Communications Act.[1] The Commission has long acquiesced in the view that the fairness doctrine was codified by these amendments,[2] and, thus, the burden of proof must rest with those who would urge that the agency itself has authority to eliminate the doctrine. In my view, nothing in the record contradicts the clear language of section 315(a) which states that licensees have an "obligation imposed upon them under [the Communications Act] to operate in the public interest and to afford reasonable opportunity for the discussion of conflicting views on issues of public importance." [3]

Since I believe that the doctrine has been codified, I concur in the decision to defer to Congress on this matter.

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BILLING CODE 6712-01-M

[1] See Act of September 14, 1959, Pub. L. 86-274, section 1, 73 Stat. 557 (amending 47 U.S.C. 315(a) (1982)).

[2] See, e.g., *Fairness Report*, 48 FCC 2d 1, 1 (1974).

[3] 47 U.S.C. 315(a) (1984).

federal register

Friday
August 30, 1985

Part VI

Department of Health and Human Services

Food and Drug Administration

21 CFR Parts 606 and 640

Current Good Manufacturing Practice for Blood and Blood Components; Uniform Blood Labeling; Final Rule

Guideline for the Uniform Labeling of Blood and Blood Components; Availability of Guideline; Notice

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 606 and 640

[Docket No. 80N-0120]

Current Good Manufacturing Practice for Blood and Blood Components; Uniform Blood Labeling

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is revising the labeling requirements for any blood and blood component product that is collected or manufactured in a blood bank establishment to combine, simplify, and update the biologics regulations. Elsewhere in this issue of the **Federal Register**, FDA is announcing the availability of a final guideline "Guideline for the Uniform Labeling of Blood and Blood Components" that is consistent with this final rule. The guideline provides criteria for the printing and use of a standardized container label for each blood and blood component product.

EFFECTIVE DATE: September 2, 1986 for all affected products initially introduced or initially delivered for introduction into interstate commerce. The labeling for all blood components collected on or after this effective date shall comply with the requirements set forth in these regulations. FDA advises that licensed establishments may begin using labeling printed in accordance with these regulations and the guideline "Guideline for the Uniform Labeling of Blood and Blood Components" without its prior approval by FDA. Concurrent with its use, licensed establishments are required to submit to the Director, Offices of Biologics Research and Review (HFN-800), Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20205, the revised labeling and instruction circular as an amendment to their product license(s). For additional information concerning the effective date, see the discussion under the heading "Paperwork Reduction Act of 1980" located at the end of the preamble.

FOR FURTHER INFORMATION CONTACT: Steven F. Falter, Center for Drugs and Biologics (HFN-364), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-3650.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of October 31, 1980 (45 FR 72416), FDA issued a proposed rule to amend the biologics regulations to revise and simplify the labeling requirements for any transfusible blood and blood component product that is collected or manufactured in a blood bank establishment and unifying these requirements under one set of regulations in §§ 606.120, 606.121, and 606.122 (21 CFR 606.120, 606.121, and 606.122). FDA believed that these proposed labeling requirements would: (1) Improve the eye-readability of the container label by limiting the amount of information required on the label; (2) provide for the use of a machine-readable code on the label; (3) unify all labeling requirements in one place in the current good manufacturing practices for blood and blood components regulations (21 CFR Part 606); and (4) encourage the use of uniform labels by all establishments engaged in the collection, processing, or labeling of blood and blood components.

I. Background

In the preamble to the October 31, 1980 proposed rule, FDA also announced the availability of a draft guideline entitled "Guidelines for the Uniform Labeling of Blood and Blood Components." The guideline provided specifications for a uniform blood label, consistent with the proposed rules, that was suitable for any blood establishment to use in labeling blood and blood components intended for transfusion. The uniform label was developed with the cooperation of the Committee for Commonality in Blood Banking Automation (CCBBA) of the American Blood Commission (ABC). Elsewhere in this issue of the **Federal Register**, FDA is announcing the availability of the final guideline based on the October 1980 draft guideline. The final guideline provides instructions for the printing and proper use of a uniform blood label consistent with the final regulations. Any changes in the final guideline are described in the notice announcing its availability.

FDA also published two other proposals in the **Federal Register** of October 31, 1980 (45 FR 72404) that are related to this final rule. The first of these proposals was intended to revise the proper names for many biological products, including the proper names for blood and blood components. In the **Federal Register** of January 28, 1985 (50 FR 4128), FDA published a final rule based on that proposal. The proper names for blood products used herein reflect the changes in names promulgated in that final rule.

In the second related proposal published in the **Federal Register** of October 31, 1980 (45 FR 72422), FDA proposed to revise certain requirements for the additional standards for human blood and blood products. FDA has withdrawn that proposed rule for reconsideration. See the **Federal Register** of July 22, 1983 (48 FR 33494). Because of that withdrawal, FDA is changing several labeling provisions of this final rule and is explaining these changes later in the preamble.

II. FDA's Response To Comments

FDA provided interested persons 60 days to submit written comments on the proposed rule concerning uniform blood labeling. In response to a request by a licensed manufacturer of blood components and blood derivatives, FDA extended the comment period another 60 days by a notice published in the **Federal Register** of December 9, 1980 (45 FR 81065). FDA received 54 letters of comment in response to the proposal, and most letters contained more than one comment. Most of the comments supported FDA's proposed actions. A summary of the comments and FDA's responses follow.

1. A comment noted that in proposed § 606.121(a), Source Plasma is exempt from the labeling requirements in § 606.121, but products such as Source Plasma Liquid or Source Plasma Salvaged are not mentioned. The comment asked whether these products also were exempt from the labeling requirements.

FDA advises that when a name of a biologic product is used in a regulation (excluding any modifiers or the identification of the anticoagulant), the requirement applies to all products using that name alone or together with any required modifiers in the product's proper name. See definition of "proper name" in 21 CFR 600.3(k). Thus, the exemption for Source Plasma in § 606.121 applies to all forms of Source Plasma—Source Plasma, Source Plasma Liquid, Source Plasma Salvaged, etc. If a requirement in the regulations for biologics does not apply to all products using a name, the requirement identifies the particular products to which it applies. FDA believes that it is unnecessary and cumbersome to list in the regulations the proper name of each product with each approved modifier.

2. One comment on proposed § 606.121(b) stated that the language used incorrectly implies that the only instance in which labels are permitted to be altered is where blood components are removed from the product. The comment suggested that the provision permit the revision of a label to indicate the proper name and other information to describe the "* * * contents

remaining in a container after processing."

FDA partially agrees with the comment. In certain cases, such as the deglycerolizing of red flood cells, no blood components are removed, but the unit may require relabeling. Accordingly, in the final rule FDA is revising § 606.121(b) to provide that the labeling shall not be removed, altered, or obscured except to indicate information required to identify accurately the contents of a container after blood components have been prepared from the unit. FDA believes that use of the word "processing" would not be appropriate, because the word is interpreted in the laboratory to include test performed on the blood , such as the test for hepatitis, that do not require changes in the container label.

3. A comment stated that the phrase "the label provided by the collection facility" in proposed § 606.121(b) implies that the collecting facility and initial processing facility always add a label to the collected unit. The comment noted that the manufacturer of the blood collection unit (blood bag) often provides preprinted labeling, and the collecting facility merely adds additional required information to that labeling during collection and processing.

FDA disagrees with the comment. Whether or not the blood container is prelabeled or partially or wholly labeled by the collecting facility, under this final rule the collecting (and processing) facility is responsible for the labeling used on the blood product, including the product label. Thus, for enforcement purposes, FDA considers that the collection facility provides the labeling used. Accordingly, the agency concludes that the reqirement is clear and correct, and FDA is issuing § 606.121(b) without change.

4. Four comments on proposed § 606.121 (b) and (c)(13)(iv) asked whether an additional unit number could be added to the label of a unit of blood by a receiving facility when the unit is received from another location. Two of these comments stated that renumbering of a unit of blood should be permitted. One comment asked for instructions on how to renumber a unit of blood if it is received from another facility.

FDA agrees that a second unit number may be added to the label of a unit of blood, although the agency discourages this practice. When two unit numbers are present on a container of blood, someone may not identify the product correctly, resulting in a transfusion error. Where adequate labeling controls are present, the receiving facility may add to a unit of blood a second unit number that is consistent with the receiving facility's numbering system. FDA recommends that the receiving facility place the added unit number on the label in a uniform location and suggests that the added unit number (or label) be placed in the space reserved for the optional collection date or directly above the original unit number. Under § 606.121(b), the added unit number shall not conceal the original unit number on the container.

5. One comment noted that there is no space on the uniform label for including the identification of more than one establishment when the blood is collected and processed by separate facilities.

FDA disagrees with the comment. The uniform label provides space to record the name and address of the facility that receives blood. The space is located on the uniform label directly below the space for recording the name and address of the collecting facility.

6. One comment on proposed § 606.121(c)(2) recommended that the facility's registration number be included on the label if the registration number is to serve as the encoded collection center identifier required by § 606.121(c)(13)(iii).

FDA agrees with the comment. The registration number, assigned to each location involved in the collection or processing of blood, should be included on the container label for the proper identification of the collecting establishment. Accordingly, in the final rule, FDA is amending § 606.121(c)(2) to require the inclusion on the label of the registration number of the collecting establishment. Many establishments have multiple locations for the collection of blood, each with a different registration number. FDA advises that such an establishment may select one registration number, preferably that of the primary locaton, for inclusion on the container label in eye-readable form and in encoded form as the collection center identifier. However, an establishment with multiple locations that uses one registration number on the container label for all locations is required to have adequate internal methods for determining the specific collection site of a unit of blood.

7. One comment on proposed § 606.121(c)(2) requested that FDA clarify the provision by stating that the license number should appear only on a licensed product.

FDA agrees with the comment. Section 351 of the Public Health Service Act (42 U.S.C. 262) requires that the license number of the manufacturer be marked on the label of a container of a licensed biological product. Conversely, the label of an unlicensed biological product must not be marked with a license number. Accordingly, in the final rule FDA is clarifying § 606.121(c)(2) to require that the license number of each manufacturer be included on the container label only for licensed products.

8. A comment asked that FDA clarify the discrepancy between proposed § 606.121(c)(3), which requires that the container label include the "donor, pool, or lot number" and current § 640.24(a) (21 CFR 640.24(a)), which states that platelets shall not be pooled during processing.

FDA disagrees with the comment. FDA believes that §§ 606.121(c)(3) and 640.24(a) are consistent. Section 606.121(c)(3) lists several possible alternatives for identifying a unit and relating it to the donor. Because platelets may not be pooled during processing, a pool number would not exist for such units and therefore could not be included on the container label. However, after preparation of individual platelet units is completed, units of platelets intended for a specific patient often are pooled by the transfusing facility. A pool number, relating the pooled platelets to the individual donor numbers comprising the pool, may then be assigned the pooled platelet product and included on its label.

9. Two comments on proposed § 606.121(c)(4) recommended that the expiration date indicate the month of expiration as well as the day and year.

FDA agrees with the comment. The word "month" was inadvertently omitted in the proposed rule. The final rule is amended accordingly.

10. Two comments on proposed § 606.121(c)(5) argued that because the majority of blood banks use only volunteer donors, the identification on the blood label of volunteer donors should not be required. The comments suggested that only paid donors be identified on the label, relieving the majority of blood banks from this labeling requirement.

FDA disagrees with the comments. In the Federal Register of January 13, 1978 (43 FR 2142), FDA promulgated the requirement that a donor classification statement be included on the label to protect the public health. FDA based its regulation on data showing that blood from paid donors generally presents a higher risk of transmitting hepatitis than blood from volunteer donors. At a June 1982 meeting, FDA's Blood Products Advisory Committee was asked to consider, among other things, FDA's donor classification requirements. The

Blood Products Advisory Committee recommended that the current donor classification requirements be retained without change. A number of States have enacted legislation that requires donor classification on blood labels, with specific labeling requirements varying from State to State. FDA is providing a uniform label for blood products shipped in interstate commerce and is protecting the public health by continuing to require a statement of donor classification on the label of each unit of blood.

11. One comment recommended that the definition of "paid donor" under proposed § 606.121(c)(5)(i) be revised to include a donor who receives nonmonetary payment.

FDA disagrees with the comment. FDA believes that the higher risk of posttransfusion hepatitis associated with blood from paid donors results primarily because direct monetary payment for blood attracts donations from persons from socioeconomic groups with prevalent transmissible hepatitis. When persons donating blood obtain nonmonetary long-term benefits that are not readily convertible to cash, such benefits provide incentives for persons from groups at low risk of hepatitis to donate blood, while such incentives are not as likely to attract persons from groups with a high risk of hepatitis. FDA continues to believe that a donor who receives nonmonetary long-term benefits is properly classified as a "volunteer donor." Accordingly, in the final rule FDA did not change the definitions of "paid donor" and "volunteer donor."

12. One comment on proposed § 606.121(c)(6), which concerns the accuracy of the label declaration of the volume of certain blood products, recommended that this proposed requirement be revised to permit use of a preprinted volume range on the label of Platelets.

FDA agrees with the comment. In a final rule promulgated on October 29, 1982 (47 FR 49017), FDA eliminated the volume limits formerly required on labels for Platelets and permitted the product to be resuspended in an appropriate volume of plasma. Because FDA now permits use on labels of an unspecified range of volumes for Platelets, it may not be possible to always achieve a Platelet volume accurate to within ±10 percent, as required in proposed § 606.121(c)(6). Therefore, in the final rule FDA is permitting a reasonable range of Platelet volumes on the label for the product. To date, on the uniform blood labels submitted to the agency for review and approval, industry has used a range of up to 20 milliliters (mL) for the preprinted volume range for Platelets, e.g., 45 mL to 65 mL. FDA will consider and approve other volume ranges for Platelets, provided that the labeled volume range is informative and consistent with current good manufacturing practices.

13. Two comments on § 606.121 (c)(8)(iii) and (d)(2) recommended that the statement "PROPERLY IDENTIFY INTENDED RECIPIENT" be of the most prominence on the label and the only label element printed in red. As a basis for this recommendation, the comment noted that a transfusion given to the wrong patient is the most common cause of an avoidable fatal reaction.

FDA disagrees with the recommendation. FDA recognizes that this labeling statement is important for the reason stated in the comment. On the uniform label presented in the final guideline, the statement "PROPERLY IDENTIFY INTENDED RECIPIENT" is printed all in capitals in 6-point size type and is one of three statements in red. The prototype label, modified to meet FDA requirements, was field tested by 16 blood banking establishments. The uniform label was found to be functional through field testing and through its voluntary use since the time of the proposed rule. As practical experience is gained through the label's use, FDA may revise the format of the uniform label to improve its utility. Until such experience clearly demonstrates the need for improvements, FDA intends to support, through regulations and the guideline, the use of the uniform label.

14. One comment on proposed § 606.121(c)(9) (redesignated as § 606.121(c)(9)(i) in the final rule) recommended that the required statement "This product may transmit the agent of hepatitis" be revised editorially to read: "This product may transmit one or more agents of hepatitis."

FDA agrees in part and disagrees in part with the comment. FDA agrees that the wording of the proposed statement was not precise. However, FDA disagrees that the exact suggested language be used. FDA believes that the suggested language is not broad enough in scope to meet current circumstances. Since the proposed rule was published, scientists have determined that human T-lymphotropic virus type III (HTLV-III), the suspected causative agent of acquired immunodeficiency syndrome (AIDS), may be transmitted by blood transfusion. Although blood establishments are now voluntarily testing blood for antibody to HTLV-III, FDA believes that the possibility of transmitting the causative agent of AIDS by blood transfusion will be reduced but not eliminated. Additionally, on rare occasions other infectious agents, such as cytomegalovirus or malaria, may be carried in blood. Accordingly, because infectious agents other than hepatitis may be carried in blood, FDA is amending the final rule in § 606.121(c)(9) to require that the container label include the cautionary statement "This product may transmit infectious agents."

15. One comment on proposed § 606.121(c)(9) (redesignated as § 606.121(c)(9)(i) in the final rule) recommended that the provision not apply to the labeling of products intended for autologous infusion.

FDA agrees with the comment. The labeling provisions necessary for blood intended for autologous infusion (return of blood by infusion to the original donor) are those that ensure that such blood is infused into the donor and not mistakenly used homologously. Many of the general labeling requirements, such as the volunteer donor statement, unexpected antibody information, and blood grouping information, are not necessary and may be omitted for blood intended solely for autologous use. However, as provided in § 606.121(i)(5), blood originally intended for autologous purposes is sometimes diverted for homologous use, in which case all labeling requirements for homologous transfusion must be met.

16. One comment on § 606.121(c)(10) asked whether the volume of source material should include the volume of anticoagulant. If the anticoagulant volume was not included, the comment contended that the provision would be inconsistent with § 606.121(c)(6). The comment also asked why a volume range (±10 percent) is permitted in paragraph (c)(6) and not in (c)(10).

FDA believes that § 606.121(c) (6) and (10) are consistent. Under § 606121(c)(6), FDA requires that the product label provide the user with a reasonably accurate statement of the total volume of the product, including the volume of anticoagulant. Under § 606.121(c)(10), FDA requires that the label for blood components include a statement of the name and volume of the source material. The statement of the source material volume will aid the user in estimating the final product's biological activity. Because the anticoagulant does not contribute directly to the final product's activity, FDA does not require that the anticoagulant volume be included as part of the source material volume. Often a blood facility will obtain source material from another facility for the manufacture of blood components. The receiving facility is not responsible for

confirming the accuracy of the volume statement on the label of the source material. Accordingly, FDA does not require the facility to assure that the statement of source material volume is within specific limits of accuracy.

17. One comment objected to the requirements of § 606.121(c)(12). The comment contended that there is one definitive report that clearly establishes the D^u antigen to be far less immunogenic than the D(Rh_o) antigen and that the remaining examples of claimed Rh immunization by the D^u antigen are most questionable. In addition, the comment noted that there are several grades of D^u antigen which vary greatly in ease of detection and potential for acting as an immunogen. The comment recommended that blood found nonreactive by automated testing procedures or by manual methods using the indirect antiglobulin procedure be labeled as Rh negative.

FDA agrees with the comment, but finds revision of the regulations to be unnecessary. The regulation requires that a test for D^u antigen be performed if the test using Anti-D Blood Grouping Serum is negative; the method of testing for the D^u antigen is not specified. Both the indirect antiglobulin procedure and some automated testing procedures in current use have been found acceptable by the agency for detecting the D^u antigen, even though some of the weakest variants may not be detected by these methods. Licensed blood banks may incorporate any of the approved test methods by requesting an amendment to their product license. Labeling accompanying the various reagents and automated equipment indicates whether the product is suitable for detecting the D^u antigen.

18. Six comments on § 606.121(c)(12) argued that a label identifying the Rh group should not be required on Cryoprecipitated AHF or Plasma. The comments stated that the rare occasions in which transfusion with Rh-positive Plasma or Cryoprecipitated AHF causes Rh antibody production in Rh-negative recipients does not justify the additional expense of retaining additional labeling. Two comments noted that labeling these products with the Rh group could confuse an uninformed individual who may not know when matching of the Rh groups of the blood product and recipient is necessary.

FDA partially agrees with the comments. As stated in the preamble to the October 1980 proposal, some clinicians believe that only Rh negative units of Plasma should be used for transfusing certain patients, such as potentially child-bearing Rh negative females for whom the consequences of immunization are most serious. To omit the Rh group from the label would deprive the clinician of the information necessary to implement this option. Furthermore, the agency believes that only thoroughly trained personnel, acting in accordance with written standard operating procedures, should be given the responsibility of determining the appropriate handling and testing of blood products. Accordingly, the agency does not believe that the labeling of blood components with the Rh group will create confusion on the part of the individuals using the blood components.

FDA also proposed to require that the donor's Rh group be on the container label of Cryoprecipitated AHF. However, unlike Plasma, Cryoprecipitated AHF undergoes a second centrifugation during processing through which red blood cell fragments, containing the Rh antigen, are removed. FDA is not aware of a documented case of Cryoprecipitated AHF causing Rh antibody production in an Rh-negative recipient. Accordingly, FDA is amending § 606.121(c)(12) in the final rule to permit the omission of the Rh group on Cryoprecipitated AHF. FDA expects that many blood banks will continue to identify the Rh group on Cryoprecipitated AHF labels. On the uniform label, the ABO and Rh groups are printed on one labeling unit. To omit the Rh group, an establishment would have to purchase additional labels containing only the ABO group, thereby increasing its label inventory and labeling costs. Accordingly, FDA advises that establishments may continue to include the Rh group on Cryoprecipitated AHF labels to limit labeling costs and to provide maximum information to the using clinician.

19. Eleven comments on proposed § 606.121(c)(13) objected to the required inclusion of encoded information on the labels of transfusible blood and blood components. A variety of reasons were given for this objection, but the majority of comments said that the additional expense of encoded labels cannot be justified by any potential benefits, especially for those establishments that are not computerized to allow use of the machine-readable codes. Some of the comments expressed the belief that machine-readable encodement was useful only for those establishments extensively engaged in the interregional exchange of blood and blood components. Accordingly, many of the comments suggested that encoded information be prescribed only on an optional basis. One comment stated specifically that the encoded unit number should not be required on container labels. One comment from registered but unlicensed blood bank asked whether unlicensed establishments would be required to adopt the bar code system for blood labeling.

FDA agrees that it is unnecessary to require encoding. From the time the October 1980 proposed rule was published, FDA has encouraged the voluntary adoption of the uniform label, including bar coding. Currently, approximately two-thirds of the blood distributed in the United States is labeled with the bar-coded uniform label. Because of the benefits that may be derived from the use of computer technology, FDA believes that use of machine-readable symbols on blood labels will continue to expand whether or not FDA required their use.

The use of computer technology in blood banking will be of substantial benefit in reducing labeling and recording errors, providing a more efficient means of recording and storing information, controlling inventory and assisting in the interchange of blood among establishments. In addition, the use of a uniform label will reduce overall labeling costs in contrast to the expense of each establishment developing and printing its own customs labels. It is expected that blood establishments will be able to purchase the uniform label as a standard catalogue item from its hospital supply service. Large regional blood centers often supplement their blood inventories with blood collected and labeled at local blood banks within their region. Because of recordkeeping difficulties, computerized regional blood centers have found it impractical to include blood with unencoded labels in their inventories. If a significant percentage of blood in a center's region is unencoded and, therefore, unavailable to the center, the center's ability to efficiently supply a region's blood needs may be hindered, especially in an emergency situation. However, for those establishments that are not yet computerized and do not frequently exchange blood and blood components with computerized establishments, the direct benefit of including encoded information on the container label would be minimal. Upon reconsideration, FDA has determined that the voluntary adoption of encoded labeling is adequate to support the efficient use of blood resources by computerized facilities and it is unnecessary to require use of bar-coded blood labels at this time.

Accordingly, FDA is amending § 606.121(c)(13) in the final rule by removing the requirement that certain

information be encoded on the container label of blood and blood components. Instead, in § 606.121(c)(13), FDA is requiring that any machine-readable coding system used voluntarily for labeling blood and blood components be one approved for such use by the Director, Office of Biologics Research and Review.

20. Two comments on § 606.121(c)(13) argued that FDA has not adequately investigated the economic impact of the proposed regulations and that the information placed on file with Dockets Management Branch is inadequate to substantiate the economic effects of requiring encodement of information on the labels of blood and blood components.

FDA disagrees with the comment. FDA primarily based its economic assessment upon a cost comparison of the then current labeling and the uniform label, including bar codes, provided by a major blood banking organization. The costs were verified by data supplied by a printer of blood container labels. No specific data were received contradicting the estimates provided in FDA's economic assessment. FDA believes that the cost estimates provided in its economic assessment that accompanied the proposed rule were valid at that time. For its final rule, FDA has reassessed the economic impact, with the encoded uniform label serving as the basis for cost estimates, and an updated revised economic assessment is on file with the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

21. Five comments on § 606.121(c)(13) agreed with the principle of encoding information on container labels; however, the comments recommended that a means of encodement be used that is readable both by the eye and machine. Four of the comments specifically recommended the use of the Optical Character Recognition (OCR) method of encoding information. One manufacturer of equipment compatible with the OCR system submitted extensive technical information on the OCR system. Another comment related the perceived merits of the OCR system in comparison with the bar-code method.

FDA cannot accept the OCR system as an alternative method for encoding information at this time. CCBBA considered a number of candidate symbol systems, including the OCR system, when selecting the CODABAR™ symbol as most appropriate for blood-banking automation. CCBBA's findings and recommendations on the symbol systems it reviewed are included as Volume III of its Final Report which is on file under Docket No. 80N-0120. In light of the comments and information received in response to the proposed rule, members of FDA and ABC again considered the merits of the OCR system compared with the CODABAR™ system. The review reaffirmed CCBBA's original finding that, based upon available data, the OCR system has several disadvantages and no significant advantage when compared with the use of its CODABAR™ system in a blood-bank setting. Of primary concern to FDA, the available data indicate that OCR symbols have a higher rate of substitution errors (errors related to unidentified misreads) than CODABAR™ symbols. Because such errors may not be identified, a labeling or transfusion error may result. FDA recognizes that the technology surrounding automated data processing is rapidly advancing and will continue to monitor alternative methods of encodement. FDA will consider data to support a change to the OCR system or other methodology at any time. If another system is found equal or superior to the current system, the Director, Office of Biologics Research and Review, may approve the candidate symbol as an alternative method of encoding information on the blood container label.

22. One comment on § 606.121(c)(13) stated that if labels containing the encoded Julian date were misprinted or misplaced, it would take 30 to 45 days to replace labeling containing bar-codes, during which time no products could be labeled.

FDA disagrees with the comment. The expiration date is not an encoded element of the uniform label and is written in the form of the day, month, and year of expiration. Julian dating, the system in which the days of the year are numbered sequentially from 1 to 365, may be used to identify the collection date of the blood unit. Use of the collection date is optional and, when used, may be presented in encoded and printed forms. It is expected that those establishments identifying the collection date on the label will use on-site bar-code printing equipment to print the bar-coded label upon demand. Accordingly, only blank collection date labels need be kept in stock by those establishments choosing to use this labeling element, and no problems in maintaining an adequate labeling inventory should result.

23. Two comments on § 606.121(c)(13)(ii) stated that identification of the type of anticoagulant should not be required on the label for frozen red blood cell products because the final product will be washed and the anticoagulant effectively removed.

FDA agrees with the comments. FDA is revising the provision in the final rule to indicate that it applies only to unfrozen red blood cell products. Similarly, FDA is revising the applicability of § 606.121(e)(2)(i) in the final rule.

24. One comment on § 606.121(c)(13)(ii) opposed the required inclusion of the type of anticoagulant on labels for Whole Blood and Red Blood Cells. The comment stated that this provision could cause problems for blood banks using more than one type of anticoagulant. The comment expressed the opinion that because the type of anticoagulant used does not affect the safety or effectiveness of the final products, this information may readily be omitted. As an alternative, the comment suggested that the information circular describe the anticoagulant solution used for each collected product.

FDA disagrees with the comment. The type of anticoagulant used is known to affect a product's physical properties, such as stability, and may influence decisions as to what blood components should be prepared. In a computerized system, expiration dates are set according to the anticoagulant and product bar code; to avoid mislabeling, the same information must appear below the bar code in eye-readable form. Although it is true that establishments using more than one type of anticoagulant will need to retain product labels for each anticoagulant, FDA does not find this an undue burden when necessary to assure the accurate identification and effective use of the product. Furthermore, FDA considers the anticoagulant to be an active ingredient of a blood product. In accordance with section 502(e)(1)(A) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 352(e)(1)(A)), information concerning each active ingredient must be provided on the container label of a drug product. Because biological products are also drugs and therefore subject to the act, section 502(e)(1)(A) requires that the labeling for Whole Blood and Red Blood Cells include the type of anticoagulant.

25. One comment on § 606.121(c)(13)(iii) argued that requiring the inclusion of the collection center identifier on the label will cause a serious labeling problem for establishments that have several collection sites and one centralized processing facility, all under a single

establishment license. The comment noted that a properly run establishment will have internal methods to determine the collection site of a unit of blood and only the identifier for the licensed establishment is necessary on the blood label.

FDA agrees with the comment. As stated above in paragraph 6 of this preamble, an establishment with multiple collection sites need select only one registration number, preferably that of the primary location, for inclusion on the container label in eye-readable form and, optionally, in encoded form as the collection center identifier. Establishments with multiple locations but using only one registration number on the label must have appropriate internal methods for determining the specific collection site of a unit of blood.

26. About 40 comments on § 606.121(d)(3) recommended that the color coding for differentiating ABO blood groups not be changed. Many of the comments argued that the current color codes have been in use for a number of years and to change them would cause confusion and possibly misidentification of the blood group. Further, the comments said that changing the color codes to be consistent with the colors used for blood grouping sera is unnecessary because different personnel are usually involved in handling each type of product and the discrepancy in color codes has not caused confusion in the past. Two comments requested clarification of the effective date for the change in color codes. Many of the comments stated that a 1-year transition period, during which color coding would not be permitted, was not long enough to prevent confusion and to dispose of the more stable blood components labeled with the old color codes.

FDA agrees with the comments. FDA is amending § 606.121(d)(3) in the final rule to prescribe the colors for designating the ABO blood group that are in current use and were formerly codified under § 640.7(d)(2). FDA proposed to change the prescribed colors designating ABO Blood groups in response to a suggestion by CCBBA that the colors be changed for consistency with those prescribed for Blood Grouping Sera in § 660.28(a)(1) (21 CFR 660.28(a)(1)). Considering the number of comments opposing the proposed change and the lack of supporting comments, FDA agrees that the color scheme should not be changed when the current scheme has functioned successfully for a number of years. Because the existing color scheme is being retained, FDA is deleting in the final rule the provision in proposed § 606.121(d)(5) for the effective date and transition period.

27. Two comments on § 606.121(d)(3) recommended that there be no color scheme for identifying ABO groups on the label.

FDA disagrees with the comments. The agency is aware that some persons involved in blood banking and blood transfusion do not support the use of color coding in designating the ABO group. However, many establishments use color coding so that persons at the transfusion site may conveniently reaffirm, even from a distance, that blood of the correct ABO group is being used. FDA is not aware of any data supporting either the required use or prohibition of ABO group color coding. Accordingly, FDA will continue to permit the optional use of color coding for identifying the ABO group of blood units.

28. One comment stated that it was unclear throughout the regulations whether the name of the anticoagulant should be considered as part of the proper name of the product. The comment suggested that, because additional new anticoagulants are continually being developed, it is unnecessary to list the anticoagulant names under § 606.121(e)(1)(ii). Accordingly, the comment suggested that § 606.121(e)(1)(ii) be revised to read: "The name of the anticoagulant shall be part of the proper name of the product, immediately preceding the term 'Whole Blood', and shall be expressed as set forth in the order approving the new anticoagulant."

FDA disagrees with the comment. The name of the anticoagulant is considered a modifier of the proper name. FDA is not aware of any regulation that implies that the anticoagulant name is part of the proper name of the blood product. FDA believes that the revision to § 606.121(e)(1)(ii) suggested in the comment is not as informative as the current wording, nor would it have the same effect. The nomenclature provided in the regulation is considerably revised from that formerly codified in labeling regulations for Whole Blood (Human) (21 CFR 640.7(b)(1)). Therefore, the suggested wording would be incorrect as it would suggest that the outdated names for anticoagulant should continue to be used. FDA does recognize that, as proposed, § 606.121(e)(1)(ii) would require amendment each time a new anticoagulant is approved. Accordingly, FDA is revising the final rule to permit the use of other anticoagulant names upon the approval of the Director, Office of Biologics Research and Review.

29. Two comments on § 606.121(e)(1)(iii) argued that there is no practical value for placing the name of an antibody on a Whole Blood container label. Rather, it is preferable to convert such units to Red Blood Cells. One of the comments asked whether the intent of this provision is to label the names of all unexpected antibodies or only the significant ones.

FDA disagrees with these comments. Although the agency agrees that often it is preferable to convert units of whole blood containing unexpected antibodies to red blood cells, there are occasions when units of whole blood containing unexpected antibodies must be transfused, such as when there are shortages of compatible blood. FDA believes such blood may safely be transfused, provided the blood is found compatible with that of the recipient. Accordingly, the blood should be labeled with any antibodies found to be present. FDA advises that the provision requires the listing of all unexpected antibodies found. However, FDA has consistently permitted the use of test methodology that can greatly minimize the number of insignificant antibodies detected. All unexpected antibodies identified should be listed so that those administering the blood may make the determination of which antibodies should be ignored for the individual recipient. In the October 31, 1980 proposal to revise the additional standards for Whole Blood, FDA proposed to require that Whole Blood from previously pregnant or transfused donors be tested for unexpected antibodies by a method that demonstrates significant alloantibodies. That proposed rule has been withdrawn (48 FR 33494; July 22, 1983). But FDA intends to repropose this requirement by separate rulemaking procedures. At present, the testing of blood from previously pregnant or transfused donors for unexpected antibodies is not explicitly required, but strongly recommended by FDA. Any unexpected antibodies found shall be listed on the container label, as prescribed in § 606.121 (e)(1)(ii), (2)(ii), and (4).

30. One comment on § 606.121 (e)(1)(iii) and (2)(ii) asked that the use of a special label or tie-tag be permitted for identifying unexpected antibodies. The comment noted that the number of units of blood that will have significant antibodies will be very small and tie-tags are less expensive, easier to apply, and easier to write on.

FDA accepts the comment. FDA supports the concept, developed by CCBBA and endorsed by the major blood banking organizations, that

standardized (uniform) container labeling should be used by blood banks for identifying all information. But the agency recognizes that for some establishments, especially those collecting and labeling a small number of units of blood each year, the use of tie-tags for specialized information may be more economical. Accordingly, FDA is amending the final rule by adding § 606.121(j) to permit the optional use of tie-tags for identifying unexpected antibodies. Provisions in proposed § 606.121 (h)(1) and (i)(2) that permit the use of tie-tags for conveying required information for blood shipped in an emergency and blood intended for autologous infusion are also combined under new § 606.121(j).

31. One comment on § 606.121(e)(3) stated that the provision implies that Platelets may be prepared in an open system; the comment asked that this provision be clarified.

FDA disagrees with the comment. Section 606.121(e)(3) does not permit the preparation of Platelets in an open system. The proposed rule listed the products, including Platelets and products prepared in an open system, that must have the hour, day, month, and year of expiration on the container label. The provision only pertains to expiration dating and does not imply that Platelets may be prepared in an open system.

32. One comment on § 606.121(e)(5) noted that the term "recovered plasma" is not defined in the regulations. The comment recommended that an official definition be included. Another comment contended that "recovered plasma" is not a proper name and it should be changed to "Salvaged Source Plasma."

FDA disagrees with the comments. Recovered plasma is plasma obtained as a byproduct of component preparation or recovered from outdated units of blood. Recovered plasma is used as a source material for a variety of injectable and noninjectable biological products. FDA routinely assigns a proper name to each licensed biological product. (See the definition of "proper name" under § 600.3(k) (21 CFR 600.3(k)).) (Because recovered plasma is not a licensed biologic, FDA sees no need to formally define the product or assign a proper name. "Recovered plasma" is the name adopted by the majority of the industry for identifying this material, and the regulations are worded consistently. Source Plasma Salvaged is a specific licensed product prepared only by pheresis; therefore, assigning the name "Salvaged Source Plasma" to an unlicensed product would be confusing.

33. One comment addressed § 606.121(e)(5), which prescribes three labeling requirements for the labels of recovered plasma. The comment stated that further definition is required to determine the circumstances under which each of the three labeling provisions would apply.

FDA believes the regulation is adequately clear to those facilities affected by its provisions; however, for the information of the reader, the circumstances for use of each labeling statement are explained below.

a. *Section 605.121(e)(5)(i).* This provision requires that all recovered plasma container labels include the date of collection of the oldest material in the container. The oldest material in the container is that prepared from whole blood collected on the earliest date.

b. *Section 606.121(e)(5)(ii).* Although recovered plasma may not be used for transfusion, it may serve as a source material for a variety of licensed and unlicensed biological products. Section 606.121(e)(5)(ii) prescribes labeling for such usage. Recovered plasma intended for use in manufacturing injectable products must be labeled with the statement "Caution: For Manufacturing Use Only." Recovered plasma intended for use in manufacturing noninjectable products must be labeled "Caution: For Use in Manufacturing Noninjectable Products Only."

c. *Section 606.121(e)(5)(iii).* This provision governs the use of recovered plasma that does not meet the requirements for use in licensable products. Recovered plasma can only be used in manufacturing a licensable product if plasma is in "short supply" and the recovered plasma is shipped under a "short supply agreement" as required by § 601.22. Section 606.121(e)(5)(iii) requires that plasma not shipped under a "short supply agreement" and therefore not usable in a licensed biological product be labeled "Not For Use in Products Subject to Licensure Under Section 351 of the Public Health Service Act."

34. One comment recommended that the requirements of § 606.121(f), which requires that blood and blood components unsuitable for transfusion be labeled "NOT FOR TRANSFUSION", apply only if the product is not labeled according to §606.121(e)(5)(ii) for noninjectable use only.

FDA agrees with the comment. Recovered plasma labeled in accordance with § 606.121(e)(5) would contain the statement "Caution: For Manufacturing Use Only" or "Caution: For Use in Manufacturing Noninjectable Products Only," and thus would not need to be labeled "Not For Transfusion." FDA has therefore modified § 606.121(f) to provide that it does not apply to recovered plasma labeled in accordance with § 606.121(e)(5).

35. One comment noted that no mention is made in the regulations of the use of a biohazard label for units of blood which are not intended for further manufacturing. The comment asked whether this omission meant that a biohazard label should not be used.

The use of a biohazard label is optional. A biohazard label is commonly used to identify contaminated units or units of blood known to be positive for an infectious agent, such as HBsAg. A recommended biohazard label is included in the guideline. The labeling regulations do not require the use of a biohazard label, although FDA encourages its use. FDA does require that contaminated units and HBsAg positive units not intended for further manufacture be segregated from transfusable units of blood and properly disposed of by autoclaving or incineration.

36. One comment on § 606.121(g) recommended that the labeling provisions for blood and blood components positive for HBsAg and intended for further manufacturing use be clarified beyond simply referencing § 610.40 (21 CFR 610.40).

FDA accepts the comment. Section 610.40 includes not only provisions for the proper labeling of HBsAg positive units but also requirements for testing the blood, conditions for the use of HBsAg positive units, and procedures for notifying the agency of the shipment of HBsAg positive blood. These requirements are necessary because HBsAg positive blood is a highly infectious agent and any person who comes into contact with the blood, due to mishandling or misuse of the blood, may contract hepatitis. Because of the importance of these requirements, the agency cautions that they should be viewed and understood as a unit. However, FDA agrees that an important objective of this rulemaking is to incorporate all requirements for the labeling of blood and blood components into one set of regulations. Accordingly, FDA is amending § 606.121(g) in the final rule to reiterate the labeling requirements specified in § 610.40 applicable to HBsAg reactive blood and blood components.

37. One comment on proposed § 606.121(h)(1) (combined into § 606.121(j) in the final rule) objected to the use of the term "tie-tag." The comment contended that this term implies that the only acceptable means

of attaching a tag to the container is by use of a string and that other better means of making the attachment are available.

FDA disagrees with the comment. The term "tie-tag" in these regulations is generically descriptive and does not imply any requirements relative to the means of attachment of the tag. Various plastic ties, similar to those used to attach price-tags to clothing articles, are used routinely. The agency cautions that the means of attachment should not pierce the blood container and should ensure continuous attachment under normal conditions of use.

38. One comment on proposed § 606.121 (h)(1) and (i)(1) (combined into § 606.121(j) in the final rule) asked why use of a tie-tag is allowed considering that special labels are available that can be securely attached to the container. The comment contended that the use of a tie-tag appears to compromise the special label concept.

While the agency agrees that the use of special labels is preferable, FDA does not intend to prohibit the use of tie-tags for conveying specialized information. Many establishments have been using tie-tags successfully for a considerable time to convey information that is needed infrequently or for information that may later be removed. Because of the anticipated infrequent use of tie-tags, FDA believes that the concept of providing all information on a uniform label to encourage the free exchange of blood is not compromised. The agency will continue to encourage the use of special labels by providing instructions for the content and format of special labels in the guideline.

39. One comment on proposed § 606.121(h)(2) contended that it would be advantageous to label blood intended for emergency release with the name of the intended recipient.

FDA agrees with the comment. Although the agency recommends that the name of the intended recipient should be omitted on the special label or tie-tag for emergency blood in most situations, FDA is deleting from the final regulations the requirement that the intended recipient's name be omitted from the label. Blood is labeled for emergency use when, because of the immediate need for the blood, one or more of the required tests on the blood cannot be completed before transfusion. When the crisis has passed, a unit of incompletely tested blood is less likely to be transfused if the intended recipient's name is not on the label. In addition, the attending clinician administering the blood is more likely to examine thoroughly the emergency blood label and identify what tests have not yet been completed and what extra precautions should be taken. However, FDA agrees there are some circumstances, such as when several patients are to receive emergency-released blood simultaneously, for which the inclusion of the recipient's name on the label may be appropriate.

40. One comment on § 606.121(i) stated that to ensure safe transfusions to patients receiving autologous units of blood (blood intended to be returned to the original donor by infusion), designation of the ABO and $Rh_o(D)$ blood group may provide an additional precaution.

FDA believes that the regulations adequately respond to the comment. Section 606.121(i)(1) requires the identification of the patient on the special label for autologous blood, and the blood group of the patient may be used as part of that identification. FDA does not require the identification of the blood group on the label of autologous blood because blood returned to the original donor is assuredly blood group compatible. On the uniform label, the usual blood grouping label is not attached to blood intended for autologous purposes, thereby assuring that the autologous blood is not mistaken for blood intended for routine homologous transfusion purposes.

41. One comment on proposed § 606.121(i)(1)(ii) (redesignated as § 606.121(i)(2) in the final rule) argued that the date of donation is not valuable information on the label of a product for autologous transfusion and only the expiration date should be required on the label.

FDA disagrees with the comment. Usually blood is collected for autologous purposes when it is difficult or impossible to obtain suitable blood from homologous sources for transfusing a certain patient, for example, when the patient has a rare blood type. Because of limitations both on the amount of blood that can be collected from a patient and the collection frequency restrict the amount of fresh autologous blood available, it is occasionally necessary to transfuse autologous blood that may have marginally exceeded its expiration date. Also, to assure an adequate supply of fresh blood at the time it is needed, it is a recognized practice for the attending physician to reinfuse the oldest unit of autologously collected blood into the patient at the same time that two fresh units are collected. In either of the situations cited above, it is the age of the blood that is of the utmost importance, and this information is best conveyed by showing the date of collection on the label. Accordingly, the agency concludes that the date of collection is required on the label of autologous blood and the final rule so provides.

42. Two comments asked that proposed § 606.121(i)(2) (§ 606.121(i)(5) in the final rule) be revised to provide for the overlabeling or obliteration of special labels because it is often difficult to remove a well-adhered tape label.

FDA agrees with the comment. The agency considers overlabeling or obliteration (inking over a label statement) to be equivalent to removal of the label. For clarity, FDA is revising the regulation in the final rule to provide that the special label for blood intended for autologous purposes shall be removed or otherwise obscured if the unit is issued for homologous transfusion.

43. One comment recommended that the following statements be required on the label of all transfusable blood products: "Do Not Add Medication To This Blood"; "Infuse Through A Filter"; "Do Not Warm Except By Specifically Authorized Procedures"; and "Infuse Immediately; Do Not Store Outside Of The Blood Bank. Return Any Unused Portion To The Blood Bank Immediately". The comment contended that these labeling statements would help inform relatively untrained and unsupervised personnel who occasionally administer blood products, thereby avoiding some potential transfusion errors. Another comment stated that while cautions on a label may be disregarded or unread, statements on the label do have greater immediacy and are more likely to be read than those in a circular. This comment suggested no specific information for inclusion on the label.

FDA disagrees with the comments. One of the purposes of CCBBA's review of blood labeling and the proposed rules was to delete from the blood container label information that is not essential for the proper processing and administration of the product. FDA considers the suggested label statements in the comment to be educational and therefore unnecessary for adequately trained personnel. The agency believes that brief statements on the container label are inadequate for educating untrained personnel. Furthermore, untrained and unsupervised personnel should not be given the responsibility for administering blood and blood products. Persons administering blood should be properly trained and supervised and should be working under written standard operating procedures. FDA believes that the information given in the comment is better understood when given in the blood establishment's

training program by the trainee's supervisor. The written standard operating procedures and instruction circular can then serve to remind personnel of these procedures. FDA also disagrees with the comment that the instruction circular is unread. While it is often unnecessary to consult the instruction circular during the routine operation of a transfusion service, the circular is useful in providing necessary information when a question arises concerning characteristics of a blood product or its proper administration.

44. One comment suggested that the agency issue the labeling requirements as tentative final regulations and simultaneously issue a new draft guideline (presumably for further comment). At that time the agency could encourage voluntary compliance with either the tentative final regulations or the guideline. Subsequently, when final regulations and a final guideline are issued, establishments could continue to use labeling in compliance with the tentative final regulations or draft guideline until depleted. The comment contended that this means of implementation would allow for inconsistencies and questions to be resolved while holding down health care costs.

FDA believes that the procedures being used by the agency to promulgate its labeling regulations and make available its guidelines are consistent with the intent of the comment. By permitting the voluntary use of the uniform label since October 1980 when these labeling regulations were proposed and the draft guideline was made available, FDA effectively instituted a trial period. Only minor discrepancies between the proposed rule and the guideline were found during the trial period, and any discrepancies have been corrected.

45. One comment on § 606.122(c) objected to the required labeling statement "Do not add medications" because the addition of 0.9 percent Sodium Chloride Injection U.S.P. may be considered addition of a medication and yet may be appropriate.

FDA disagrees with the comment. While 0.9 percent Sodium Chloride Injection U.S.P. may be construed to be a medication in the broadest sense of the term, FDA believes that the statement "Do not add medications" will not cause misunderstanding. The addition of 0.9 percent Sodium Chloride Injection U.S.P. would be appropriate only for certain blood components and when its addition is appropriate its use is noted only in the sections of the instruction circular discussing the applicable blood components.

46. Two comments on § 606.122(d) requested that the term "known sensitizing substances" be further defined. One of the comments asked whether such substances include protein and cellular antigens, allergens, and drugs, or some other substances.

The provision was intended to apply to substances that may be used in the processing of certain blood components, such as hydroxyethyl starch, that are known to be potentially sensitizing. FDA has reconsidered this provision and finds that it is unclear, applies to only a few substances, and it overlaps proposed § 606.122(h), which would require the naming of any additives that still may be present in the product. Accordingly, in the final rule FDA is removing § 606.122(d) and redesignating paragraphs (e) through (o) as (d) through (n), respectively. Despite the deletion of this paragraph, FDA advises that the instruction circular must continue to note, when applicable, that a particular additive may be potentially sensitizing.

47. Two comments noted that § 606.122(f) (redesignated as § 606.122(e) in the final rule) requires a statement in the labeling instruction circular concerning the serologic test for syphilis while this statement is not in the example labeling included in the guideline.

A statement concerning the serologic test for syphilis is required in the instruction circular. The current American Association of Blood Banks/ American Red Cross instruction circular states "serologic test for syphilis may also have been performed, as required, and found to be negative." FDA finds that this wording complies with § 606.122(e).

48. One comment objected to the labeling statement required under proposed § 606.122(k). Proposed § 606.122(k) would have required that the instruction circular contain a statement that Whole Blood Platelets and/or Cryoprecipitate Removed should not be used for patients requiring, as applicable, platelets or antihemophilic factor. The comment stated that administration of Whole Blood Platelets and/or Cryoprecipitate Removed to patients requiring platelets or antihemophilic factor would be permitted if the product is not intended as a source of platelets or antihemophilic factor. The comment noted that the labeling requirement does not apply to older units of Whole Blood which would also be deficient in functional platelets and AHF.

FDA agrees with the comment. Accordingly, FDA is deleting proposed § 606.122(k) in the final rule. FDA also advises that, as announced in the "Changes in Proper Names" final rule, the proper name of a product where the cryoprecipitate has been removed shall be "Whole Blood Cryoprecipitate Removed" and the removal of platelets need not be noted on the label.

49. Four comments on § 606.122(l)(1) (redesignated as § 606.122(k)(1) in the final rule) recommended that the labeling suggest, but not require, the use of a suitable plasma volume expander if red blood cells are substituted for whole blood. The comments also noted that the use of a volume expander is proper only if additional volume is immediately necessary and that this is a decision that should be made by the attending physician. The comments noted that the provision incorrectly implies that the plasma volume expander should be added directly to the Red Blood Cells, a procedure that is contrary to currently accepted practice and to the labeling caution not to add medications. Three of the comments suggested that the labeling statements in proposed § 606.122(c), (l)(1), and (l)(2) be combined to read: "Instructions not to add medication to a unit of red blood cells except 0.9 percent Sodium Chloride Injection USP when indicated. Additional plasma volume expanders may be administered separately if necessary."

FDA agrees in part and disagrees in part with the comments. In the case of a massive transfusion, where the blood's oxygen carrying capacity must be restored and the patient must be treated for extreme hypovolemia, Whole Blood is the indicated product. In such cases, Red Blood Cells may be substituted, but suitable plasma volume expanders should be administered concurrently. Although it is ultimately the attending physician's decision as to what blood products should be administered, the product's labeling instruction circular must provide adequate instructions for the use of the product. The instructions should include information about other forms of therapy, such as the administration of suitable plasma volume expanders, that may be necessary concurrent with the administration of the product. However, FDA agrees that the proposed labeling statement incorrectly implies that the plasma volume expander should be added directly to the Red Blood Cells. Accordingly, FDA is amending § 606.122(k)(1) in the final rule to clarify that the instructions apply only when Whole Blood is the indicated product and that plasma volume expanders should be administered concurrently. FDA sees no benefit in combining the labeling provisions cited in the

comment. For clarity, each labeling provision is listed in the regulations separately. However, such required information may be associated together in the instruction circular.

50. One comment on § 606.122(l)(2) (redesignated as § 606.122(k)(2) in the final rule) recommended that a statement warning that only saline should be added to red blood cell products should replace the warning not to add Lactated Ringer's Injection (U.S.P.) solution. The comment stated that it is obvious that a strong sucrose solution should not be added to blood components, and therefore the labeling provision is unnecessary.

FDA disagrees with the comment. FDA concludes that the warning against the addition of Lactated Ringer's Injection (U.S.P.) solution remains appropriate. FDA acknowledges that most persons administering blood are aware that such a solution should not be added to a blood product. This is especially true for Lactated Ringer's Injection, which contains calcium and interferes with the function of the anticoagulant. Unfortunately, FDA is aware of several instances in which transfusion of a blood product with Lactated Ringer's Injection added was attempted. To lessen the chance of a recurrence of this error, FDA is requiring a specific warning in the instruction circular.

51. One comment on § 606.122(m)(1) (redesignated as § 605.122(l)(1) in the final rule) recommended that the provision be corrected editorially to read: "The approximate volume of plasma from which the platelets were prepared."

FDA agrees and § 601.122(l)(1) is amended in the final rule as recommended by the comment.

52. One comment on § 606.122(m)(1) (redesignated as § 606.122(l)(1) in the final rule) asked whether the volume of plasma should be stated in the labeling for platelets obtained from single units and for pooled platelets.

FDA advises that the volume of plasma from which the product was prepared is required only in the labeling for single units of platelets. The provision is clarified in the final rule accordingly.

53. One comment on § 606.122(m)(2) (redesignated as § 606.122(l)(2) in the final rule) noted that the American Association of Blood Banks (AABB) Standards Committee currently permits the use of platelets 6 hours after entering the container or pooling. The comment recommended that, because of the absence of data contradicting the recommendation, the regulations should be revised consistently. A comment on § 606.122(n)(3) (redesignated as § 606.122(m)(3) in the final rule) recommended that the provision be revised consistent with the current AABB standard that permits the storage of thawed plasma at 1 to 6 °C for a maximum of 24 hours before transfusion. Two comments on § 606.122(o)(5) (redesignated as § 606.122(n)(5) in the final rule) noted that the AABB Standards Committee currently permits the use of Cryoprecipitated AHF 6 hours after entering the container or pooling. The comments recommended that because of the absence of data contradicting the AABB recommendation, the regulation should be revised consistently.

FDA cannot accept these recommendations at this time. Proposed §§ 606.122 (m)(2), (n)(3), and (o)(5) (redesignated as §§ 606.122 (l)(2), (m)(3), and (n)(5) in the final rule) are labeling requirements formerly codified in §§ 640.26(k), 640.35(l), and 640.57(l), respectively. FDA is unaware of convincing data supporting the changes recommended by the comments. The agency believes that these changes could affect the safety and effectiveness of the products and that the changes recommended should not be implemented without notice and comment rulemaking procedures. Further, as part of FDA's retrospective review of regulations that is required by E.O. 12291 and the Regulatory Flexibility Act (Pub. L. 96-354), FDA now is reviewing its regulations for blood and blood products. During its review of these regulations, FDA will consider the differences between its regulations and the standards issued by AABB. If FDA believes that the changes recommended by the comments have merit, FDA will include the changes in its proposed rule to be issued as part of FDA's retrospective review of the blood regulations. Interested persons will be offered an opportunity to submit comments, data, and other information at that time.

54. One comment suggested that a new labeling requirement for platelets be included under § 606.122(m) (redesignated as § 606.122(l) in the final rule) to read: "Good patient management requires monitoring treatment responses to Platelets by periodic posttransfusion platelet counts." This statement parallels a similar statement for Cryoprecipitated AHF required under § 606.122(n)(8).

FDA disagrees with the comment. It is always a sound medical practice to monitor a patient's response when undergoing an intensive form of therapy, such as a blood or blood component transfusion. When the monitoring of a patient by specific methodology has been found by scientific consensus to be necessary for assuring the effective use of a product, FDA believes such information should be included in the product labeling. FDA is not aware of a consensus as to the most appropriate means of monitoring a patient's response to Platelet transfusion. For example, monitoring may be accomplished by platelet count, testing the clotting function of the blood, or by observing the patient for reduced bleeding. Because a variety of means of monitoring the patient are acceptable, FDA will not require that the labeling recommend any specific means for monitoring a patient's progress after Platelet transfusion.

55. One comment on § 606.122(o)(1) (redesignated as § 606.122(n)(1) in the final rule) stated the potency of Cryoprecipitated AHF should be expressed as International Units of antihemophilic factor.

FDA agrees with the comment. The only potency unit currently established for measuring antihemophilic factor is obtained by measurement against the international standard (or against a standard that has been compared with the international standard). FDA is amending § 606.122(n)(1) in the final rule accordingly.

56. One comment on § 606.122(o)(2) (redesignated as § 606.122(n)(2) in the final rule) asked whether the provision is an indirect requirement to assay Cryoprecipitated AHF for fibrinogen.

The provision does not require, either directly or indirectly, the testing of Cryoprecipitated AHF for its fibrinogen content. Cryoprecipitated AHF is occasionally used to treat the hypofibrinogenemic patient; therefore, an approximation of the product's fibrinogen content should be included in the instruction circular. As an option, the instruction circular may include the statement, "Usually contains at least 150 mg of fibrinogen." The agency has found through a review of assays of a representative number of units that Cryoprecipitated AHF usually contains at least 150 milligrams of fibrinogen. No additional testing is required by manufacturers to verify this value. Recognizing that a manufacturer may want to present a more precise value in the labeling, the regulations offer the option to the manufacturer of determining the average fibrinogen content of its Cryoprecipitated AHF through the assay of a representative number of units and including the determined value in the instruction circular. In the final rule, FDA is revising § 606.122(n)(2) for clarity.

57. One comment on § 606.122(o)(4) (redesignated as § 606.122(n)(4) in the final rule) stated that 15 minutes should be the maximum time for thawing Cryoprecipitated AHF at 37 °C. Two comments stated that there is no evidence that Cryoprecipitated AHF must be thawed for no more or less than 15 minutes, and the regulation should be revised accordingly.

FDA agrees that 15 minutes should be the maximum time for thawing Cryoprecipitated AHF. The primary component of Cryoprecipitated AHF, antihemophilic factor (Factor VIII), is heat labile. Therefore, extended exposure of the product to elevated temperatures will significantly lower product yield. Accordingly, Cryoprecipitated AHF should be thawed at 37 °C for the minimum time necessary to ensure complete resuspension of the precipitate. Through practical experience, 15 minutes has been found to be ample time for the complete thawing of Cryoprecipitated AHF. FDA agrees that Cryoprecipitated AHF may be thawed in less time, although care should be taken to ensure that the precipitate is completely resuspended. Accordingly, FDA is amending the final rule to require a statement in the instruction circular that Cryoprecipitated AHF should be thawed for no more than 15 minutes at a temperature of 37 °C.

58. Two comments recommended that § 606.122(o)(6) (redesignated as § 606.122(n)(6) in the final rule) be revised by substituting the term "0.9 percent Sodium Chloride Injection U.S.P." for "saline."

FDA agrees with the comment and is amending § 606.122(n)(6) accordingly.

59. One comment on § 606.122(o)(8) (redesignated as § 606.122(n)(8) in the final rule), which requires that the instruction circular for Cryoprecipitated AHF note the importance of careful patient monitoring, argued that the required labeling statement infringes on the practice of medicine and is not authorized by section 351 of the Public Health Service Act.

FDA disagrees with the comment. FDA does not believe that the provision infringes on the practice of medicine. It is not FDA's intent to require a physician to perform certain tests to monitor the patient's response to Cryoprecipitated AHF. However, in accordance with section 502(f) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352(f)), FDA does require that labeling provided to the physician for all prescription drugs, including biologics, contain adequate instructions for the product's use. FDA and most members of the scientific community agree that careful patient monitoring is necessary to ensure the effective use of Cryoprecipitated AHF. Accordingly, FDA is requiring that the instruction circular for Cryoprecipitated AHF note the importance of careful patient monitoring when administering Cryoprecipitated AHF.

60. FDA is amending § 606.121(e)(1)(ii) in the final rule to include the approved nomenclature for a new anticoagulant, Anticoagulant Citrate Phosphate Double Dextrose (CP2D), which FDA recently approved for the collection of Whole Blood and the preparation of various blood components.

61. FDA is amending § 606.121(e)(3) in the final rule to state that products with a dating period of 72 hours or less shall be labeled with the hour of expiration. The revised wording will provide greater flexibility if a dating period for a product should change. Indeed, Platelets collected in certain container systems are being granted dating periods of up to 5 days, in which case the hour of expiration is not required on the container label.

62. Proposed § 606.122 (m)(2), (n)(3), and (o)(5) (redesignated as § 606.122 (l)(2), (m)(3), and (n)(5) in the final rule) contains labeling requirements formerly codified in §§ 640.26(k), 640.35(l), and 640.57(l), respectively. In the final rule, FDA is adopting these provisions with a minor clarifying change. The agency advises that instruction circulars that conform to the proposed requirements and the former codified language continue to be acceptable until the effective date of this final rule. To assure uniform wording among instruction circulars in use, FDA recommends that manufacturers revise their instruction circulars to be in agreement with § 606.122 (l)(2), (m)(3), and (n)(5) when labeling is reordered.

63. In the Federal Register of October 31, 1980, FDA published a proposal to revise the additional standards for Whole Blood (21 CFR Part 640, Subpart A) in which FDA proposed to revise the requirements concerning the emergency issue of blood in § 640.2(f). In view of the withdrawal of the proposal (48 FR 33494; July 22, 1983), FDA, in this final rule, is amending § 640.2 in paragraph (f) (4) and (5) to delete the labeling provisions and in paragraph (f)(3) to reference the labeling requirements in § 606.121(h).

Environmental Impact

The agency has determined pursuant to 21 CFR 25.24(a)(11) (April 26, 1985; 50 FR 16636) that this action is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Paperwork Reduction Act of 1980

In accordance with the Paperwork Reduction Act of 1980 and 5 CFR 1320.13(g) of OMB's regulations implementing the provisions of that act, FDA has submitted the final rule to OMB for approval of the collection of information requirements contained in §§ 606.121 and 606.122 of the rule. These requirements will not be effective until FDA obtains OMB approval. In accordance with 5 CFR 1320.13(j), prior to November 29, 1985, FDA will publish in the Federal Register a notice of OMB's decision to approve, modify, or disapprove these requirements. Other organizations and individuals desiring to submit comments on the collection of information requirements should direct them to FDA's Dockets Management Branch (address above) and to the Office of Information and Regulatory Affairs, OMB, Rm. 3208, New Executive Office Bldg., Washington, DC 20503, Attn: Bruce Artim.

Various current sections of Part 606 contain collection of information requirements that were submitted to OMB for review and approval as required by section 3507 of the Paperwork Reduction Act. The requirements were approved and assigned OMB control number 0910-0116.

The requirement for a regulatory flexibility analysis under the Regulatory Flexibility Act does not apply to this final rule because the proposed rule was issued prior to January 1, 1981, and is therefore exempt. The economic impact of this rule has been assessed in accordance with Executive Order 12291. FDA concludes that approximately 178 licensed establishments and 1,300 registered but unlicensed establishments are affected by this final rule. The assessment assumes that all establishments will adopt the uniform label described in the guideline "Guideline for the Uniform Labeling of Blood and Blood Components," although some establishments may not use an encoded unit number label. FDA estimates that the rule could result in savings of $2,400 per year for each establishment; if each establishment elected to use the least expensive uniform label. However, because many establishments are expected to use voluntarily more expensive, fully bar-coded labels, label cost may be up to $312,000 more per year ($2,000 per establishment). The anticipated costs are insufficient to warrant designation

of the rule as a major rule under any of the criteria specified under section 1(b) of Executive Order 12291. The assessment done to make this determination is on file with the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

List of Subjects

21 CFR Part 606

Blood, Laboratories, Reporting and recordkeeping requirements.

21 CFR Part 640

Blood, Reporting and recordkeeping requirements.

Therefore, under the Food, Drug, and Cosmetic Act, the Public Health Service Act, and the Administrative Procedure Act and under authority delegated to the Commissioner of Food and Drugs, Parts 606 and 640 are 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: Secs. 201, 502, 505, 701, 52 Stat. 1040-1042 as amended, 1050-1053 as amended, 1055-1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321, 352, 355, 371) and the Public Health Service Act (sec. 351, 58 Stat. 702 as amended (42 U.S.C. 262)) and the Administrative Procedure Act (secs. 4, 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 701-706)); 21 CFR 5.10.

2. By revising § 606.120 to read as follows:

§ 606.120 Labeling, general requirements.

(a) Labeling operations shall be separated physically or spatially from other operations in a manner adequate to prevent mixups.

(b) The labeling operation shall include the following labeling controls:

(1) Labels shall be held upon receipt, pending review and proofing against an approved final copy, to ensure accuracy regarding identity, content, and conformity with the approved copy.

(2) Each type of label representing different products shall be stored and maintained in a manner to prevent mixups, and stocks of obsolete labels shall be destroyed.

(3) All necessary checks in labeling procedures shall be utilized to prevent errors in translating test results to container labels.

(c) All labeling shall be clear and legible.

3. By adding new §§ 606.121 and 606.122 to read as follows:

§ 606.121 Container label.

(a) The container label requirements are designed to facilitate the use of a uniform container label for blood and blood components (except Source Plasma) by all blood establishments. Single copies of an FDA guideline entitled "Guideline for the Uniform Labeling of Blood and Blood Components" are available upon request (under Docket No. 80N-0120) from the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857 (copies of the guideline are available also from the American Blood Commission, 1901 North Ft. Myer Drive, Suite 300, Arlington, VA 22209).

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

(c) The container label shall 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, and modifier(s), if appropriate.

(2) The name, address, registration number, and, if a licensed product, the license number of each manufacturer.

(3) The donor, pool, or lot number relating the unit to the donor.

(4) The expiration date, including the day, month, and year, and, if the dating period for the product is 72 hours or less, the hour of expiration.

(5) If the product is intended for transfusion, the appropriate donor classification statement, i.e., "paid donor" or "volunteer donor", in no less prominence than the proper name of the product.

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

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

(iii) 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.

(6) 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.

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

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

(i) "Caution: Federal law prohibits dispensing without prescription."

(ii) "See circular of information for indications, contraindications, cautions, and methods of infusion."

(iii) "Properly identify intended recipient."

(9) The statement: "This product may transmit infectious agents."

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

(11) The statement: "Caution: For Manufacturing Use Only", when applicable.

(12) If the product is intended for transfusion, the ABO and Rh groups of the donor shall be designated conspicuously. For Cryoprecipitated AHF, the Rh group may be omitted. The Rh group shall be designated as follows:

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

(ii) If the test using Anti-D Blood Grouping Serum is negative but the test for D^u is positive, the product shall be labeled: "Rh positive."

(iii) If the test using Anti-D Blood Grouping Serum is negative and the test for D^u is negative, the product shall be labeled: "Rh negative."

(13) The container label may bear encoded information in the form of machine-readable symbols approved for use by the Director, Office of Biologics Research and Review (HFN-800), Center for Drugs and Biologics.

(d) Except for recovered plasma intended for manufacturing use or as otherwise approved by the Director, Office of Biologics Research and Review (HFN-800), Center for Drugs and Biologics, the paper of the container label shall be white and print shall be solid black, with the following additional exceptions:

(1) The Rh blood group shall be printed as follows:

(i) Rh positive: Use black print on white background.

(ii) Rh negative: Use white print on black background.

(2) The proper name of the product, any appropriate modifier(s), the donor classification statement, and the statement "properly identify intended recipient" shall be printed in solid red.

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

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

(4) Ink colors used for the optional color coding system described in paragraph (d)(3) of this section shall be a visual match to specific color samples designated by the Director, Office of Biologics Research and Review (HFN–800), Center for Drugs and Biologics.

(5) Special labels, such as those described in paragraphs (h) and (i) of this section, may be color coded using the colors recommended in the guideline (see paragraph (a) of this section), or colors otherwise approved for use by the Director, Office of Biologics Research and Review (HFN–800), Center for Drugs and Biologics.

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

(1) Whole Blood labels shall include:

(i) The volume of anticoagulant.

(ii) The name of the applicable anticoagulant immediately preceding and of no less prominence than the proper name and expressd as follows: (*a*) ACD, (*b*) CPD, (*c*) Heparin, (*d*) CPDA–1, (*e*) CP2D, or by other nomenclature approved for use by the Director, Office of Biologics Research and Review (HFN–800), Center for Drugs and Biologics.

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

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

(i) The volume and kind of Whole Blood, including the type of anticoagulant, from 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) Labels for products with a dating period of 72 hours or less, including any product prepared in a system that may compromise sterility, shall bear the hour of expiration.

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

(5) Recovered plasma labels shall include:

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

(ii) The statement: "Caution: For Manufacturing Use Only"; or "Caution: For Use in Manufacturing Noninjectable Products Only", as applicable.

(iii) 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."

(f) Blood and blood components determined to be unsuitable for transfusion shall be prominently labeled: "NOT FOR TRANSFUSION", and the label shall state the reason the unit is considered unsuitable. The provision does not apply to recovered plasma labeled according to paragraph (e)(5) of this section.

(g) As required under § 610.40 of this chapter, labels for blood and blood components that are reactive for Hepatitis B Surface Antigen, but that are intended for further manufacturing, shall state conspicuously that the material is reactive when tested for hepatitis B surface antigen and may transmit viral hepatitis or, as applicable, that blood was collected from a donor known to be reactive for hepatitis B surface antigen and is presumed to be infectious, although confirmatory hepatitis testing has not been done.

(h) The following additional information shall appear on the label for blood or blood components shipped in an emergency, prior to completion of required tests, in accordance with § 640.2(f) 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 and not completed before shipment.

(i) The following additional information shall appear on the label for Whole Blood or Red Blood Cells intended for autologous infusion:

(1) Information adequately identifying the patient, e.g., name, blood group, hospital, and identification number.

(2) Date of donation.

(3) The statement: "FOR AUTOLOGOUS USE ONLY."

(4) In place of the 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 in the hepatitis tests prescribed under § 610.40 of this chapter shall be prominently and permanently labeled: "FOR AUTOLOGOUS USE ONLY."

(5) Units of blood originally intended for autologous use, except those labeled as prescribed under paragraph (i)(4) of this section, may be issued for homologous 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 paragraph (i) (1), (2), and (3) of this section shall be removed or otherwise obscured.

(j) A tie-tag attached to the container may be used for providing the information required by paragraph (e) (1)(iii), (2)(ii), and (4), (h), or (i)(1), (2), and (3) of this section.

§ 606.122 Instruction circular.

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

(a) Instructions to mix the product before use.

(b) Instructions to use a filter in the administration equipment.

(c) The statement "Do Not Add Medications" or an explanation concerning allowable additives.

(d) A description of the product, its source, and preparation, including the name and proportion of the anticoagulant used in collecting the Whole Blood from each product is prepared.

(e) Statements that the product was prepared from blood that was nonreactive when tested for hepatitis B surface antigen by an FDA required test and nonreactive when tested for syphilis by a serologic test for syphilis (STS).

(f) The statements: "Warning. The risk of transmitting hepatitis is present. Careful donor selection and available laboratory tests do not eliminate the hazard."

(g) The names of cryoprotective agents and other additives that may still be present in the product.

(h) The names and results of all tests performed when necessary for safe and effective use.

(i) The use of the product, indications, contradications, side effects and hazards, dosage and administration recommendations.

(j) [Reserved]

(k) For Red Blood Cells, the instruction circular shall contain:

(1) Instructions to administer a suitable plasma volume expander if Red Blood Cells are substituted when Whole Blood is the indicated product.

(2) A warning not to add Lactated Ringer's Injection U.S.P. solution to Red Blood Cell products.

(l) For Platelets, the instruction circular shall contain:

(1) The approximate volume of plasma from which a sample unit of Platelets is prepared.

(2) Instructions to begin administration as soon as possible, but not more than 4 hours after entering the container.

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

(1) A warning against further processing of the frozen product if there is evidence of breakage or thawing.

(2) Instructions to thaw the frozen product at a temperature between 30 and 37 °C.

(3) When applicable, instructions to begin administration of the product within 6 hours after thawing.

(4) Instructions to administer to ABO-group-compatible recipients.

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

(n) For Cryoprecipitated AHF, the instruction circular shall contain:

(1) A statement that the average potency is 80 or more International Units of antihemophilic factor.

(2) The statement: "Usually contains at least 150 milligrams of fibrinogen"; or, alternatively, the average fibrinogen level determined by assay of representative units.

(3) A warning against further processing of the product if there is evidence of breakage or thawing.

(4) Instructions to thaw the product for no more than 15 minutes at a temperature of 37 °C.

(5) Instructions to store at room temperature after thawing and to begin administration as soon as possible but no more than 4 hours after entering the container or after pooling and within 6 hours after thawing.

(6) A statement that 0.9 percent Sodium Chloride Injection U.S.P. is the preferred diluent.

(7) Adequate instructions for pooling to ensure complete removal of all concentrated material from each container.

(8) The statement: "Good patient management requires monitoring treatment responses to Cryoprecipitated AHF transfusions with periodic plasma factor VIII or fibrinogen assays in hemophilia A and hypofibrinogenemic recipients, respectively."

4. By adding a new clause regarding the OMB control number at the end of § 606.170 to read as follows:

§ 606.170 Adverse reaction file.

* * * * *

(Information collection requirements approved by the Office of Management and Budget under OMB control number 0910-0116)

PART 640—ADDITIONAL STANDARDS FOR BLOOD AND BLOOD PRODUCTS

5. The authority citation for 21 CFR Part 640 continues to read as follows:

Authority: Secs. 215, 351, 58 Stat. 690 as amended; 702 as amended (42 U.S.C. 216, 262); 21 CFR 5.10.

6. In § 640.2 by revising paragraph (f) to read as follows:

§ 640.2 General requirements.

* * * * *

(f) *Issue prior to determination of test results.* Notwithstanding the provisions of § 610.1 of this chapter, blood may be issued by the manufacturer on the request of a physician, hospital, or other medical facility before results of all tests prescribed in § 640.5 and the test for hepatitis B surface antigen prescribed in § 610.40(a) of this chapter have been completed, where such issue is essential to allow time for transportation to ensure arrival of the blood by the time it is needed for transfusion: *Provided,* That (1) the blood is shipped directly to such physician or medical facility, (2) the records of the manufacturer contain a full explanation of the need for such issue, and (3) the label on each container of such blood bears the information required by § 606.121(h) of this chapter.

§§ 640.7, 640.18, 640.26, 640.35, and 640.57 [Removed]

7. By removing § 640.7 *Labeling,* § 640.18 *Labeling,* § 640.26 *Labeling,* § 640.35 *Labeling,* and § 640.57 *Labeling.*

8. In § 640.70 by revising the introductory text of paragraph (a) to read as follows:

§ 640.70 Labeling.

(a) In addition to the labeling requirements of § 610.62 of this chapter, and in lieu of the requirements in §§ 606.121, 610.60, and 610.61 of this chapter, the following information shall appear on the label affixed to each container of Source Plasma:

* * * * *

Dated: August 1, 1985.

Frank E. Young,

Commissioner of Food and Drugs.

[FR Doc. 85-20739 Filed 8-29-85; 8:45 am]

BILLING CODE 4160-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICE

Food and Drug Administration

[Docket No. 80N-0120]

Guideline for the Uniform Labeling of Blood and Blood Components; Availability of Guideline

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a revised guideline for the uniform labeling of blood and blood components. The guideline describes in detail the specifications for a uniform container label for blood-banking use which conform with a final rule published elsewhere in this issue of the Federal Register.

ADDRESS: Written comments and requests for a copy of the guideline (identified with the docket number found in brackets in the heading of this document) to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Mary Ann Tourault, Center for Drugs and Biologics (HFN-830), Food and Drug Administration, 8800 Rockville Pike, Bethesda, Md 20205, 301-496-4396.

SUPPLEMENTARY INFORMATION: FDA is making available a final guideline prepared by the Office of Biologics Research and Review in the Center for Drugs and Biologics to describe the uniform container label for blood and blood components. In the Federal Register of October 31, 1980 (45 FR 72416), FDA published a proposed rule to revise the labeling requirements for blood and blood components. In the same document, FDA announced the availability of a proposed guideline entitled "Guidelines for the Uniform Labeling of Blood and Blood Components." Preparation of the guideline is part of a program supported by FDA, the American Blood Commission (ABC), and other organizations representing the blood banking industry, to encourage the use of blood container labels of a standard content and format, with certain label elements present in both eye-readable and machine-readable form. Since the time of the announcement of the proposed guideline's availability, FDA has permitted the voluntary use of uniform labeling consistent with the proposed rule and guideline.

Elsewhere in this issue of the Federal Register, FDA is publishing a final rule revising the labeling requirements for blood and blood components. In the Federal Register of January 29, 1985 (50 FR 4128), FDA published a final rule revising the proper names for certain biological products, including blood and blood component products. FDA is announcing the availability of a revised guideline which reflects the labeling requirements and new proper names established in the respective final rules. In cooperation with ABC, FDA has revised the final guideline to correct several errors found in the guideline made available in October 1980. The final guideline provides labeling information for several additional products, including additional blood components, anticoagulants, preservatives, and blood container systems. Although many of these products are not currently licensed or approved by FDA for general use in the United States, FDA expects that these additional products will gain wide acceptance and use in the next few years.

Included with the guideline as Appendix A is "Suggested Evaluation Protocol for Bar-Coded Pressure Sensitive labels" intended for use by printers of labels to determine the acceptability of their products for use in blood banks.

ABC also has made the proposed guideline of October 1980 available to its constituents, along with other instructions for the uniform labeling of blood and blood components. Base upon the practical experience gained through the use of the proposed guideline, ABC has recommended revisions to clarfiy the guideline, to provide additional information concerning the printing and use of the uniform label, and to delete certain unnecessary information. The revised final guideline incorporates ABC's recommendations.

This notice is issued under § 10.90(b) (21 CFR 10.90(b)), which provides for the use of guidelines to outline procedures or standards of general applicability that are acceptable to FDA for a subject matter than falls within the laws administered by FDA. Although these guidelines are not a legal requirement, a person may be assured that in following an agency guideline the procedures followed and standards used will be acceptable to FDA. A person may also choose to use alternative procedures or standards for which there is scientific rationale even though they are not provided for in a guideline. A person who chooses to use procedures or standards not in a guideline may discuss the matter further with the agency to prevent an expenditure of resources for work that FDA may later determine to be unacceptable.

FDA is permitting the immediate voluntary use of container labels printed in accordance with the revised final guideline that are consistent with the final regulations published elsewhere in this issue of the Federal Register. Licensed establishments may begin using the new container label and instruction circular without their prior review and approval by FDA, provided that the label is printed in accordance with the specifications described in the guideline. As an amendment to the product license(s), a licensed establishment is required to submit the revised label and instruction circular to the Director, Office of Biologics Research and Review (HFN-800), Center for Drugs and Biologics, 8800 Rockville Pike, Bethesda, MD 20205.

In accordance with the Paperwork Reduction Act of 1980 (44 U.S.C. 35), the reporting and recordkeeping requirements in §§ 606.121 and 606.122 of the final rule on uniform blood labeling (Docket No. 80N-0120) have been submitted for approval to the Office of Management and Budget (OMB). The guideline being made available by the agency has been developed in accordance with the provisions of these sections. The requirements under §§ 606.121 and 606.122 for uniform blood labeling, as described in the final rule published elsewhere in this issue of the Federal Register, will not be effective until FDA obtains OMB approval of the recordkeeping and reporting requirements in §§ 606.121 and 606.122. Prior to November 29, 1985, FDA will publish a notice concerning OMB review of these requirements.

Single copies of the final guideline are available from the Dockets Management Branch (address above). Copies of the final guideline are available also from the American Blood Commission, 1901 N. Ft. Meyer Drive, Suite 300, Arlington, VA 22209 for $5.00 per copy. (The price of the guideline is subject to change.)

Interested persons may submit written comments on the guideline to the Dockets Management Branch. These comments will be considered in determining whether further amendments to, or revisions of, this guideline are warranted. Two copies of any comments are to be submitted, except that individuals may submit one 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 office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: August 1, 1985.

Frank E. Young,

Commissioner of Food and Drugs.

[FR Doc. 85-20734 Filed 8-29-85; 8:45 am]

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