruction circular must be available for distribution if the product is intended for transfusion. The instruction circular must provide adequate directions for use, including the following information:

* * * * *

(e) A statement that the product was prepared from blood that was tested and found negative for evidence of infection due to the infectious agents (include the name of each infectious agent for which the blood was tested, including all FDA required tests).

(f) The statement: "Warning: The risk of communicable disease agents is present. Careful donor selection and available laboratory tests do not eliminate the hazard."

* * * * *

(m) For Plasma, the instruction circular must contain:

(1) * * *

(2) Instructions to thaw the frozen product at a temperature appropriate for the product.

(3) When applicable, instructions to begin administration of the product within a specified time after thawing.

(4) * * *

(5) A statement that this product has the same risk of transmitting communicable disease agents as Whole Blood; other plasma volume expanders without this risk are available for treating hypovolemia.

* * * * *

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.

7. Section 610.53 is amended by revising paragraph (c) in the table for

Cryoprecipitated AHF, and Plasma products for the item Fresh Frozen Plasma to read as follows:

§ 610.53 Dating periods for licensed biological products.

(c) * * *

* * * * *

Table with 4 columns: A (Product), B (Manufacturer's storage period 1 to 5 °C), C (Manufacturer's storage period 0 °C or colder), D (Dating period after leaving manufacturer's storage). Rows include Cryoprecipitated AHF and Plasma products.

* * * * *

PART 640—ADDITIONAL STANDARDS FOR HUMAN BLOOD AND BLOOD PRODUCTS

8. 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.

9. Section 640.34 is amended by revising paragraphs (b) and (g)(2) to read as follows:

§ 640.34 Processing.

(a) * * *

(b) Fresh Frozen Plasma. Fresh Frozen Plasma must be prepared from blood collected by uninterrupted venipuncture with minimal damage to and minimal manipulation of the donor's tissue...

* * * * *

(g) * * *

(2) With the exception of Platelet Rich Plasma and Liquid Plasma the final product must be inspected for evidence of thawing or breakage at the time of

issuance. The containers need not be stored in a manner that shows evidence of thawing if records of continuous monitoring can establish that the appropriate storage temperature recommended on the labeling for the product was maintained throughout the storage period...

* * * * *

10. Section 640.54 is amended by revising paragraph (a)(3) to read as follows:

§ 640.54 Processing.

(a) * * *

(3) Immediately after separation and freezing of the plasma, the plasma must be stored and maintained at the appropriate storage temperature recommended on the labeling for the product until thawing of the plasma for further processing to remove the Cryoprecipitated AHF.

* * * * *

11. Section 640.69 is amended by revising paragraph (c) to read as follows:

§ 640.69 General requirements.

* * * * *

(c) Inspection. Source Plasma intended for further manufacturing into injectable products must be inspected for evidence of thawing at the time of

issuance, except that inspection of individual plasma containers need not be made if the records of continuous monitoring of the storage temperature establish that the temperature remained at -30 °C or colder. If there is evidence that the storage temperature has not been maintained at -30 °C or colder, the plasma may be relabeled and issued as provided in § 640.76(a) of this chapter.

* * * * *

§ 640.70 [Removed]

12. Section 640.70 Labeling is removed.

§ 640.76 [Amended]

13. Section 640.76 Products stored or shipped at unacceptable temperatures is amended as follows:

- a. In paragraphs (a)(1) and (a)(2) by removing "-20 °C" and adding in its place "-30 °C" wherever it appears;
b. In paragraphs (a)(1), (a)(2), and (b) by removing "shall" and adding in its place "must" wherever it appears;
c. In paragraphs (a)(2) and (b) by removing "-5 °C" and adding in its place "-15 °C" wherever it appears.

Dated: July 12, 2003.

Jeffrey Shuren,

Assistant Commissioner for Policy.

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