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Department of Health and Human Services

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21 CFR Parts 606 and 610

Current Good Manufacturing Practice for Blood and Blood Components; Notification of Consignees and Transfusion Recipients Receiving Blood and Blood Components at Increased Risk of Transmitting HCV Infection ("Lookback"); Proposed Rule

Health Care Financing Administration

42 CFR Part 482

Medicare and Medicaid Programs; Hospital Conditions of Participation: Laboratory Services; Proposed Rule

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 606 and 610

[Docket No. 99N–2337]

RIN 0910–AB76

Current Good Manufacturing Practice for Blood and Blood Components; Notification of Consignees and Transfusion Recipients Receiving Blood and Blood Components at Increased Risk of Transmitting HCV Infection (''Lookback'')

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to amend the biologics regulations to require that blood establishments (including plasma establishments) prepare and follow written procedures for appropriate action when it is determined that blood and blood components at increased risk of transmitting hepatitis C virus (HCV) infection have been collected from a donor who tested repeatedly reactive for evidence of HCV infection at a later date. This proposed rule would require blood establishments to quarantine prior collections from such a donor, perform further testing on the donor, and notify transfusion recipients, as appropriate, when such a donor is identified at the time of a repeat donation or after performing a review of historical testing records to identify donations at increased risk of transmitting HCV. In addition, FDA is proposing to extend the record retention period to 10 years to create opportunities for disease prevention many years after recipient exposure to such a donor. This action is taken as part of FDA's ''Blood Initiative'' to comprehensively review and, as necessary, revise its regulations, policies, guidances, and procedures related to the licensing and regulation of blood products. This proposed rule is intended to help ensure the continued safety of the blood supply and to help ensure that information is provided to consignees and to prior recipients of blood and blood components from a donor whose subsequent donation tests positive for antibody to HCV or otherwise is determined to have been at increased risk of transmitting HCV.

DATES: Submit written comments on the proposed rule by February 14, 2001. Submit written comments on the information collection provisions by December 18, 2000. See section VII of this document for the proposed effective date of a final rule based on this document.

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit written comments on the information collection provisions to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., Washington, DC 20503, Attn: Wendy Taylor, Desk Officer for FDA.

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

SUPPLEMENTARY INFORMATION:

I. Background

A. Blood Initiative

For a variety of reasons FDA has decided to comprehensively review and, as necessary, revise its regulations, policies, guidance, and procedures related to the licensing and regulation of blood products. In the **Federal Register** of June 3, 1994 (59 FR 28821 and 59 FR 28822, respectively), FDA issued two documents entitled ''Review of General Biologics and Licensing Regulations'' (Docket No. 94N–0066) and ''Review of Regulations for Blood Establishments and Blood Products'' (Docket No. 94N–0080). These two documents announced the agency's intent to review biologics regulations in 21 CFR parts 600, 601, 606, 607, 610, 640, and 660 (21 CFR 600, 601, 606, 607, 610, 640, and 660) and requested written comments from the public. Interested persons were given until August 17, 1994, to respond to the documents. In response to requests for additional time, FDA twice extended the comment period, as announced in the **Federal Register** of August 17, 1994 (59 FR 42193), and November 14, 1995 (59 FR 56448). In addition, FDA responded to requests for a public meeting to allow for the presentation of comments regarding the agency's intent to review the biologics regulations. On January 26, 1995, FDA held a public meeting to provide an opportunity for all interested individuals to present their comments and to assist the agency in determining whether the regulations should be revised, rescinded, or continued without change. Since the time of the regulation review, FDA has implemented a number of changes to its regulations and policies applicable to the general biologics and licensing regulations, some of which applied to blood products as well as other biological products. (See, *e.g.,* the final rules issued on May 14, 1996 (61 FR 24313); August 1, 1996 (61 FR 40153); November 6, 1996 (61 FR 57328); July 24, 1997 (62 FR 39890); and October 15, 1997 (62 FR 53536)).

Because of the importance of a safe national blood supply, the U.S. House of Representatives Committee on Government Reform and Oversight, Subcommittee on Human Resources and Intergovernmental Relations (the Subcommittee) and other groups such as the General Accounting Office (GAO), and the Institute of Medicine (IOM) have reviewed the agency's policies, practices, and regulations. Reports issued following the respective reviews made a number of recommendations as to how FDA might improve the biologics regulations, particularly as they apply to the continued safety of blood products. The relevant reports are: (1) ''Protecting the Nation's Blood Supply From Infectious Agents: The Need for New Standards to Meet New Threats,'' by the Subcommittee (August 2, 1996); (2) ''Blood Supply: FDA Oversight and Remaining Issues of Safety,'' by GAO (February 25, 1997); (3) ''Blood Supply: Transfusion-Associated Risks,'' by GAO (February 25, 1997); and (4) ''HIV and the Blood Supply: An Analysis of Crisis Decisionmaking,'' by IOM (July 13, 1995). These reports are on file with the Dockets Management Branch (address above) under the docket number given in the heading of this document.

FDA has reviewed these reports and agrees with the majority of the recommendations contained within them. However, rather than only responding specifically to the recommendations from the Subcommittee, GAO, IOM, and the public, FDA convened a number of internal task forces to review a variety of issues related to the regulation of blood and blood products, including how to most appropriately update the existing regulations applicable to blood and blood products. In the future, FDA intends to issue a number of blood-related rulemakings that various FDA task groups are currently preparing. FDA is not describing the specific recommendations it has received and the numerous objectives of the Blood Initiative in this document. Future rulemaking and other notices will describe and discuss specific recommendations and regulatory objectives.

B. Existing Donor Screening and Testing Requirements

FDA has developed five ''layers of safety'' to help ensure a safe blood supply: Donor screening, donor deferral registries, testing blood, blood quarantining, and monitoring and investigating problems. The five layers of safety are designed to overlap so that they will prevent the distribution of blood and blood products that are at increased risk of transmitting communicable disease agents such as human immunodeficiency virus (HIV) and hepatitis B virus (HBV). With regard to screening donors and testing blood, FDA has defined an extensive system of donor screening and testing procedures, two of the five layers of safety, performed by blood establishments. These procedures include the initial screening of individuals that volunteer to donate blood using a questionnaire, interview, and physical examination. This initial screening process is designed to protect the donor and to establish whether the donor is in good health, to rule out possible exposure to disease, such as through travel to an area endemic for malaria, or through close contact with an infected individual, and to identify whether the donor has engaged in behavior that would indicate increased risk of a communicable disease. Individuals who satisfactorily answer the questionnaire, pass the physical examination, and then donate blood are further screened by laboratory testing for evidence of infection due to communicable disease agents such as HIV and HBV. In the **Federal Register** of August 19, 1999 (64 FR 45340), FDA issued a proposed rule entitled ''Requirements for Testing Human Blood Donors for Evidence of Infection Due to Communicable Disease Agents'' (hereinafter referred to as the testing proposed rule), to update, revise, and redesignate the testing requirements of § 610.45. The relevance of the testing proposed rule to this proposed rule is discussed in section III of this document.

As a result of the extensive screening and testing procedures and the other layers of safety, the risk of transmitting infection through blood transfusion is very low. Despite the best practices of blood establishments, however, a person may donate blood early in infection, during the period when the testable marker is not detectable by a screening test, but the infectious agent is present in the donor's blood (a ''window'' period). For example, if a donor donates blood on a number of occasions and each donation tests negative for antibody to HIV, but the donor returns and tests repeatedly reactive for antibody to HIV at a later date, prior collections from such a donor would be at increased risk of transmitting HIV. In addition, a recipient of a transfusion of blood or blood components collected during the ''window'' period would not know that he or she may have become infected with HIV through the transfusion unless notified.

Under such circumstances, FDA requires clarification of the donor's status and procedures to ''lookback'' at prior collections, as specified in §§ 610.46 and 610.47 (the HIV ''lookback'' regulations). (See the final rule issued in the **Federal Register** of September 9, 1996 (61 FR 47413).) The HIV ''lookback'' regulations require facilities involved in the collection, processing, and administration of blood to quarantine blood and blood components which were collected from a donor who tested negative at the time of previous donations but subsequently tests repeatedly reactive for antibody to HIV. The regulations require blood establishments to inform consignees (e.g., hospital transfusion services and manufacturers of plasma derivatives) of the collection and distribution of such previously donated blood and blood components, to perform further testing on the donor, and to notify transfusion recipients, as appropriate.

C. History of HCV Testing

HCV frequently causes a clinically inapparent, but chronic infection of the liver. Approximately 4 million individuals in the United States are believed to be chronically infected with HCV. Despite progression of disease, HCV infection is usually asymptomatic for about 20 years, but in many cases causes serious liver injury that is thought to be the leading cause of late stage cirrhosis and liver failure in the United States and to play a significant role in the development of liver cancer. Therapy with licensed interferon produces long-term benefit in only about 15 percent of cases, but a newly available therapeutic modality, combination therapy using interferon plus ribavirin, may improve this outcome.

The greatest risk for transmission of HCV is through direct percutaneous exposure to infectious blood, such as through transfusion of infectious blood or blood products, sharing of contaminated equipment among injection drug users, or transplantation of organs or tissues from infectious donors. Hemodialysis patients and health-care workers exposed to needle sticks in the occupational setting are also at risk for exposure to infectious blood. Direct percutaneous exposures to infectious blood, particularly in the setting of drug abuse, account for the majority of HCV infections acquired in the United States (Ref. 1). The incidence of transfusion transmitted HCV infection has decreased markedly since the implementation of donor screening for HCV and viral inactivation of clotting factors and intravenous immune globulins. However, approximately 7 percent of the 3.9 million Americans believed to be chronically infected with HCV were infected as a result of transfusion of blood components prior to the availability of donor screening tests or due to past use of nonviral-inactivated plasma derivative products (Ref. 2).

HCV was established as a causative agent of transfusion associated hepatitis only since its discovery in the late 1980's. In October 1989, FDA's Blood Products Advisory Committee (BPAC) first discussed ''lookback'' for HCV, prior to the availability of donor screening tests for HCV. BPAC advised that there was insufficient information available concerning HCV infection to propose either product quarantine or notification of recipients transfused with products prepared from prior collections from donors later determined to be at increased risk for transmitting HCV. Blood establishments implemented donor screening tests after a single antigen, enzyme linked immunosorbent assay (EIA) for antibody to HCV (HCV EIA 1.0 screening test) was licensed in May 1990. FDA issued a memorandum to all registered blood establishments in November 1990, entitled ''Testing for Antibody to Hepatitis C Virus Encoded Antigen (Anti-HCV),'' recommending use of approved donor screening tests for antibody to HCV. A ''lookback'' program was not recommended because: (1) Screening tests available at the time could not distinguish between ongoing infection and recovery, and thus, the meaning of a reactive test result for any one individual was not clear; (2) donor screening for antibody to HCV did not include confirmatory testing and most notifications would have been based on false-positive donor test results; (3) there was limited knowledge of routes of transmission for HCV other than parenteral; and (4) no potential long-term benefits of therapy were known.

A significantly more sensitive multiantigen screening test (HCV EIA 2.0 screening test) was licensed in March 1992. In June 1993, FDA licensed an HCV 2.0 strip immunoblot assay (HCV RIBA 2.0), a supplemental (additional, more specific) test for antibody to HCV. Supplemental tests for

antibody to HCV are used to distinguish false positive from true positive repeatedly reactive screening test results. Except for tests available for investigational use, supplemental tests for antibody to HCV have only been available since the HCV RIBA 2.0 supplemental test was licensed in June 1993.

In an August 1993 memorandum to all registered blood establishments entitled ''Revised Recommendations for Testing Whole Blood, Blood Components, Source Plasma and Source Leukocytes for Antibody to Hepatitis C Virus Encoded Antigen (Anti-HCV),'' FDA did not recommend a ''lookback'' program pending the outcome of discussions on the issue at the December 1993 BPAC meeting. Following the discussions on HCV at the meeting in December 1993, BPAC unanimously recommended product quarantine of prior collections from a donor who later tests repeatedly reactive for antibody to HCV and tests positive or indeterminate on a supplemental test, but only marginally endorsed consignee notification for the purpose of transfusion recipient notification, and reiterated many of the reservations regarding the lack of an established public health benefit in performing this activity. FDA issued a memorandum to all registered blood establishments in July 1996 entitled ''Recommendations for the Quarantine and Disposition of Units from Prior Collections from Donors with Repeatedly Reactive Screening Tests for Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), and Human T-Lymphotropic Virus Type I (HTLV–I).'' The July 1996 memorandum recommended testing, consignee notification, and quarantine of affected products but did not provide recommendations for the notification of recipients of such donations because the public health benefit of such notification was not clear.

The Public Health Service Advisory Committee on Blood Safety and Availability (the PHS Advisory Committee) discussed improvements in the treatment and management of HCV infection and improvements in testing for antibody to HCV at public meetings held on April 24 and 25, 1997, and August 11 and 12, 1997. The PHS Advisory Committee also discussed the public health benefits of notification of transfusion recipients receiving prior collections from a donor who subsequently tests repeatedly reactive for evidence of HCV infection. Following acceptance by the Department of Health and Human Services (DHHS) of recommendations for HCV ''lookback'' made in August of 1997 by the PHS Advisory Committee, FDA issued a notice in the **Federal Register** of March 20, 1998 (63 FR 13675), announcing the availability of a document entitled ''Guidance for Industry: Supplemental Testing and the Notification of Consignees of Donor Test Results for Antibody to Hepatitis C Virus (Anti-HCV)'' (the March 1998 guidance) in which FDA recommended that blood establishments implement HCV ''lookback'' procedures. In the March 1998 guidance, FDA recommended that donors currently testing repeatedly reactive for antibody to HCV in a licensed test be further tested for antibody to HCV using a licensed, multiantigen supplemental test. Additionally, FDA recommended that consignees of certain blood and blood components collected since January 1, 1988, which were anti-HCV negative or untested, be notified when donors subsequently test repeatedly reactive for anti-HCV in a licensed multiantigen screening test and reactive in a licensed or investigational supplemental test. This notification would enable recipients to be informed that they had been transfused with units that may have contained HCV so that they may obtain further medical counseling. The March 1998 guidance provided FDA's recommendations for donor screening, a review of past testing records, further testing for antibody to HCV, notification of consignees, and transfusion recipient notification and counseling by physicians regarding transfusion with blood or blood components at increased risk of transmitting HCV. The March 1998 guidance was intended to supplement the July 1996 memorandum.

In response to comments received, the March 1998 guidance was withdrawn on September 8, 1998, and FDA issued a revised guidance on October 21, 1998 (63 FR 56198, October 23, 1998) entitled ''Guidance For Industry: Current Good Manufacturing Practice for Blood and Blood Components: (1) Quarantine and Disposition of Units from Prior Collections from Donors with Repeatedly Reactive Screening Tests for Hepatitis C Virus (HCV); (2) Supplemental Testing, and the Notification of Consignees and Blood Recipients of Donor Test Results for Antibody to HCV (Anti-HCV),'' (the September 1998 guidance). The September 1998 guidance replaced the March 1998 guidance, and provided recommendations to enable quarantine and disposition of blood and blood components from prior collections from donors with repeatedly reactive screening test results. The September 1998 guidance was provided on the CBER Home Page for comment and implementation on September 23, 1999. Additionally, the guidance document was mailed to all blood establishments on November 20, 1998.

The September guidance addressed several significant comments and requests from industry: (1) FDA revised several time periods for ''lookback'' actions in response to concerns about impact on industry, the need for additional time for testing due to availability problems with certain test kits, and to allow time for the physician education to be completed (ensuring that counseling messages would be available for use in notification of recipients); (2) FDA clarified options for further testing with an HCV enzyme linked immunosorbent assay 3.0 (HCV EIA 3.0 screening test); (3) FDA made revisions to clarify recommendations on labeling of products released from quarantine and for consistency with existing regulations on product labeling; (4) FDA provided flow chart diagrams to assist industry in implementing procedures contained in the guidance; and (5) To permit easier, more rapid notification of the recipient, FDA recommended the option of transfusion services notifying the transfusion recipient directly as an alternative to notifying the transfusion recipient's physician of record.

At public meetings on November 24, 1998, and January 28, 1999, the PHS Advisory Committee reconsidered the issue of recipient notification related to repeatedly reactive results on the single antigen screening test. The PHS Advisory Committee recommended that targeted ''lookback'' should be initiated based on a repeatedly reactive HCV EIA 1.0 screening test result on a repeat donor unless a supplemental test was performed and the result did not indicate increased risk of HCV infection, or, in the absence of a supplemental test result, the signal to cut off (S/CO) value of the repeatedly reactive HCV EIA 1.0 screening test was less than 2.5, or follow-up testing of the donor was negative. FDA published a notice in the **Federal Register** of June 22, 1999 (64 FR 33309), announcing the availability of a draft guidance entitled, ''Guidance For Industry: Current Good Manufacturing Practice for Blood and Blood Components: (1) Quarantine and Disposition of Prior Collections from Donors with Repeatedly Reactive Screening Tests for Hepatitis C Virus (HCV); (2) Supplemental Testing, and the Notification of Consignees and Transfusion Recipients of Donor Test Results for Antibody to HCV (Anti-HCV).'' Consistent with the

recommendations of the PHS Advisory Committee, this revised draft guidance addressed ''lookback'' actions related to donor screening by HCV EIA 1.0 and also recommended that the search of historical testing records of prior donations from donors with repeatedly reactive EIA 1.0, EIA 2.0, or EIA 3.0 screening tests for HCV should extend back indefinitely to the extent that electronic or other readily retrievable records exist. In addition, FDA revised the flow chart diagrams to reflect the changes to the guidance. FDA added specific recommendations for prior collections from a repeatedly reactive autologous donor and clarified recommendations on implementing ''lookback'' for repeatedly reactive plasma donations.

Based on comments submitted to the docket, FDA will revise the June 1999 draft guidance and issue a final guidance document for implementation. These comments and comments submitted on any additional guidance issued by the agency in the future will be considered in the preparation of the final rule for HVC ''lookback.''

In addition to these recommendations, FDA is proposing in § 610.40(c) of the testing proposed rule to require ''Each donation found to be repeatedly reactive by a screening test shall be further tested whenever a supplemental (additional, more specific) test has been approved for such use by FDA.''

II. Legal Authority

FDA is proposing to issue this new rule under the authority of sections 351 and 361 of the Public Health Service Act (the PHS Act) (42 U.S.C. 262 and 264 *et seq.*) and the provisions of the Federal Food, Drug, and Cosmetic Act (the act) which apply to drugs (21 U.S.C. 201 *et seq.*). Under section 361 of the PHS Act, FDA may make and enforce regulations necessary to prevent the introduction, transmission, and spread of communicable disease between the States or from foreign countries into the States. (See Sec. I, 1966 Reorg. Plan No. 3 at 42 U.S.C. 202 for delegation of section 361 authority from the Surgeon General to the Secretary, Health and Human Services; see 21 CFR 510(a)(4) for delegation from the Secretary to the Food and Drug Administration.) Intrastate transactions may also be regulated under section 361. (See *Louisiana* v. *Mathew*, 427 F.Supp. 174, 176 (E.D.La. 1977).) A major purpose of the HCV ''lookback'' proposed rule is to prevent the introduction, transmission, and spread of HCV.

All blood and blood components introduced or delivered for introduction into interstate commerce also are subject to section 351 of the PHS Act (42 U.S.C. 262). Section 351(a) requires that manufacturers must have a license which has been issued upon a showing that the manufacturing establishment meets all applicable standards, prescribed in the biologics regulations, designed to insure the continued safety, purity, and potency of the blood and that the product is safe, pure, and potent.

FDA's license revocation regulations provide for the initiation of revocation proceedings, among other reasons, if the establishment or the product fails to conform to the standards in the license application or in the regulations designed to ensure the continued safety, purity, or potency of the product (§ 601.5). Section 351 of the PHS Act also provides for criminal penalties for violation of the laws governing biologics. Violations can be punishable by fines or imprisonment, or both.

The act also applies to biological products (42 U.S.C. 262(d), as amended). Blood and blood components are considered drugs, as that term is defined in section 201(g)(1) of the act (21 U.S.C. 321(g)(1)). (See *United States* v. *Calise*, 217 F.Supp. 705 (S.D.N.Y. 1962)). Because blood and blood components are drugs under the act, blood and plasma establishments must comply with the substantive provisions and related regulatory scheme of the act. Under section 501 of the act (21 U.S.C. 351), drugs are deemed ''adulterated'' if the methods used in their manufacturing, processing, packing or holding do not conform with current good manufacturing practices (CGMP's). Under the proposed HCV ''lookback'' rule, blood and plasma establishments would be required to develop standard operating procedures (SOP's) for HCV ''lookback'' quarantine of affected blood and blood components and consignee and transfusion recipient notification. A blood or plasma establishment that failed to comply with HCV ''lookback'' procedures would violate CGMP's and, therefore, would be subject to the act's enforcement provisions.

III. Highlights of the Proposed Rule

FDA and the Health Care Financing Administration (HCFA) are proposing steps designed to further protect the blood supply and to notify recipients of the possibility that they may have received blood or blood components contaminated with HCV. FDA's proposed rule, along with HCFA's companion proposed rule published elsewhere in this Federal Register, would require facilities involved in the collection, processing, and administration of blood to quarantine certain blood and blood components and to inform the consignee. The consignee, as appropriate, would inform the recipient's attending physician or the recipient, of the possibility that blood previously used for transfusion was obtained from a donor who subsequently tested repeatedly reactive for antibody to HCV. FDA believes that this proposed rule, in conjunction with HCFA's companion proposed rule will provide a more efficient means of notification.

As previously discussed in section I.C of this document, chronic hepatitis due to HCV is a major health problem in the United States because the infection is usually clinically silent, and infected people usually are unaware of their disease until serious damage has been caused to the liver. Although transfusion transmitted HCV infection accounts for only a small proportion of those infected with HCV, it is possible to identify and quarantine affected blood and blood components, perform further testing, and notify some transfusion recipients who have received blood from a donor later determined to be at increased risk of transmission of HCV. This process is commonly referred to as ''lookback.''

FDA is issuing this proposed rule for HCV ''lookback'' as a consequence of numerous public discussions, and extensive discussion within DHHS, of the benefits of notifying recipients of blood at increased risk of transmitting HCV. In parallel to this proposed rule, there will be a major PHS educational campaign on HCV aimed at both the medical community and the public. This proposed rule would establish requirements, similar to those now in effect for HIV ''lookback,'' to identify and quarantine prior collections later suspected as possible window period donations because they were collected from a donor who returned to donate and tested repeatedly reactive for evidence of HCV infection, and to notify transfusion recipients based on further testing of such a donor, as appropriate. In addition to HCV ''lookback'' requirements based on current testing that are similar to those for HIV and that are triggered when a donor returns to donate and tests repeatedly reactive on a screening test, this proposed rule would require a review of historical testing records to identify prior collections from donors at increased risk of transmitting HCV.

The review of historical testing records would extend back indefinitely for computerized electronic records, and to January 1, 1998, for other readily retrievable records.

The requirements for ''lookback'' activity based on multiantigen screening test results are handled in separate sections from those based on single antigen screening test results because the proposed requirements differ. For the purpose of this proposed rule, any reference to ''blood or blood components'' will include Source Leukocytes and Source Plasma unless specifically addressed. The proposal would not require quarantine of products that have already been pooled for further processing because the process of fractionation inactivates or removes the HCV. For the purpose of this proposed rule, any reference to blood establishments will include plasma establishments.

FDA is also proposing conforming amendments to certain provisions of §§ 610.46 and 610.47, the HIV ''lookback'' regulations. The proposed revisions to §§ 610.46 and 610.47 are discussed under the corresponding sections of this proposal and are intended to clarify and provide consistency between the HIV and HCV ''lookback'' requirements.

The proposed HCV ''lookback'' regulations are particular to the testing methodologies currently used. As testing technology continues to develop, the ''window'' period might vary with the testing methodology and FDA may determine that it is necessary to amend the final rule that results from this proposal. In this section III, FDA discusses each of the proposed requirements, the redesignation of certain regulations and revisions to existing requirements.

A. Related Rulemaking

As previously stated, in the **Federal Register** of August 19, 1999 (64 FR 45340), FDA issued, as part of the Blood Initiative, a proposed rule entitled ''Requirements for Testing Human Blood Donors for Evidence of Infection Due to Communicable Disease Agents'' (the testing proposed rule). In the testing proposed rule, FDA proposed to revise the general biological product standards by adding testing requirements for HCV, and by adding requirements for performing a licensed, supplemental test when a donation is found to be repeatedly reactive for any of the required screening tests for evidence of infection due to communicable disease agents. The testing proposed rule would delete § 610.45, ''Human Immunodeficiency Virus (HIV) requirements,'' because its requirements would be included in the revision of proposed § 610.40. The use of the term ''repeatedly reactive'' in this rulemaking is consistent with the testing proposed rule, which states that ''according to the manufacturer's instructions, initially reactive samples are to be tested again, generally in duplicate, and a sample that is found to be reactive on any single retest (i.e., on one or more of the duplicate retests), is considered to be repeatedly reactive.'' Refer to the testing proposed rule for additional discussion of repeatedly reactive test results in section D., Further Testing. In § 610.40(a) and (c) of the testing proposed rule, FDA would revise the requirements for performance of donor screening tests and for supplemental testing of a donor who tests repeatedly reactive for evidence of infection due to a communicable disease agent, including HCV. As discussed in section III.D, this rule proposes that § 610.40(g), include the proposed requirements to initiate HCV ''lookback'' and requirements to initiate HIV ''lookback'' (currently in § 610.45(d), which would be deleted as part of the testing proposed rule). Initiation of the ''lookback'' processes would be based on results of HIV and HCV testing proposed in § 610.40(a) and (c) of the testing proposed rule. (Refer to section III.D of this document for discussion of the proposed changes to § 610.45(d).)

B. Proposed Revisions to § 606.100(b)(19)

FDA is proposing to amend § 606.100(b)(19), which currently prescribes requirements for SOP's, in accordance with §§ 610.46 and 610.47, to look at in-date prior collections from a donor who later tests repeatedly reactive on a required test for HIV, or is otherwise determined to be unsuitable when tested for HIV, and to notify transfusion recipients. FDA is proposing to amend § 606.100(b)(19) to include requirements for blood establishments to have SOP's, in accordance with proposed §§ 610.48 and 610.49, for HCV ''lookback,'' including procedures for quarantine and testing, and notification of transfusion recipients. The revised regulations would require SOP's to look at prior collections from a donor who has donated blood and later tests repeatedly reactive on a required test for HIV or HCV, or when the blood establishment has been made aware of other test results indicating evidence of HIV or HCV infection, and to notify transfusion recipients, if appropriate.

C. Proposed Revisions to § 606.160

FDA is proposing to amend § 606.160. Section 606.160(b)(1)(viii) currently prescribes requirements for maintaining records of quarantine, notification, testing, and disposition performed under §§ 610.46 and 610.47, whenever a donor subsequently tests repeatedly reactive for evidence of HIV infection. FDA is proposing to revise § 606.160(b)(1)(viii), to include requirements for maintaining records of quarantine, notification, testing, and disposition performed under proposed §§ 610.48 and 610.49, whenever a donor subsequently tests repeatedly reactive for evidence of HCV infection.

Section 606.160(d) currently prescribes that the retention period for required processing records shall be no less than 5 years after completion of the record or 6 months after the latest expiration date for the individual product, whichever is a later date. FDA is proposing to revise § 606.160(d) by increasing the required retention period to no less than 10 years after the records of processing have been completed, or 6 months after the latest expiration date for the individual product, whichever is a later date. FDA is proposing this change in the retention period because advances in medical diagnosis and therapy have created opportunities for disease prevention or treatment many years after recipient exposure to a donor later determined to be at increased risk of transfusion transmitted disease. Additionally, methods of recordkeeping have advanced, improving the ability of blood establishments to more easily maintain and retrieve records.

D. Proposed Revisions to § 610.45

As previously discussed, in the **Federal Register** of August 19, 1999 (64 FR 45340), FDA issued a proposed rule to revise § 610.40, and to delete § 610.45, ''Human Immunodeficiency Virus (HIV) requirements,'' because, except as discussed below, the requirements of § 610.45 would be included in proposed § 610.40.

Section 610.45(d) currently requires blood establishments to comply with §§ 610.46 and 610.47, the HIV ''lookback'' requirements for quarantine, consignee notification, further testing and transfusion recipient notification, when applicable, whenever a donor's ''test results for antibody to HIV are repeatedly reactive or otherwise determined to be unsuitable when tested in accordance with paragraph (a) of this section * * *.'' As previously discussed in section III.A of this document, the testing proposed rule would delete § 610.45. This proposed rule would include the requirements of current § 610.45(d) into proposed § 610.40(g). Proposed § 610.40(g) would require blood establishments to comply with §§ 610.46 and 610.47, and with proposed §§ 610.48 and 610.49, thereby requiring compliance with the HIV and

HCV ''lookback'' regulations, respectively.

E. Proposed Revisions to Headings of §§ 610.46 and 610.47

As a result of the addition of HCV ''lookback'' requirements, FDA is proposing to revise the headings of the sections applicable to the ''lookback'' requirements for HIV. FDA is proposing to revise the heading of § 610.46 to read ''Human Immunodeficiency Virus (HIV) 'Lookback;' quarantine, consignee notification and further testing'' to distinguish it from the new § 610.48, ''Hepatitis C Virus (HCV) '''lookback;''' quarantine, consignee notification and further testing.'' Likewise, FDA is proposing to amend the heading of § 610.47, ''Lookback'' Notification requirements for transfusion services,'' to read ''Human Immunodeficiency Virus (HIV) ''Lookback;'' notification of transfusion recipients'' to distinguish it from the new § 610.49, ''Hepatitis C Virus (HCV) ''Lookback;'' notification of transfusion recipients.'' As previously noted, FDA is proposing to amend § 610.46 for consistency with proposed § 610.48 of this proposed rule, and to amend § 610.47 for consistency with § 610.49 of this proposed rule. The corresponding revisions to § 610.46 and to § 610.47 are noted in the discussion of proposed § 610.48 and proposed § 610.49.

F. Proposed § 610.48(a), Quarantine and Consignee Notification

Proposed § 610.48(a) identifies the circumstances that would trigger the ''lookback'' process when a donor returns to donate and tests repeatedly reactive on a screening test, and states the requirements for quarantine of blood and blood components, notification of consignees, and quarantine of blood and blood components by consignees. Under proposed § 610.48(a)(1), blood establishments would be required to take appropriate action within 3-calendar days after the date on which a donor returns to donate blood or blood components and tests repeatedly reactive for evidence of HCV infection on a required test, performed in accordance with proposed § 610.40(a), or the date on which the blood establishment was made aware of other test results indicating evidence of HCV infection, provided the testing was performed by a laboratory certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), using a test approved by FDA. In the testing proposed rule (64 FR 45340, August 19, 1999) proposed § 610.40(a) requires tests for specified communicable disease agents, including for HCV, and requirements for further testing of repeatedly reactive samples. For example, a blood establishment completing a screening test on Tuesday afternoon with a repeatedly reactive test result would have until the end of the day on Friday to complete the requirements for quarantine and consignee notification.

FDA is specifically requesting comments on the appropriateness of 3 calendar days proposed for exemptions of the quarantine of prior collections and consignee notification under proposed §§ 10.48(a), (e), and (f) and the conforming amendment to 610.46(a). FDA is also proposing that the ''lookback'' measures specified in § 610.48(a) be initiated by a blood establishment upon receipt of information that a person who has been a donor at that establishment has other test results indicating evidence of HCV infection and that the test was performed by a CLIA-certified laboratory, using a test approved by FDA, regardless of the purpose of the testing. FDA recognizes that blood establishments do not routinely receive such information, but should a blood establishment become aware of such reliable test results, the proposal would require appropriate ''lookback'' measures. State laws and public health practices vary widely, making it impossible to specify all circumstances under which test results may be provided to the blood establishment. However, FDA believes that the blood establishment has the obligation, upon the receipt of such reliable test results, to initiate appropriate action to protect the blood and plasma supply. In addition, the reliability of test results may vary, depending on the quality of the test method used and on the qualifications of the testing facility to perform the test. Accordingly, FDA is proposing to require the initiation of ''lookback'' procedures when the test results originate from a laboratory certified under CLIA and when the laboratory has used FDA-approved tests.

Proposed § 610.48(a) would require blood establishments and their consignees to identify and quarantine all affected blood and blood components collected prior to the donor's repeatedly reactive screening test for HCV. Under proposed § 606.160(d), blood establishments would retain records for ''* * * no less than 10 years * * *'' or, for products that remain in inventory, for 6 months after the latest expiration date of the product, whichever is the later date, and under proposed § 610.48(a) blood establishments would quarantine any in-date prior collections that remain in inventory. If the blood establishment has information to assure that there are no in-date prior collections, there is no need to trace those products.

Proposed § 610.48(a)(1)(i) would require blood establishments to quarantine all in-date prior collections from a donor testing repeatedly reactive for evidence of HCV infection. Proposed § 610.48(a)(1)(ii) would require blood establishments to notify consignees of the repeatedly reactive HCV screening test result so that the consignee may quarantine all in-date prior collections of blood and blood components. Proposed § 610.48(a)(2) would require consignees to quarantine all in-date prior collections of blood and blood components that remain in inventory.

For consistency, FDA is also proposing conforming amendments to the corresponding HIV ''lookback'' requirements of § 610.46(a). FDA is proposing to amend § 610.46(a) by changing the title of the paragraph to ''Quarantine and consignee notification'' and to clarify that blood establishments would be required to complete the quarantine and consignee notification requirements within 3-calendar days after the date on which the donor tests repeatedly reactive for evidence of HIV infection. FDA is proposing to replace the phrase ''or otherwise determined to be unsuitable when tested in accordance with § 610.45'' with ''or when the blood establishment has been made aware of other test results indicating evidence of HIV infection, provided the testing was performed by a laboratory certified under the Clinical Laboratory Improvement Amendments of 1988, using a test approved by FDA'' to eliminate any confusion that might be caused by different wording. Likewise, for clarity and consistency, FDA is proposing to replace ''For Whole Blood, blood components, Source Plasma and Source Leukocytes collected from that donor within the 5 years prior to the repeatedly reactive test, if intended for transfusion, or collected within the 6 months prior to the repeatedly reactive test, if intended for further manufacture into injectable products, * * *.'' with ''For in-date blood and blood components collected from that donor at any time prior to the repeatedly reactive test, whenever records are available, if intended for transfusion or for further manufacture into injectable products, * * *.'' Also, FDA recognizes that it is not necessary for ''lookback'' requirements to distinguish collections intended for transfusion from those intended for further manufacturing. FDA is clarifying that ''lookback'' requirements should be followed for any

prior collection that has not expired because records are held for 6 months after the latest expiration date of the individual product.

G. Proposed § 610.48(b), Further Testing and Consignee Notification of Results

Proposed § 610.48(b) would require further testing whenever a donor returns to donate and tests repeatedly reactive for evidence of HCV infection, as described in § 610.48(a), and notification of consignees of the results of the further testing. Proposed § 610.48(b) would require blood establishments to perform further testing, in accordance with proposed § 610.40(c) of the testing proposed rule (as previously discussed), after a donor with a record of prior collections tests repeatedly reactive for evidence of HCV infection when tested in accordance with proposed § 610.40(a) of the testing proposed rule. Blood establishments would be required to notify consignees of the results of the further testing within 45-calendar days after the day on which the donor tests repeatedly reactive on a screening test for evidence of HCV infection.

FDA is proposing a conforming amendment to § 610.46(b) for HIV ''lookback'' by changing the maximum time provided for a blood establishment to notify consignees of the results of the further testing from 30 to 45 days. This change is proposed for consistency between the HIV and HCV ''lookback'' regulations and in response to comments that although further testing for HIV and HCV can be completed within 30 days, additional time is needed to notify consignees following completion of the further testing.

H. Proposed § 610.48(c), Review of Historical Testing Records and Identification of Donors Tested Using a Multiantigen Screening Test Prior to the Effective Date of this Regulation

As discussed in section I.C of this document in this preamble, blood establishments routinely have been testing blood donations for antibody to HCV since 1990. In the guidance documents issued in March 1998, September 1998 and June 1999, FDA issued recommendations (draft guidance was issued in June 1999) for blood establishments to initiate ''lookback'' procedures consistent with those now being proposed, including when, through a review of historical testing records, previous instances are identified when a donor had tested repeatedly reactive on a multiantigen screening test for evidence of HCV infection. FDA believes that since 1990, many blood establishments have routinely initiated ''lookback'' procedures consistent with the regulations now being proposed, and with the issuance of the recommendations in 1998 and 1999, many additional establishments have undertaken the review of historical testing records and have initiated appropriate ''lookback'' procedures. However, because HCV is a chronic, often asymptomatic disease that may ultimately have serious consequences, FDA believes that it is imperative to identify and notify recipients who have been transfused with blood or blood components for which there is an increased risk of transmission of HCV as determined by subsequent donor testing. Such transfusion recipients should be made aware that they should seek further testing to see if they are infected and, if so, to receive appropriate counseling and medical care.

The requirements of proposed § 610.48(c) and (d) are based on the agency's understanding of current research in hepatitis testing. FDA specifically invites comments on these provisions and requests individuals to submit data in support of the comments. To the extent the data do not support these provisions, FDA would revise the rule accordingly. FDA recognizes that the review of historical testing records (performed in accordance with proposed § 610.48(c) and (d)) will identify tests performed using both licensed and unlicensed tests, HCV EIA 1.0, 2.0, and 3.0, as well as, HCV RIBA 2.0 and 3.0 supplemental tests. For that reason, the proposed requirements for testing performed prior to the effective date of any final rule resulting from this proposal (that is, test results identified in the review of historical testing records) would take into account the use of unlicensed tests, under specific circumstances. In addition, testing performed following the effective date of any final rule resulting from this proposal (such as further testing performed in accordance with proposed § 610.48(h) or (i)) would require use of a currently licensed test, as specified.

The purpose of § 610.48(c) is to identify, through a search of available historical testing records, those prior collections that might have been collected during the window period, that is, a donation that may have been made after the donor became infected with HCV but before it was possible for a screening test to detect antibody to HCV. The identification of prior collections would be based on the multiantigen screening test result and would be followed by appropriate steps to perform quarantine, further testing and notification of consignees and transfusion recipients, as discussed in detail in this and other sections of this proposed rule. Blood establishments would be required to perform a review of historical testing records to identify, within 1 year of the effective date of any final rule resulting from this proposal, prior collections at increased risk of transmitting HCV infection because they are from a donor who later tested repeatedly reactive for evidence of HCV infection on a multiantigen screening test and who either: (1) Has no record of further testing for HCV performed on the repeatedly reactive sample and no record of a negative licensed, multiantigen screening test performed at a later date (as specified in § 610.48(c)(4) and (c)(5); or (2) has a record of further testing (as specified in § 610.48(c)(1), (c)(2), and (c)(3)) that potentially indicates evidence of HCV infection, as discussed in detail later in this proposed rule. As discussed in the following paragraph, after the review of historical testing records, ''lookback'' actions would be triggered for certain prior collections. Blood establishments would be required to quarantine any in-date prior collections still in inventory where records show that they were collected from donors later found to have a repeatedly reactive multiantigen screening test for evidence of HCV infection (unless exempt from quarantine under § 610.48(g)(2)), and to notify consignees to quarantine such prior collections, as specified under proposed § 610.48(e)(2); to perform further testing, as specified in proposed § 610.48(h)(1), on donors identified in accordance with proposed § 610.48(c)(4) and (c)(5); or optionally to perform further testing in accordance with § 610.48(h)(2) on donors identified in accordance with § 610.48(c)(2) and (c)(3); and to notify consignees of the test result, in accordance with proposed § 610.48(h)(3), as described in the following paragraph. Transfusion services notified by blood establishments of prior receipt of blood or blood components at increased risk of transmitting HCV would either notify the transfusion recipients directly or notify the recipient's physician of record (i.e., physician of record or physician who ordered the blood or blood component), as specified in proposed § 610.49(b).

Under proposed § 610.48(c), the review would include records, if available, dating back indefinitely for computerized electronic records, and to January 1988 for other readily retrievable records, or 12 months prior to the donor's most recent negative

multiantigen screening test for antibody to HCV, whichever is the lesser period. This 12-month time period requirement is intended to identify any potential ''window period'' donation. Review of historical testing records dating back indefinitely would not be necessary for prior collections from many donors (i.e., prior collections from donors who have a record of a prior negative multiantigen screening test result because the prior collections would not be considered to be window period donations.) Examples are provided in the following paragraph. In addition, many donors who test repeatedly reactive for evidence of HCV infection are first-time donors with no previous history of donation. Thus, no ''lookback'' action is needed for such a first-time donor because ''lookback'' activity targets prior collections and no prior collections exist for a first time donor.

Proposed § 610.48(c) would limit the review of records to the identification of prior collections dating back to ''the date 12 months prior to the donor's most recent negative multiantigen screening test for HCV.'' FDA believes that this 12-month period prior to the last negative multiantigen screening test for HCV establishes with high confidence that, prior to that date, possible HCV infection would have been detected by a screening test; if any ''window period'' donation was collected, it would have occurred after that date. For example, it would not be necessary to identify collections dating back indefinitely for a donor who has donated every 6 months from January 1983 until testing repeatedly reactive on a screening test for evidence of HCV infection in January 1998, with the last negative multiantigen screening test on July 1, 1997. In this example, the last negative multiantigen screening test for antibody to HCV is July 1, 1997, and 12 months prior to that would be July 2, 1996. Under the proposal, the blood establishment would use the later date of July 2, 1996 (rather than the maximum time period back to January 1983), and the blood establishment would identify donations made on or after July 2, 1996, to July 1, 1997, as possible ''window period'' donations. In this example, donations made prior to July 2, 1996, would not be suspected to be ''window period'' donations, capable of transmitting HCV infection to a transfusion recipient. Note that a negative test result on a single antigen EIA screening test for HCV may not be used as the ''most recent negative multiantigen screening test'' and is not a basis to limit the ''lookback'' activity, as described previously, due to the limited sensitivity of the single antigen HCV EIA test.

FDA is proposing the review of historical testing records to identify five specific instances following a repeatedly reactive multiantigen screening test that should be used to identify increased risk of transmitting HCV from the donor's prior collections. Under § 610.48(c), blood establishments would identify prior collections from donors who tested repeatedly reactive for evidence of HCV infection on a licensed, multiantigen screening test and who: (1) Tested positive on a supplemental test for HCV performed on the repeatedly reactive sample (as specified in § 610.48(c)(1)); or (c)(2) tested indeterminate on a supplemental test for HCV (as specified in § 610.48(c)(2)); or (c)(3) testing repeatedly reactive on licensed HCV EIA 3.0 screening test and negative on a licensed HCV RIBA 2.0 supplemental test but with no records of a negative licensed HCV RIBA 3.0 supplemental test performed on the repeatedly reactive sample or a later sample from the same donor; or (4) tested repeatedly reactive for evidence of HCV infection on an HCV EIA 2.0 screening test with no record of a supplemental test for HCV performed on the repeatedly reactive sample or on a later sample from the donor and no record of a negative licensed HCV EIA 3.0 screening test performed on the repeatedly reactive sample or later on the same donor; or (5) tested repeatedly reactive for evidence of HCV infection on a licensed, HCV EIA 3.0 screening test with no record of a supplemental test for HCV performed on the repeatedly reactive sample or on a later sample from the same donor. As discussed previously, the requirements of proposed § 610.48(c) for review of historical testing records to identify prior collections from affected donors are particular to the testing methods used and exceptions are specified in § 610.48(g), Exemption from Quarantine. Prior collections that would not be identified as possible ''window period'' donations and would not require further action are exempted from quarantine as described in § 610.48(g)(2). For donors identified in accordance with § 610.48(c)(4) and (c)(5) for whom no records of further testing exist to clarify the status of prior collections determined to be at increased risk of transmitting HCV infection, blood establishments would be required, as described under proposed § 610.48(e), to perform quarantine and consignee notification for any in-date prior collections that remain in inventory and to perform further testing, as described under proposed § 610.48(h)(1).

I. Proposed § 610.48(d), Review of Records and Identification of Donors Testing Repeatedly Reactive on a Single Antigen Screening Test Prior to the Effective Date of this Regulation

The purpose of § 610.48(d), which parallels the requirements of § 610.48(c), is to identify, through a review of historical testing records, those prior collections that might have been collected during the window period of HCV infection, based on a single antigen screening test result. Similar to the requirements of § 610.48(c), which is based on the multiantigen screening test, proposed § 610.48(d) would: (1) Require blood establishments to review available historical records of donor testing that occurred prior to the effective date of this regulation to identify prior collections that are potential window period donations; (2) require the review of available historical testing records dating back indefinitely for computerized electronic records and to January 1988 for other readily retrievable records; and (3) require that blood establishments complete the review or historical testing records within 1 year of the effective date of any final rule that results from this proposal.

Under § 610.48(d), blood establishments would identify previously distributed blood and blood components in any of the following four instances: (1) As proposed in § 610.48(d)(1), where the donor tested repeatedly reactive for evidence of HCV infection on the single antigen screening test and repeatedly reactive on an HCV EIA 2.0 or HCV EIA 3.0 screening test for HCV performed on the repeatedly reactive sample or a fresh sample from the same donor; (2) as proposed in § 610.48(d)(2), where the donor tested repeatedly reactive for evidence of HCV infection on the single antigen screening test and either positive or indeterminate on an HCV 2.0 or HCV 3.0 strip immunoblot assay (HCV RIBA 2.0 or HCV RIBA 3.0 supplemental test, respectively) supplemental test for HCV; or (3) as proposed in § 610.48(d)(3), where the donor tested repeatedly reactive for evidence of HCV infection on an HCV EIA 1.0 screening test, with a signal to cut off (S/CO) value less than 2.5 for at least two out of the three EIA tests (i.e., the initial EIA screening test and the duplicate retests) with no record of a supplemental test or multiantigen screening test for HCV performed on the repeatedly reactive sample or on a later sample from the same donor ; or (4) as proposed in § 610.48(d)(4), where the donor tested repeatedly reactive for

evidence of HCV infection on an HCV EIA 1.0 screening test, with a S/CO value equal to or greater than 2.5 for at least two out of the three EIA tests or with no determination of S/CO value for all three EIA tests, and with no record of a supplemental test or multiantigen screening test for HCV performed on the repeatedly reactive sample or on a later sample from the same donor. (The S/CO value for each test result is calculated as the ratio of the absorbency value obtained for the donor sample divided by the absorbency value for the cutoff in that assay run.)

As previously discussed in section I.C of this document, the PHS Advisory Committee met on January 28, 1999, to consider options for expanding the targeted HCV ''lookback'' program to include recipients of blood from donors subsequently identified as repeatedly reactive by the single antigen HCV EIA 1.0 screening test. Approximately 80 percent of the HCV EIA 1.0 repeatedly reactive donations were identified before the first confirmatory test became available. The PHS Advisory Committee concluded that it would be reasonable to limit the ''lookback'' for EIA 1.0 based on the S/CO value of the screening tests in cases where supplemental testing had not been done and further testing of the original repeatedly reactive sample or a later sample from the same donor was impractical. The PHS Advisory Committee concluded that it would be appropriate to perform HCV ''lookback'' on a subset of the donors testing repeatedly reactive on EIA 1.0 screening tests to capture the vast majority of the true positives and minimize the unnecessary false recipient notifications. The requirements proposed in § 610.48(d) and (i) reflect the PHS Advisory Committee's recommendations for use of the S/CO value based on a critical ratio of 2.5 in evaluating risk of HCV transmission under ''lookback'' circumstances identified in the review of historical testing records.

As discussed previously, the requirements of proposed § 610.48(d) for review of historical testing records to identify prior collections from affected donors are particular to the testing methods used and exceptions are specified in § 610.48(g), Exemption from quarantine. Prior collections that would not be identified as possible ''window period'' donations and would not require further action are exempted from quarantine as described in § 610.48(g)(3).

J. Proposed § 610.48(e), Quarantine and Consignee Notification Following the Review of Historical Testing Records Based on Screening Performed Using a Multiantigen Screening Test

The purpose of proposed § 610.48(e) is to require quarantine of prior collections that were identified in the review of historical testing records, based on a multiantigen screening test in accordance with proposed § 610.48(c), until further testing is completed, if necessary, and the blood establishment can make a determination to release the prior collections from quarantine (under proposed § 610.48(j)(2)), or to destroy or relabel them (under proposed § 610.48(k)). Proposed § 610.48(e) would require blood establishments to quarantine certain prior collections until further testing is completed to clarify the status of the prior collections, and to notify consignees so that prior collections they hold can be quarantined. This requirement is intended to prevent the transfusion of a prior collection from a donor identified in the review of records as being at increased risk of transmitting HCV infection while further testing is performed.

Proposed § 610.48(e)(1) would require blood establishments to quarantine in-date prior collections of blood and blood components collected from donors identified in the review of records, under proposed § 610.48(c), while further testing is performed, as required in proposed § 610.48(h)(1) or as optional testing is performed in accordance with § 610.48(h)(2).

As previously mentioned, some exceptions to quarantine are specified in proposed § 610.48(g)(2). Prior collections that meet the criteria under proposed § 610.48(g)(2) would not be suspected as ''window period'' donations and would be exempt from quarantine, as discussed in following sections. If no exemption to quarantine applies, blood establishments would be required to perform quarantine within 3 days of the date on which the establishment identifies a donor's repeatedly reactive multiantigen screening test. All identification performed in accordance with § 610.48(c) and the resulting quarantine and notification must be completed within a maximum of 1 year from the effective date of any final rule resulting from this proposal.

Proposed § 610.48(e)(2) would require blood establishments, within 3-calendar days of the date on which the donor's repeatedly reactive multiantigen screening test is identified, to notify consignees of the donor's test results, including supplemental test results, if available, so that consignees may quarantine all in-date prior collections of blood and blood components subject to quarantine under proposed § 610.48(e)(1). FDA is specifically requesting comments on the appropriateness of the 1-year timeframe to complete all quarantine and notification.

K. Proposed § 610.48(f), Quarantine and Consignee Notification Following the Review of Records Based on Screening Performed Using a Single Antigen Screening Test

The purpose of § 610.48(f), which parallels the requirements of § 610.48(e), is to require quarantine of prior collections that were identified in the review of historical testing records based on single antigen testing, in accordance with proposed § 610.48(d), until further testing is completed, if necessary, and a determination can be made to release the prior collections from quarantine (under proposed § 610.48(j)(3)), or to destroy or relabel them (under proposed § 610.48(k)). Proposed § 610.48(f) would require blood establishments to quarantine certain prior collections until further testing is completed to clarify the status of the prior collections, and to notify consignees so that prior collections they hold can be quarantined. This requirement is intended to prevent the transfusion of a prior collection from a donor identified in the review of records as being at increased risk of transmitting HCV infection while further testing is performed.

Proposed § 610.48(f)(1) would require blood establishments to quarantine in-date prior collections of blood and blood components from donors identified in the review of historical testing records, under proposed § 610.48(d), while further testing is performed, as required in proposed § 610.48(i)(1) or as optional testing is performed in accordance with § 610.48(i)(2).

Under this proposal, blood establishments would be required to perform quarantine within 3 calendar days of the date on which the blood establishment identifies a donor's repeatedly reactive single antigen screening test. All identification performed in accordance with § 610.48(d) and the resulting quarantine and notification must be completed within a maximum of 1 year from the effective date of any final rule resulting from this proposal. As previously mentioned, some exceptions to quarantine are specified in proposed § 610.48(g)(3). Prior collections that

meet the criteria under proposed § 610.48(g)(3) would not be suspected as ''window period'' donations and would, therefore, be exempt from quarantine, as discussed in following sections.

Proposed § 610.48(f)(2) would require blood establishments, within 3-calendar days of the date on which the donor's repeatedly reactive single antigen screening test is identified, to notify consignees of the donor's test results, including supplemental test results, if available, so that consignees may quarantine all in-date prior collections of blood and blood components subject to quarantine under proposed § 610.48(f)(1). FDA is specifically requesting comments on the appropriateness of 3-calendar days proposed for completion of the quarantine of prior collections and consignee notification under § 610.48(f) and the appropriateness of the 1-year timeframe to complete all quarantine and notification.

Proposed § 610.48(f)(3) would require consignees notified in accordance with proposed § 610.48(f)(2) to quarantine all prior collections of blood and blood components subject to quarantine under proposed § 610.48(f)(1), except as provided in proposed § 610.48(g)(3).

L. Proposed § 610.48(g), Exemption From Quarantine

Proposed § 610.48(g) specifies which prior collections are not suspected as being window period donations and, therefore, are not subject to quarantine under proposed § 610.48(a), (e), and (f). Proposed § 610.48(g)(1) would exempt from quarantine certain prior collections otherwise subject to quarantine under proposed § 610.48(a) when a donor tests repeatedly reactive on a multiantigen screening test for evidence of HCV infection. Proposed § 610.48(g)(1)(i) is intended to identify certain donations that are not suspected of being collected during the ''window period'' because they were collected prior to the time a possible window period could have existed, and would not be subject to quarantine under proposed § 610.48(a). Under proposed § 610.48(g)(1)(i), for donations collected more than 12 months prior to the donor's most recent negative multiantigen screening test, a high confidence level exists that no infection could have existed at the time of donation and remain undetected by a screening test, and, therefore, blood establishments would not be required to quarantine blood or blood components ''collected more than 12 months prior to the donor's most recent negative multiantigen screening test when tested for HCV in accordance with § 610.40(a). An explanation of ''window period'' donations and a corresponding example are provided previously in the description of proposed § 610.48(c).

In addition, proposed § 610.48(g)(1)(ii) would provide that when an appropriate licensed supplemental test for HCV (discussed in this section III.L) is found to be negative and is completed within the 3-day time period provided for completion of quarantine and consignee notification, quarantining of prior collections of blood and blood components from that donor would not be required. Thus, if the supplemental test is found negative within 3-calendar days after the date on which the donor tested repeatedly reactive for evidence of HCV infection (the time provided for completion of quarantine and consignee notification), then the repeatedly reactive screening test result would be interpreted as a ''false positive,'' would not indicate HCV infection, and prior collections from that donor would not be considered to be at increased risk of transmitting HCV. If, however, the supplemental testing is completed more than 3 days after the date of the repeatedly reactive screening test result (the time provided for completion of quarantine and consignee notification), the blood and blood components would be quarantined but could then be released from quarantine if the supplemental test is negative, as provided in proposed § 610.48(j).

As specified in proposed § 610.48(g), the supplemental test must be appropriately chosen, i.e., the appropriately chosen supplemental test should contain all the antigens of the screening test that was performed. Under proposed § 610.48(g)(1)(ii), if the repeatedly reactive screening test was obtained using an HCV EIA 2.0 screening test, then an appropriate supplemental test would be either an HCV RIBA 2.0 or an HCV RIBA 3.0. However, if the repeatedly reactive screening test result was obtained using an HCV EIA 3.0 screening test, then the appropriate supplemental test would be an HCV RIBA 3.0. The HCV RIBA 2.0 supplemental test would not be an appropriately chosen supplemental test following an HCV EIA 3.0 screening test because the HCV RIBA 2.0 supplemental test does not include all antigens contained in the HCV EIA 3.0 screening test.

Proposed § 610.48(g)(2) provides for exceptions from quarantine performed in accordance with proposed § 610.48(e) following the review of historical testing records based on screening performed using a multiantigen screening test. Similar to the provisions of proposed § 610.48(g)(1), proposed § 610.48(g)(2) is intended to exempt from quarantine those prior collections that are not suspected as being collected during the ''window period.'' Under proposed § 610.48(g)(2), prior collections of blood and blood components would not be subject to quarantine under proposed § 610.48(e) if they meet any of the following criteria: (1) The prior collection was donated more than 12 months prior to the donor's most recent negative multiantigen screening test for evidence of HCV infection that preceded the repeatedly reactive screening test; or (2) records show that the repeatedly reactive screening test result was obtained using an HCV EIA 2.0 screening test, and either the original sample or a later sample from the same donor was tested and found negative using an HCV RIBA 2.0, or an HCV RIBA 3.0 supplemental test or an HCV EIA 3.0 screening test. (As previously discussed, a negative test result on a single antigen EIA screening test for HCV may not be used as the ''most recent negative multiantigen screening test'' and is not a basis to limit the ''lookback'' activity, as described previously, due to the limited sensitivity of the HCV EIA 1.0 screening test); or (3) records show that the repeatedly reactive screening test result was obtained using an HCV EIA 3.0 screening test, and either the original sample or a later sample from the same donor was tested and found negative using an HCV RIBA 3.0 supplemental test.

Proposed § 610.48(g)(3) provides for exceptions from quarantine (performed in accordance with proposed § 610.48(f)) following the review of records based on screening performed using a single antigen screening test. Similar to the provisions of proposed § 610.48(g)(1) and (g)(2), proposed § 610.48(g)(3) is intended to exempt from quarantine those prior collections that are not suspected as being collected during the ''window period.'' Under proposed § 610.48(g)(3), prior collections of blood and blood components would not be subject to quarantine under proposed § 610.48(f) if they meet any of the following four criteria: (1) Records show that the repeatedly reactive screening test result was obtained using an HCV EIA 1.0 screening test, and either the original sample or a later sample from the same donor was tested and found negative using an HCV EIA 2.0 or an HCV EIA 3.0 screening test (exempted under proposed § 610.48(g)(3)(i)); or (2) records show that the repeatedly reactive screening test result was obtained using an HCV EIA 1.0

screening test, and either the original sample or a later sample from the same donor was tested and found negative using a HCV RIBA 2.0 or a HCV RIBA 3.0 supplemental test (exempted under proposed § 610.48(g)(3)(ii)); or (3) the donor identified in accordance with proposed § 610.48(d)(1), as testing repeatedly reactive on an HCV EIA 2.0 or 3.0 screening test, was further tested using an HCV RIBA 2.0 or HCV RIBA 3.0 supplemental test, using a fresh sample, or frozen sample from the repeatedly reactive donation and the result was negative (exempted under § 610.48(g)(3)(iii)); or (4) the donor identified in accordance with proposed § 610.48(d)(2), as testing indeterminate on an HCV RIBA 2.0 supplemental test, was further tested using either an HCV EIA 3.0 or a HCV RIBA 3.0 supplemental test using a fresh sample, or frozen sample from the repeatedly reactive donation and the result was negative (exempted under proposed § 610.48(g)(3)(iv)).

FDA is also proposing a conforming amendment to § 610.46(c), which specifies requirements for exemption from quarantine for HIV ''lookback,'' for consistency with the HCV ''lookback'' requirements by changing ''Whole Blood, blood components, Source Plasma and Source Leukocytes'' to ''blood and blood components.''

M. Proposed § 610.48(h), Further Testing Following Review of Historical Testing Records and Consignee Notification Based on Screening Performed Using a Multiantigen Screening Test

Proposed § 610.48(h) is intended to require that prior collections identified in accordance with § 610.48(c)(4) and (c)(5), based on multiantigen screening test results, either be further tested and consignees notified so that blood establishments can determine if the prior collection should be released from quarantine (under § 610.48(j)), or destroyed or relabeled (under § 610.48(k)), and if notification of transfusion recipients is necessary (under § 610.49(a)). In addition, blood establishments would have the option to perform further testing for prior collections identified in accordance with § 610.48(c)(2) and (c)(3). Proposed § 610.48(h)(1) would require blood establishments, by 1 year from the effective date of any final rule resulting from this proposal, to perform further testing to clarify the status of prior collections collected from a donor identified, in accordance with § 610.48(c)(4) and (c)(5), as being at increased risk of transmitting HCV. Proposed § 610.48(h)(1) would require that further testing be performed as follows: (1) As proposed in § 610.48(h)(1)(i)(A), if the repeatedly reactive test result was obtained using a licensed HCV EIA 2.0 screening test, blood establishments would perform a licensed supplemental test for HCV on a frozen sample from the repeatedly reactive donation, if it is available. If such a frozen sample is not available, blood establishments would obtain a fresh sample from the donor and perform a licensed supplemental test for HCV; or alternatively, (2) as proposed in § 610.48(h)(1)(i)(B), if the repeatedly reactive test result was obtained using a licensed HCV EIA 2.0 screening test, blood establishments would perform a licensed HCV EIA 3.0 screening test on a frozen sample, if it is available. If such a frozen sample is not available, blood establishments would obtain a fresh sample from the donor and perform a licensed HCV EIA 3.0 screening test and a licensed supplemental test if the HCV EIA 3.0 screening test is repeatedly reactive; or (3) as proposed in § 610.48(h)(1)(ii), if the repeatedly reactive test result was obtained using a licensed HCV EIA 3.0 screening test, blood establishments would perform a licensed supplemental test for HCV on a frozen sample, if available. If such a frozen sample is not available, blood establishments would obtain a fresh sample from the donor and perform a licensed supplemental test for HCV; or (4) as proposed in § 610.48(h)(1)(iii), blood establishments would make a determination that neither a frozen sample from the repeatedly reactive donation nor a fresh sample from the donor is available for further testing. For example, the blood establishment might make a determination that additional testing is not possible because the sample was not stored properly, or the donor could not be located or the donor declined further testing.

Under proposed § 610.48(h)(2), blood establishments would have the option to perform further testing on prior collections identified in accordance with § 610.48(c)(2) and (c)(3). This provision would make it possible to clarify the status of the prior collections and, in some instances, based on further testing, it might not be necessary to destroy the prior collections or notify transfusion recipients. Under proposed § 610.48(h)(2), blood establishments that have performed the review of records and identified prior collections in accordance with proposed § 610.48(c)(2) or (c)(3) of this section may further test a frozen sample from the repeatedly reactive donations or a fresh sample from the same donor by 1 year from the effective date of any final rule resulting from this proposal, as follows: (1) As proposed in § 610.48(h)(2)(i), if the donor was identified in accordance with proposed § 610.48(c)(2) of this section as testing repeatedly reactive using an HCV EIA 2.0 screening test, and indeterminate on a HCV RIBA 2.0 supplemental test, blood establishments have the option to perform further testing using either an HCV EIA 3.0 screening test or a currently available licensed supplemental test for HCV; or (2) as proposed in § 610.48(h)(2)(ii), if the donor was identified in accordance with proposed § 610.48 (c)(2) of this section as testing repeatedly reactive using an HCV EIA 2.0 screening test, indeterminate on a HCV RIBA 2.0 supplemental test, and repeatedly reactive on an HCV EIA 3.0 screening test, blood establishments have the option to perform further testing using an appropriately chosen licensed supplemental test for HCV (refer to section L of this document that discusses proposed § 610.48(g) for more information regarding use of ''an appropriately chosen supplemental test''); or (3) as proposed in § 610.48(h)(2)(iii), if the donor was identified in accordance with (c)(2) of this section as testing repeatedly reactive using an HCV EIA 3.0 screening test, and indeterminate on a HCV RIBA 2.0 supplemental test, blood establishments have the option to perform further testing using an appropriately chosen licensed supplemental test for HCV; or (4) as proposed in § 610.48(h)(2)(iv), if the donor was identified in accordance with proposed § 610.48 (c)(3) of this section as testing repeatedly reactive using an HCV EIA 3.0 screening test, and negative on a HCV RIBA 2.0 supplemental test, blood establishments have the option to perform further testing using an appropriately chosen licensed supplemental test for HCV. Based on the results of the further testing, the blood establishment can make a decision regarding the next appropriate step under proposed § 610.48(j), to release from quarantine, or under proposed § 610.48(k), to destroy or appropriately label prior collections, or under proposed § 610.49(a), to notify any transfusion recipients.

Under proposed § 610.48(h)(3), blood establishments would be required to notify consignees of the results of the additional testing, performed in accordance with proposed § 610.48(h)(1) or (h)(2), upon completing the additional testing and prior to 1 year from the effective date of any final rule resulting from this proposal. Blood

establishments would be required to notify the consignee of any risk of HCV transmission that exists for such prior collections, based on the results of the additional testing. If the prior collection was from a donor identified in the review of historical testing records in accordance with proposed § 610.48(c)(1) through (c)(5), and no additional testing was performed, or if no sample was available for further testing, as provided in proposed § 610.48(h)(1)(iii), the blood establishment would be required, within 1 year from the effective date of a final rule that results from this proposal, to notify consignees of any risk of HCV transmission for such prior collections.

The review of historical testing records identifies those donors whose test results indicate some degree of risk of HCV transmission for prior collections. If the testing records do not include supplemental testing, further testing of the original repeatedly reactive sample or a fresh sample from the donor is needed. The purpose of further testing is to provide the opportunity for blood establishments to evaluate the test results and determine the next appropriate step in the ''lookback'' process. Blood establishments must consider several significant issues when evaluating HCV screening and supplemental tests. Prior collections from donors who subsequently test positive or indeterminate on a supplemental test for HCV (except donors testing indeterminate on a RIBA 3.0 supplemental test as described below), are at increased risk of transmitting HCV. Prior collections from such donors would be destroyed or relabeled as proposed in § 610.48(k), or, if transfused, would trigger notification of recipients because of the increased risk of transmission of HCV infection.

However, in the case of a donor whose screening test was repeatedly reactive by HCV EIA 2.0, if an indeterminate RIBA 2.0 supplemental test result is followed by a negative result on an HCV EIA 3.0 screening test or an HCV RIBA 3.0 supplemental test, prior collections may be released from quarantine, as proposed in § 610.48(j), and transfusion recipients need not be notified. This release from quarantine is based on current research that indicates absence of polymerase chain reaction (PCR) reactivity for HCV RNA in HCV RIBA 2.0 indeterminate/HCV EIA 3.0 negative samples or in HCV RIBA 2.0 indeterminate/HCV RIBA 3.0 negative samples. Conversely, prior collections from donors who subsequently test repeatedly reactive on an EIA screening test and indeterminate on an HCV RIBA 3.0 supplemental test must also be destroyed or relabeled because they represent an increased risk of HCV transmission (under proposed § 610.48(k)). However, if these prior collections have been transfused, consignee notification for the purpose of recipient notification need not be performed (as noted in relevant sections of proposed § 610.49(a)) due to infrequent PCR positivity (only 1.6 percent) in HCV EIA 3.0 repeatedly reactive/HCV RIBA 3.0 indeterminate samples and infrequent (0.5 percent to 4 percent) PCR reactivity in HCV RIBA 2.0 indeterminate/HCV RIBA 3.0 indeterminate samples.

N. Proposed § 610.48(i), Further Testing and Consignee Notification Following Review of Records Based on Screening Performed Using a Single Antigen Screening Test

The purpose of proposed § 610.48(i), which parallels the requirements of proposed § 610.48(h), is to require that prior collections, identified in the review of historical testing records and based on single antigen testing in accordance with § 610.48(d)(4), be further tested and consignees notified so that blood establishments can determine if the prior collections should be released from quarantine (under § 610.48(j)), or destroyed or relabeled (under § 610.48(k)), and if notification of transfusion recipients is necessary (under § 610.49(a)). In addition, blood establishments would have the option to perform further testing for prior collections identified in accordance with § 610.48(d)(1), (d)(2), and (d)(3). Proposed § 610.48(i)(1) would require blood establishments, within 1 year of the effective date of any final rule resulting from this proposal, to perform further testing to clarify the status of prior collections collected from a donor identified, in accordance with § 610.48(d)(4), as being at increased risk of transmitting HCV.

Proposed § 610.48(i)(1) would require that further testing for donors identified in accordance with proposed § 610.48(d)(4) be performed as follows: (1) As proposed in § 610.48(i)(1)(i), blood establishments would be required to perform a licensed supplemental test for HCV on a frozen sample from the repeatedly reactive donation, if available. If such a frozen sample is not available, blood establishments would be required to obtain a fresh sample from the donor and perform a licensed RIBA 3.0 supplemental test for HCV; or (2) as proposed under § 610.48(i)(1)(ii), blood establishments would be required to make a determination that neither a frozen sample from the repeatedly reactive donation nor a fresh sample from the donor is available for further testing. For example, under certain circumstances, the blood establishment could make a determination that additional testing is not possible because the sample was not stored properly, or the donor could not be located or the donor declined further testing.

Under proposed § 610.48(i)(2), blood establishments would have the option to perform further testing on prior collections identified in accordance with § 610.48(d)(1) and (d)(2). This provision would make it possible to clarify the status of the prior collections and, in some instances, based on further testing, it might not be necessary to destroy the prior collections or notify transfusion recipients. Under proposed § 610.48(i), blood establishments that have performed the review of historical testing records and identified prior collections in accordance with proposed § 610.48 (d)(1) or (d)(2) of this section may further test a frozen sample from the repeatedly reactive donation or a fresh sample from the same donor by 1 year from the effective date of any final rule resulting from this proposal, as follows: (1) As proposed under § 610.48(i)(2)(i), if the donor was identified in accordance with proposed § 610.48 (d)(1) of this section as testing repeatedly reactive on an HCV EIA 1.0 screening test and repeatedly reactive on either an HCV EIA 2.0 or HCV EIA 3.0 screening test, blood establishments have the option to perform further testing using an appropriate licensed supplemental test for HCV; or (2) as proposed under § 610.48(i)(2)(ii), if the donor was identified in accordance with paragraph (d)(2) of this section as testing repeatedly reactive on an HCV EIA 1.0 screening test with an indeterminate test result obtained using a HCV RIBA 2.0 supplemental test, blood establishments have the option to perform further testing using a currently available licensed supplemental test for HCV or an HCV EIA 3.0 screening test. If such optional further testing is performed using an HCV EIA 3.0 screening test and the result is repeatedly reactive, blood establishments have the additional option to perform further testing using an appropriately chosen licensed supplemental test for HCV; or (3) as proposed under § 610.48(i)(2)(iii), if the donor was identified in accordance with paragraph (d)(3) of this section as testing repeatedly reactive on an HCV EIA 1.0 screening test with a S/CO value less than 2.5 for at least two out of the three EIA tests, and with no record of a supplemental test or multiantigen

screening test for HCV performed on the repeatedly reactive sample or on a later sample from the same donor, blood establishments have the option to perform further testing using a licensed multiantigen screening test for HCV or a licensed supplemental test for HCV.

Under proposed § 610.48(i)(3), blood establishments would be required to notify consignees of the results of the additional testing, performed in accordance with proposed § 610.48(i)(1) or (i)(2), upon completing the additional testing and prior to 1 year from the effective date of any final rule resulting from this proposal. Blood establishments would be required to notify the consignee of any risk of HCV transmission that exists for such prior collections, based on the results of the additional testing. If the prior collection was from a donor identified in the review of historical testing records in accordance with proposed § 610.48(d)(1) through (d)(4), and no additional testing was performed, or if no sample was available for further testing, as provided in proposed § 610.48(i)(1)(ii), the blood establishment would be required to notify consignees, within 1 year from the effective date of a final rule that results from this proposal, of any risk of HCV transmission for such prior collections.

O. Proposed § 610.48(j), Release From Quarantine

The purpose of proposed § 610.48(j) is to identify those prior collections of blood and blood components intended for transfusion or for manufacture into injectable products that have been quarantined and further tested that may be released from quarantine, based on the results of the additional testing. Under proposed § 610.48(j)(1), those prior collections subject to quarantine under proposed § 610.48(a) would be released for use only if the donor's current, repeatedly reactive sample is further tested using a licensed, supplemental test for HCV, as required in proposed § 610.48(b), and the result of the supplemental test is negative. Because the negative supplemental test result indicates that the repeatedly reactive screening test result was a ''false positive,'' prior collections from the donor are not suspected as being a possible window period donation, are not at increased risk of transmitting HCV and therefore, may be released from quarantine.

Under proposed § 610.48(j)(2), prior collections subject to quarantine under proposed § 610.48(e)(1) (as a result of the review of historical testing records and based on a multiantigen screening test) would be released from quarantine only if such prior collections were not suspected as being ''window'' period donations. Such prior collections, if not exempt from quarantine under proposed § 610.48(g)(2), would be released from quarantine if certain conditions are met as follows: (1) As proposed in § 610.48(j)(2)(i)(A), if the donor's testing records meet the conditions specified in proposed § 610.48(c)(4) (repeatedly reactive HCV EIA 2.0 screening test without additional test results) and further testing was performed in accordance with § 610.48(h)(1)(i)(A) on a frozen sample from the repeatedly reactive donation or a fresh sample from the same donor, and the result of the licensed supplemental test for HCV is negative; or (2) as proposed in § 610.48(j)(2)(i)(B), if the donor's testing records meet the conditions specified in proposed § 610.48(c)(4) and the blood establishment performed further testing in accordance with proposed § 610.48(h)(1)(i)(B) on a frozen sample from the repeatedly reactive donation or a fresh sample from the same donor, using either a licensed HCV EIA 3.0 screening test and the result is negative, or the result of the licensed HCV EIA 3.0 screening test is repeatedly reactive and further testing is performed using a licensed supplemental test for HCV and the result is negative; or (3) as proposed in § 610.48(j)(2)(ii), if the donor's testing records meet the conditions specified in proposed § 610.48(c)(5) (repeatedly reactive HCV EIA 3.0 screening test without additional test results) and the blood establishment performed further testing in accordance with proposed § 610.48(h)(1)(ii) of this section on a frozen sample or a fresh sample from the same donor using a licensed, supplemental test for HCV and the result is negative; or (4) as proposed in § 610.48(j)(2)(iii), if the donor's testing records meet the conditions specified in proposed § 610.48(c)(2) (repeatedly reactive multiantigen screening test and indeterminate supplemental test) and the blood establishment performed further testing in accordance with proposed § 610.48(h)(2), and one of three conditions specified in proposed § 610.48(j)(2)(iii)(A), (j)(2)(iii)(B) or (j)(2)(iii)(C) applies. (Proposed § 610.48(j)(2)(iii)(A) addresses repeatedly reactive sample that was tested using an HCV EIA 2.0 screening test, or a later sample from the same donor that was further tested in accordance with proposed § 610.48(h)(2)(i) of this section using either an HCV EIA 3.0 screening test or a licensed supplemental test for HCV and the result is negative. Proposed § 610.48(j)(2)(iii)(B) addresses the repeatedly reactive sample that was tested using an HCV EIA 2.0 screening test or a later sample from the donor that was further tested in accordance with proposed § 610.48(h)(2)(ii) of this section using a HCV RIBA 3.0 and the result is negative. Proposed § 610.48(j)(2)(iii)(C) addresses the repeatedly reactive sample that was tested using an HCV EIA 3.0 screening test or a later sample from the same donor that was further tested in accordance with proposed § 610.48(h)(2)(iii) of this section using a licensed supplemental test for HCV and the result is negative) or; (5) under proposed § 610.48(j)(2)(iv), if the donor's testing records meet the conditions specified in proposed § 610.48(c)(3) (repeatedly reactive HCV EIA 3.0 screening test and indeterminate HCV RIBA 2.0 supplemental test) and further testing was performed in accordance with proposed § 610.48(h)(2)(iv) of this section on a frozen sample or a fresh sample from the same donor using a licensed supplemental test for HCV and the result is negative.

Under proposed § 610.48(j)(3), prior collections subject to quarantine under proposed § 610.48(f)(1) (as a result of the review of historical testing records and based on a single antigen screening test) would be released from quarantine only if such prior collections were not suspected as being ''window'' period donations. Such prior collections, if not exempt from quarantine under proposed § 610.48(g)(3), would be released from quarantine if certain conditions are met as follows: (1) Under proposed § 610.48(j)(3)(i), if the donor's testing records meet the conditions specified in proposed § 610.48(d)(4) (repeatedly reactive HCV EIA 1.0 screening test with an S/CO value greater than or equal to 2.5) and further testing was performed in accordance with proposed § 610.48(i)(1)(i) on a fresh sample, or frozen sample from the repeatedly reactive donation using a licensed supplemental test for HCV and the result is negative; or (2) under proposed § 610.48(j)(3)(ii), if the donor's testing records meet the conditions specified in proposed § 610.48 (d)(1) (repeatedly reactive HCV EIA 1.0 screening test and repeatedly reactive HCV EIA 2.0 or 3.0 screening test) and further testing was performed in accordance with proposed § 610.48(i)(2)(i) on a fresh sample, or frozen sample from the repeatedly reactive donation and the result of the appropriate supplemental test for HCV is negative; or (3) under proposed § 610.48(j)(3)(iii), if the donor's testing records meet the conditions specified in

proposed § 610.48 (d)(2) and further testing (in the case of a repeatedly reactive HCV EIA 1.0 and indeterminate HCV RIBA 2.0 supplemental test) was performed in accordance with proposed § 610.48 (i)(2)(ii) on a fresh sample, or frozen sample from the repeatedly reactive donation and the result when further tested using either an HCV EIA 3.0 screening test or a licensed supplemental test for HCV is negative; or (4) under proposed § 610.48(j)(3)(iv), if the donor's testing records meet the conditions specified in proposed § 610.48 (d)(3) (repeatedly reactive HCV EIA 1.0 with an S/CO less than 2.5) and further testing was performed in accordance with proposed § 610.48(i)(2)(iii) on a fresh sample, or frozen sample from the repeatedly reactive donation and the result when further tested using a licensed multiantigen screening test for HCV or a licensed supplemental test for HCV is negative.

FDA is proposing a conforming amendment to § 610.46(d), which specifies requirements for release from quarantine for HIV ''lookback,'' for consistency with the HCV ''lookback'' requirements by changing ''Whole Blood, blood components, Source Plasma and Source Leukocytes'' to ''blood and blood components.''

P. Proposed § 610.48(k), Destruction or Labeling of Prior Collections Held in Quarantine

The purpose of proposed § 610.48(k) is to identify prior collections that must be destroyed or appropriately labeled, that is, those prior collections that are not exempt from quarantine under proposed § 610.48(g) and do not meet the conditions for release from quarantine in accordance with proposed § 610.48(j). Proposed § 610.48(k) would require that blood establishments and consignees take appropriate action for prior collections subject to quarantine under proposed § 610.48(a), (e), and (f). Blood establishments would be required to either destroy the quarantined prior collections or appropriately label the collections for in vitro use unless: (1) The prior collection was determined to be exempt from quarantine in accordance with proposed § 610.48(g), or (2) the prior collection was subject to release from quarantine under proposed § 610.48(j). FDA recognizes there may be some limited uses for quarantined prior collections which are not suitable for release from quarantine for the product's original intended use. Such prior collections should not be used for transfusion or for further manufacturing into injectable products. FDA recommends that these prior collections be destroyed as a general practice; however, in limited situations, release for research or manufacture into in-vitro diagnostic reagents may be acceptable. If released for these uses, prior collections should be relabeled consistent with §§ 606.121 and 640.70. In addition, these prior collections must be relabeled as ''Biohazard'' with the cautionary statements as follows:

Collected from a donor who subsequently tested reactive for anti-HCV. An increased risk of transmission of hepatitis C is present.''; in addition, the label must contain one of the following cautionary statements, as appropriate: ''Caution: For Further Manufacturing Into In-Vitro Diagnostic Reagents For Which There Are No Alternative Sources.'' or ''For Laboratory Research Use Only.

FDA is proposing a conforming amendment to § 610.46, the HIV ''lookback'' requirements, for consistency and to clarify the actions to be taken for prior collections subject to quarantine under § 610.46(a). FDA is proposing to redesignate § 610.46(e) as § 610.46(f) and to add new § 610.46(e) *Destruction or labeling of prior collections held in quarantine*, consistent with this proposal.

Q. Proposed § 610.48(l)

Proposed § 610.48(l) specifies that actions taken under proposed § 610.48 do not constitute a recall. This regulation is consistent with current § 610.46(e) applicable to the HIV ''lookback'' requirements (as noted previously, FDA is proposing to redesignate paragraph (e) as paragraph (f)). While there are similarities between the product recall process and ''lookback,'' there are several important differences: (1) The recall procedures described in part 7 (21 CFR part 7) are intended as a guideline while ''lookback'' would be a regulatory requirement; (2) additional steps are required in ''lookback'' which are not ordinarily performed in a product recall; (3) because each ''lookback'' would be initiated due to similar circumstances, a health hazard evaluation and recall classification by the agency (see § 7.41) is unnecessary; and (4) the products being quarantined may not be in violation of applicable laws (see § 7.40). FDA recognizes that a ''lookback'' action does not mean that an establishment has erred or did not meet its obligations under the regulations and the law in assuring the safety of the blood supply. Failure to take appropriate action in accordance with the proposed ''lookback'' regulations, however, would be a violation and FDA would take enforcement action, when appropriate, in such situations.

R. Proposed § 610.49(a), Hepatitis C Virus (HCV) ''Lookback;'' Notification of Transfusion Recipients

The purpose of proposed § 610.49 is to identify the circumstances under which it is necessary to notify transfusion recipients; who is responsible for performing the notification; and the timeframes for completing the notification process. The notification process is intended to result in the notification of transfusion recipients who have received prior collections of blood and blood components from a donor later determined to be at increased risk of transmitting HCV infection because they are possible ''window period'' donations. Refer to the discussion in the description of proposed § 610.48(c) for more information on ''window period'' donations. As previously discussed, there are two sets of circumstances which trigger ''lookback'' activity. The notification of transfusion recipients would be performed as a result of: (1) The identification of a donor who returns to donate again and tests repeatedly reactive for evidence of HCV infection on a licensed multiantigen screening test (as specified in § 610.48(a)) and further testing (performed as specified in proposed § 610.48(b)) indicates an increased risk of transmitting HCV; or (2) the identification of a donor, as a result of the review of historical testing records (in accordance with proposed § 610.48(c) or (d)), and further testing (as shown in historical records or as performed under proposed § 610.48(h) or (i)) indicates an increased risk of transmitting HCV. Under the proposal, transfusion recipient notification need not be performed for prior collections of Source Plasma and Source Leukocytes, because they are intended for further manufacture and not for transfusion. Proposed § 610.49(a), would require transfusion services to take appropriate actions, in accordance with § 610.49(b) and (c), when a transfusion recipient has received blood or blood components, from a donor later determined to be at increased risk of transmitting HCV infection as follows: (1) The donor was identified in accordance with proposed § 610.48(a) and the result of the licensed, supplemental test performed in accordance with proposed § 610.48(b) is positive; or (2) the donor was identified in accordance with proposed § 610.48(c)(1), and the result of the supplemental test identified in the review of records is positive; or (3) the

donor was identified in accordance with proposed § 610.48(c)(2), and the result of the supplemental test identified in the review of records is indeterminate, unless either the historical testing records or further testing (in accordance with proposed § 610.48(h)) show the indeterminate supplemental test result was obtained using a licensed supplemental test, and the initial test result was determined to be a false positive because any of the conditions for exemption from quarantine or release from quarantine have been met ; or (4) the donor was identified in accordance with proposed § 610.48(c)(4) or (c)(5) as testing repeatedly reactive on a multiantigen screening test with no record of further testing and the result of the licensed, supplemental test performed, in accordance with proposed § 610.48(h)(1)(i)(A), (h)(1)(i)(B), or (h)(1)(ii) is positive; or (5) the donor was identified in accordance with proposed § 610.48(c)(4) or (c)(5) as having no record of further testing and no fresh or frozen sample is available for further testing, as specified in proposed § 610.48(h)(1)(iii); or (6) the donor was identified in accordance with proposed § 610.48(d)(1) unless the initial test result was determined to be a false positive because any of the conditions for exemption from quarantine (under proposed § 610.48(g)(3)) or release from quarantine (under proposed § 610.48(j)(3)) have been met, or the donor was further tested in accordance with § 610.48(i)(2)(i) using an appropriately chosen supplemental test for HCV and the result is negative or indeterminate; or (7) the donor was identified in accordance with proposed § 610.48(d)(2) and the result of the supplemental test performed using an HCV RIBA 2.0 or HCV RIBA 3.0 supplemental test is positive as identified in the review of historical testing records; or (8) the donor was identified in accordance with proposed § 610.48(d)(2), and the result of the supplemental test performed using HCV RIBA 2.0 is indeterminate, unless any of the conditions for exemption from quarantine (under proposed § 610.48(g)(3)), or release from quarantine (under proposed § 610.48(j)(3)) have been met, or the donor was further tested in accordance with proposed § 610.48(i)(2)(ii) using a licensed supplemental test for HCV and the result is indeterminate; or (9) the donor was identified in the review of historical testing records in accordance with proposed § 610.48(d)(3) (repeatedly reactive HCV EIA 1.0 with an S/CO value less than 2.5) and the result of the licensed, supplemental test for HCV performed in accordance with proposed § 610.48(i)(2)(iii) is positive; or (10) the donor was identified in the review of historical testing records in accordance with proposed § 610.48(d)(4) (as testing repeatedly reactive on a single antigen screening test with a S/CO value equal to or greater than 2.5 for at least two of the three EIA tests, or the S/CO value can not be calculated, and with no record of further testing) and the result of the licensed, supplemental test for HCV performed in accordance with § 610.48(i)(1) is positive; or (11) the donor was identified in the review of historical testing records, in accordance with § 610.48(d)(4), and no record of further testing is available and no fresh or frozen sample is available for further testing, as specified in § 610.48(i)(1)(ii).

FDA is proposing conforming amendments to HIV ''lookback'' requirements of § 610.47(a) for consistency with the HCV ''lookback'' requirements of proposed § 610.49(a). FDA is proposing to amend § 610.47(a) to clarify that transfusion services shall notify recipients of prior collections of blood and blood components from a donor later determined to be at increased risk of transmitting HIV infection when tested for evidence of HIV infection and the result of the additional tests required in § 610.46(b) are positive.

S. Proposed § 610.49(b), Notification of Recipients of Prior Transfusion

Proposed § 610.49(b) describes the requirements for the process of notification of transfusion recipients. Under proposed § 610.49(b), consistent with requirements for notification in the HIV ''lookback'' regulations in § 610.47, the transfusion service would either notify the physician of record (i.e., the physician of record or physician who ordered the blood) and ask him or her to inform the recipient, or would notify the recipient directly. FDA recognizes that, under certain circumstances, the physician may have developed an ongoing relationship with the patient and may agree to take responsibility for notification and counseling. The transfusion service is ultimately responsible for ensuring that the notification takes place. The transfusion service might seek assistance in the notification process. For example, the transfusion service might determine that such notification and counseling would be best conducted by staff in another department in the hospital, who may be better trained and experienced in counseling patients. Under proposed § 610.49(b) and under the proposed conforming amendment to § 610.47(b), a transfusion service may elect to notify the transfusion recipient directly, without the assistance of the patient's physician of record. FDA specifically requests comment whether the transfusion service should be required to perform concurrent notification of the physician of record whenever the transfusion service notifies the transfusion recipient directly.

Proposed § 610.49(b) would require the transfusion service to make a minimum of three attempts to notify the transfusion recipient or the recipient's physician of record. The time period provided for completion of the recipient notification would be based on the date of donor testing and the date of receipt of the supplemental test result from the blood establishment. Recipient notification based on donor testing completed after the effective date of the regulation, as specified in the final rule resulting from this proposal, would be required to be completed within a maximum of 12 weeks of receipt of the results of the donor's supplemental test for HCV from the blood establishment. Recipient notification based on donor testing completed prior to the effective date of the regulation, as specified in the final rule resulting from this proposal (historical records of donor testing), would be required to be completed within 1 year of receipt of notification of test results from the blood establishment. FDA is proposing a longer period of time for completion of transfusion recipient notification based on donor testing completed prior to the effective date of the regulation because such notification would be made as a result of the review of historical testing records performed in accordance with proposed § 610.48(c) and (d), and it is possible that a transfusion service could have a large number of notifications to complete. However, FDA believes that the transfusion recipient notification process should begin and be completed as soon as feasible because such a notification will not require a year to complete in all cases. FDA recognizes that many blood establishments may be performing such transfusion recipient notifications consistent with the recommendations of the June 1999 draft guidance. Therefore, FDA believes that if a blood establishment has a limited number of transfusion recipient notifications to perform as a result of this regulation, then the notifications could be completed in less than the 1-year period that would be provided under this proposal. In addition, donors identified in accordance with proposed § 610.48(c)(2) through (c)(5), and proposed § 610.48(d)(1) through (d)(4) generally will be further tested by the

blood establishment in accordance with § 610.48(h) and (i), respectively. In those instances, FDA would require that the notification of recipients based on such a licensed supplemental test, performed after the effective date of the regulation, be completed within 12 weeks of the date of receipt of the supplemental test result from the blood establishment.

Under proposed § 610.49(b), the transfusion service would be responsible for the basic explanation to the recipient, referral for counseling and further testing, and documentation of the notification or attempts to notify the physician of record or the recipient, under § 606.160 of this chapter. Under this proposal, each establishment should have a well-designed system for notification, and would need to develop SOP's that describe each step in the notification system, as well as the required documentation. The SOP would address the need for documentation of person(s) contacted, by whom, when and whether the transfusion recipient was notified directly, or the physician of record agreed to notify the recipient, and the outcome of the notification efforts, including the reasons for inability to notify.

FDA is requesting comment on the appropriateness of requiring a minimum of three attempts to notify affected transfusion recipients as proposed for HIV and HCV ''lookback.'' FDA is proposing to increase the record retention requirement to 10 years (proposed § 606.160(d)) and to increase the length of time for which HIV and HCV ''lookback'' must be initiated, from a maximum of 5 years as currently required in § 610.46(a) for HIV ''lookback'' (for HCV ''lookback'' in proposed § 610.48(a)). In addition, FDA is proposing to require HCV ''lookback'' based on the review of available historical testing records (proposed § 610.48(c) and (d)) for those prior collections'' * * * dating back indefinitely for computerized electronic records and to January 1, 1988, for other readily retrievable records.'' FDA specifically requests comment on the minimum number of attempts which should be required to notify affected transfusion recipients identified in the records that are more than 5 years old and who, therefore, might be more difficult to locate. FDA also requests the submission of data which support a specific number of attempts to notify affected transfusion recipients.

FDA is proposing conforming amendments to HIV ''lookback'' requirements of § 610.47(b) for consistency with the HCV ''lookback'' requirements of proposed § 610.49(b). FDA is proposing to amend § 610.47(b) to clarify that transfusion services have the option of either notifying the transfusion recipient directly or notifying the recipient's physician of record and asking him or her to notify the recipient and that notification (based on donor testing completed after the effective date of the regulation) must be completed within a maximum of 12 weeks.

T. Proposed § 610.49(c), Notification of Legal Representative or Relative

Proposed § 610.49(c) would require the transfusion service or physician to notify a legal representative, designated in accordance with State law, if the transfusion recipient has been adjudged incompetent by a State court. In addition, if the transfusion recipient is competent, but State law permits a legal representative or relative to receive the information on the recipient's behalf, proposed § 610.49(c) would require the transfusion service or physician to notify the recipient, or his or her legal representative or relative. If the transfusion recipient is a minor at the time of notification, the transfusion service would be required to notify the recipient's legal representative. Under proposed § 610.49(c), reasons for notifying the recipient's relative or legal representative on his or her behalf would be documented, as required in the recordkeeping provisions of § 606.160. Proposed § 610.49(c) would not require notification efforts to continue if the recipient is deceased because, as previously discussed, direct percutaneous exposure to infectious blood, particularly in the setting of drug abuse, accounts for the majority of HCV infections acquired in the United States. Secondary transmission of HCV to sexual partners, care providers or others with close contact is very unlikely.

FDA is proposing conforming amendments to HIV ''lookback'' requirements of § 610.47(c) for consistency with the HCV ''lookback'' requirements of proposed § 610.49(c). FDA is proposing to amend § 610.47(c) to clarify that transfusion service or physician would be required to notify the legal representative if the transfusion recipient is a minor at the time of notification and to document the result of the notification or the attempts to complete the notification.

U. Proposed § 610.49(d), Reference Tables

Proposed § 610.49(d) includes four tables intended to assist in identifying the applicable paragraphs of proposed §§ 610.48 and 610.49 and the corresponding ''lookback'' actions. In particular, the requirements of proposed §§ 610.48 and 610.49 that are based on the review of historical testing records require that many different testing sequences be addressed. These tables are intended to clarify the applicable sections and the corresponding steps of the ''lookback'' process that must be considered for a particular sequence of tests.

Table 1 identifies applicable sections for the ''lookback'' process based on current donor testing, for donors identified in accordance with proposed § 610.48(a). For example, a donor that tests repeatedly reactive for HCV upon returning to donate again, would be identified by the blood establishment in accordance with proposed § 610.48(a). Table 1 of proposed § 610.49 lists the subsequent ''lookback'' actions that must be taken and the applicable regulations. Continuing with this example, in addition to other ''lookback'' actions, table 1 shows that such a donor would be further tested in accordance with proposed § 610.48(b), and prior collections could be released from quarantine if the conditions of proposed § 610.48(j)(1) were met.

Tables 2, 3, and 4 of proposed § 610.49 identify applicable sections for the ''lookback'' process based on the review of historical testing records. A different table applies based on the specific screening test that was performed. Table 2 identifies applicable sections based on the review of historical testing records for donors identified in accordance with proposed § 610.48(c) as testing repeatedly reactive using an HCV EIA 3.0 screening test. Table 3 identifies applicable sections based on the review of historical testing records for donors identified in accordance with proposed § 610.48(c) as testing repeatedly reactive using an HCV EIA 2.0 screening test. Table 4 of proposed § 610.49 identifies applicable sections based on the review of historical testing records for donors identified in accordance with proposed § 610.48(d) and tested using a single antigen screening test, HCV EIA 1.0.

IV. Analysis of Impacts and Initial Regulatory Flexibility Analysis

FDA has examined the impacts of the proposed rule under Executive Order 12866, under the Regulatory Flexibility Act (5 U.S.C. 601–612), and under the Unfunded Mandates Reform Act (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic,

environmental, public health and safety, and other advantages; distributive impacts; and equity). The Regulatory Flexibility Act requires agencies to analyze whether a rule may have a significant impact on a substantial number of small entities and, if it does, to analyze regulatory options that would minimize the impact. Section 202(a) of the Unfunded Mandates Reform Act requires that agencies prepare a written statement of anticipated costs and benefits before proposing any rule that may result in an expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100 million in any one year (adjusted annually for inflation).

The agency has determined that the proposed rule may be a significant action as defined by the Executive Order. The analysis below details FDA's estimate of the potential costs and benefits of the rule. As described in the analysis that follows, the rule is likely to have a significant economic effect on a substantial number of small entities. FDA has therefore prepared an Initial Regulatory Flexibility Analysis. The Unfunded Mandates Reform Act does not require FDA to prepare a statement of costs and benefits for the proposed rule, because the proposed rule is not expected to result in any 1-year expenditure that would exceed $100 million adjusted for inflation. The current inflation adjusted statutory threshold is about $110 million.

A. Economic Impact

The purpose of the proposed rule is to help ensure the continued safety of the blood supply and to help ensure that information is provided to consignees and recipients of blood products in the event of a repeat donor's seroconversion to positivity for hepatitis C. The proposed action is considered necessary to interdict prior in-date collections at increased risk for transmitting HCV and to help assure that blood product recipients receive counseling and treatment if necessary, as effective therapies become available for hepatitis C. The proposed rule will further support public confidence in safety of the U.S. blood supply, recognizing priorities for the reduction of infectious disease risks to transfusion recipients. The agency further notes that the costs and benefits of the FDA and the Health Care Finance Administration (HCFA) rule are not additive, as the impacts considered in the HCFA rule are also accounted for in the FDA rule.

1. The Number and Type of Entities Affected

The proposed rule will affect establishments that collect, process, and ship blood and blood components, and establishments that transfuse those products. The affected entities include commercial plasma centers, regional and community blood collection or donation centers, hospitals that operate blood collection centers, and facilities that transfuse blood products. The HCFA estimates that there are approximately 6,200 transfusing facilities. FDA's Office of Blood Research and Review (OBRR) has a record of 2,801 registered blood and plasma establishments.

According to a 1992 survey (Ref. 3), U.S. blood establishments collect an annual total of 13,794,000 units of blood. Allogeneic donations (not directed for a specific recipient) accounted for 87.2 percent (12,035,000 units). Approximately 79 percent of allogeneic donations are provided by repeat donors. (This percentage is based on American Red Cross estimates based on donations between January 1996 and June 1997.) FDA's analysis of the HCV ''lookback'' rule focuses on allogeneic donations by repeat donors, and the subset of those donors expected to test repeatedly reactive in a screening test for evidence of HCV infection. As outlined in preceding sections of this document, the proposed rule includes a set of provisions for processes to be performed by blood establishments. In general terms, these provisions concern donor recordkeeping, record review, identification and quarantine of affected units for repeat reactive donors, notification of consignees of unpooled products concerning the HCV status of affected units, and further testing to confirm HCV positivity. The proposed rule also specifies requirements for blood product consignees that relate to quarantine of in-date unpooled products based on blood establishment notifications, and recipient notification when appropriate.

Plasma centers will be affected by the proposed rule only to the extent that these establishments store and distribute unpooled units to consignees that also retain unpooled units in their inventories. FDA currently has little information about the volume of unpooled units retained by plasma centers that would be affected by this proposal. Because this information is essential for the estimation of economic impact, FDA requests detailed industry comment on current practices for recordkeeping and retention of unpooled units of plasma (including estimated numbers of unpooled units), both at collection centers and the facilities to which these units are subsequently shipped. For the purpose of this analysis, FDA has assumed that most units will be pooled prior to the initiation of any ''lookback'' activity and, therefore, that plasma establishments will be minimally affected by the proposed rule. Plasma establishments similarly will not be affected by the proposed requirements for review of historical testing records. FDA, therefore, assumes that the primary impact on plasma establishments will involve the review of the proposed regulation by each establishment to determine how current facility SOP's would be affected.

With the exception of hospitals that both collect and transfuse blood products, most establishments affected by the rule will either act as a blood collection establishment or as a consignee (transfusion service), not as both. To distinguish the impact of the requirements for blood establishments and for consignees, the rule provisions affecting each type of entity will be treated separately in the analysis that follows. Table 1 of this document provides a summary of the estimated one-time versus the yearly costs for blood establishments and blood product consignees. The basis for these estimates are explained in sections IV.A.2 and IV.A.3 of this document.

TABLE 1.—SUMMARY OF ESTIMATED ONE-TIME YEARLY COSTS FOR BLOOD ESTABLISHMENT AND BLOOD PRODUCT CONSIGNEES

Affected Entities (number)	One-Time Cost	Yearly Cost
Blood Establishments (2,800)		
Hepatitis C Virus (HCV) ''Lookback'' Standard Operating Procedures (SOP's)	$2,875,040	
Prospective review		$4,558,442

TABLE 1.—SUMMARY OF ESTIMATED ONE-TIME YEARLY COSTS FOR BLOOD ESTABLISHMENT AND BLOOD PRODUCT CONSIGNEES—Continued

Affected Entities (number)	One-Time Cost	Yearly Cost
Historical review	$33,239,402	
Subtotal	$36,114,442	$4,558,442
Consignees (6,200)		
HCV ''Lookback'' SOP's	$2,546,464	
Prospective review		$2,114,632
Historical Review	$50,106,540	
Subtotal	$52,653,004	$2,114,632
Total	$88,767,446	$6,673,074

2. Estimated Impact on Blood and Plasma Establishments

Many of the provisions of the proposed rule will affect blood establishments. Each establishment will need to review the provisions of the rule in order to reconcile current facility practices for record review, sample quarantine, consignee notification and other related processes, and donor and blood product recordkeeping, with the requirements of the rule. FDA estimates the cost of performing such a one-time review and reconciliation of blood establishment SOP's to be approximately $1,027 per establishment, assuming that the review will require approximately 40 hours per facility and be performed by a staff medical technologist (Ref. 4). This yields a total one-time cost of $2,875,040.

The proposed rule requires that blood establishments extend the retention period for required processing records for blood donors from 5 to 10 years after the records of processing have been completed or 6 months after the latest expiration date for the individual product, whichever is a later date. FDA estimates that this provision will cost approximately $3,110,240 per year, assuming that routine maintenance of donor files for the additional period of time will require approximately 40 hours of additional programming support time per facility per year, at a cost of $27.77 per hour of programmer time, based on 1997 Bureau of Labor Statistics estimates (40 x $27.77 x 2,800).

The proposed rule requires that blood and plasma establishments act within 3-calendar days of receiving the results of an FDA-licensed HCV test performed by a blood establishment or a CLIA-certified laboratory, with repeatedly reactive HCV results for a repeat blood donor. The establishment would retain the records for all in-date products and quarantine any in-date unpooled product that remain in inventory, quarantine all in-date unpooled prior collections, and notify consignees of the repeatedly reactive test result so that they may also quarantine any in-date unpooled prior collections. However, prior collections made more than 12 months prior to the last negative multiantigen HCV screening test are exempt from the required quarantine. Following the repeatedly reactive results of the initial screening tests, the blood establishment would be required to notify consignees of the result of the more specific supplemental HCV test within 45-calendar days after the day on which the donor tests repeatedly reactive in a screening test for evidence of HCV infection. If the result of further testing with a licensed supplemental test is negative, then the initial screening test result can be considered a ''false positive'' and the in-date prior collections can be released from quarantine.

FDA's estimated cost of these provisions is based on an estimated number of consignee notifications multiplied by the unit cost of each notification. First, the number of annual affected blood donations was calculated as the product of 12 million donations, an 80 percent repeat donor rate, and a 0.12 percent HCV positive donor rate. The resulting 11,520 figure was then adjusted upward to 12,816 to reflect the difference found between the number of donors triggering ''lookback'' and the component notifications reported as interim results from a recent survey conducted by the Centers for Disease Control and Prevention (CDC) (Ref. 4). Assuming a cost of $113 per notification based on remarks from a representative of the nation's blood banks (Ref. 5) yields a consignee notification cost to blood banks of $1,448,202 per year (12,816 x $113). Thus, the prospective review in the proposed rule results in a yearly total cost of $4,558,442 ($3,110,240 + $1,448,202) for blood establishments. These costs may be slightly understated, because the CDC survey-based projections extend back only to 1988 records. Nevertheless, because the proposed rule requires pre-1988 searches only for ''computerized electronic records,'' this underestimate would be small.

The proposed rule would also require a review of historical testing records of donations collected prior to the effective date of the rule. Blood establishments will be required to review records from prior collections to identify donors that tested repeatedly reactive in a screening test for evidence of HCV infection, for whom either: (1) There is no record of further testing, (2) the donor tested indeterminate on a supplemental test for HCV (with some exceptions), or (3) the donor tested positive on a supplemental test. The purpose of the record review is to identify prior collections from donors who are likely to be infected in order to notify recipients of such donations, and quarantine affected products that remain in inventory.

Following their review of historical testing records, blood establishments would be required to do the following tasks. If the records show that the repeat donation, testing repeatedly reactive in a screening test for evidence of HCV infection, was followed by an appropriate licensed supplemental test with confirmed negative results, no further action is needed. If the repeat donation, testing repeatedly reactive in a screening test for evidence of HCV infection, was followed by a supplemental test with confirmed positive results, the blood establishment

would notify consignees of blood products from the donor's prior donations and quarantine affected products that remain in inventory. If the records show that the donation, testing repeatedly reactive in a screening test for evidence of HCV infection, was followed by a supplemental test with indeterminate result, or there is no record of supplemental testing to determine the donor's HCV status, the blood establishment would try to perform supplemental testing to clarify the status of prior collections. If a frozen sample from the donation testing repeatedly reactive in a screening test for evidence of HCV infection is available, that sample would be used in supplemental testing; otherwise, the blood establishment would attempt to contact the donor to obtain a fresh sample for testing. If further testing with fresh or frozen samples is accomplished, the blood establishment would be required to notify consignees of the test result. If no frozen sample is available and a fresh sample cannot be retrieved from the donor, the blood establishment would be required to notify consignees of the results of the repeatedly reactive screening test and the inability to clarify the donor's HCV status. Within 1 year of the effective date of the final rule, blood establishments would be required to perform the testing needed to clarify the status of prior collections. Blood establishments would be required to notify consignees of HCV positive test results within 45 days of completion of further testing performed as a result of the review of historical testing records. If no further testing could be performed, consignees would be notified within 1 year.

FDA's estimate of the cost of performing the specified review of historical testing records is based on the CDC estimate of 294,154 attempted notifications (188,448 during the period 1990 to mid-1992 and 105,706 during the period from mid-1992 to 1998) and the estimated cost of $113 per notification (Ref. 5). This yields a one-time review cost of $33,239,402. Again, this estimate does not account for pre-1988 computerized electronic records, but the agency believes there are relatively few.

In total, as shown in table 1, FDA's estimates that blood collection agencies will incur ''lookback'' related one–time costs of about $36.1 million and annual costs of about $4.6 million. As the industry has already initiated this program, it is likely that the greater part of these costs have already been incurred.

3. Estimated Impact on Blood Product Consignees

The proposed rule would require that transfusion services (i.e., consignees) notify transfusion recipients who received prior collections from a donor at increased risk of transmitting HCV. Recipient notification is included in both the prospective ''lookback'' and the review of historical testing records to identify prior collections. The transfusion service may notify the physician of record or notify the recipient directly. If the transfusion recipient is a minor or adjudged incompetent by a State court, the transfusion service or physician would be required to notify the recipient's legal representative. The proposed rule is expected to generate one-time costs and some additional annual costs for blood product consignees. One-time costs include the development of facility SOP's for recipient notification. FDA assumes that these tasks will involve the review of current SOP's (e.g., for HIV ''lookback'') and the adaptation or modification of current procedures to address the provisions of this rule and estimates that they will require an average of 16 hours per facility for facilities that act as consignees. The review would be performed by a staff medical technologist at an estimated cost of $25.67 per hour. Thus, FDA estimates the total one-time cost for the 6,200 transfusing facilities to be $2,546,464.

For notifications resulting from prospective donor testing and required quarantine, the required notification effort would include a minimum of three attempts to notify the transfusion recipient and would be completed within a maximum of 12 weeks of receipt from the blood establishment of the results of the donor's supplemental test for HCV. The agency's estimated cost of compliance with provisions concerning the prospective review and recipient notification is based on the previously described estimate of 11,520 annual affected donations. This figure was adjusted to 12,816 to reflect the CDC survey finding that the number of components sent to transfusion facilities exceeded the number of donors triggering ''lookback'' at blood centers by 11.2 percent. The cost per attempted notification is estimated at $165 which reflects the average cost quoted by a third party contractor for matching, notifying, testing, counciling, and documenting ''lookback'' efforts for over 100 hospitals (Ref. 6). Although the proposed rule does not specifically require hospitals to perform testing and counciling services, many do. These assumptions yield an annual cost of $2,114,632 (12,816 x $165) for blood consignees to conduct prospective ''lookback'' activities.

Notifications resulting from the review of historical testing records and the identification of prior collections are to be completed by the transfusion service within 1 year of receipt of notification from the blood establishment. The recipient notification provided by the transfusion service would include a basic explanation to the recipient, referral for counseling and further testing and documentation of the notification or attempts to notify the physician of record or recipient. The estimated one-time cost of recipient notification associated with the review of historical testing records is $50,106,540. This is based on the CDC estimate of about 303,676 recipients identified for notification (188,448 from 1990 to mid–1992 and 115,228 from 1990 to mid–1992), and the average cost of $165 of staff time per component for recipient notification. Thus, FDA estimates the total one-time cost to blood transfusion facilities to be $52,653,004 ($2,546,464 + $50,106,540) for conducting retrospective ''lookback''.

The cost of targeted HCV ''lookback'' notification in the United States is expected to compare favorably with the experiences reported in earlier efforts, e.g., in Canada (Ref. 7), which were likely based on less automated approaches to recordkeeping. Table 2 of this document shows the cost of the HCV ''lookback'' per recipient notified, using CDC data to project various outcomes of the ''lookback'' effort. As shown in table 2, the assumption that a total of 258,551 transfusion recipients will be identified for notification through the historical ''lookback'' effort translates to an estimated one-time cost of about $642 per recipient identified. CDC further estimates that approximately 57,885 will still be living and notified through the retrospective review. This estimate implies a one-time cost of $1,440 per notified living recipient.

TABLE 2.—ESTIMATED COST PER RECIPIENT NOTIFICATION

	Cost of ''Lookback'' and Notification[1]	Cost Per Recipient Transfused	Cost Per Recipient Notified
Prospective	$6,673,074[2]	$658	$1,541
Historial	$83,345,942	$642	$1,440

[1] Excludes cost of developing SOP's.
[2] Annual cost.

B. Benefits of the Proposed Rule

The proposed rule is intended to help ensure the continued safety and adequacy of the national blood supply. Threats to the safety of the blood supply and the importance of a timely regulatory response to assure public safety have been the focus of numerous review efforts in recent years, by the U.S. House of Representatives Committee on Government Reform and Oversight, Subcommittee on Human Resources and Intergovernment Relations, the General Accounting Office, IOM, and private organizations including the American Liver Foundation and the DHHS Advisory Committee on Blood Safety and Availability. The proposed ''lookback'' effort provides benefits both at the individual level of blood recipients and at a societal level, in terms of both the safety and continued adequacy of the national blood supply. The discussion that follows first addresses individual level benefits and then considers societal benefits.

1. Individual Benefits of HCV ''lookback''

Over the past several years, the improved accuracy of HCV testing, the increased understanding of hepatitis C outcomes, the value of counseling against risk behaviors that worsen outcomes, and the advances in treatment of HCV have collectively created a medical and ethical imperative to inform identified transfusion recipients of their HCV risk. Prior to the widespread use of HCV screening of blood donors, transfusion was one of the most common modes of transmission. Although patients with chronic hepatitis C may remain asymptomatic for a number of years, the consequences of their disease are extremely serious. For example, CDC population-based studies indicate that 40 percent of chronic liver disease is HCV-related, resulting in an estimated 8,000 to 10,000 deaths each year (Ref. 8). Current CDC estimates of medical and work-loss costs of all HCV-related acute and chronic liver disease (including cases resulting from blood transfusion) are in excess of $600 million annually, and HCV-associated end-stage liver disease is the most frequent indication for liver transplantation among adults. The cost of liver transplantation is estimated to be approximately $200,000 in the first year and $20,000 per year for subsequent years; and the cost of treatment for hepatocellular carcinoma, another sequelae of chronic liver disease, is estimated to be $10,000 per year (Ref. 9).

Timely notification of HCV infection benefits the infected blood recipient in several important ways. First, although factors predicting severity of liver disease due to HCV have not been well-defined, recent data indicate that increased alcohol intake is associated with more severe liver disease. According to CDC, even moderate amounts of alcohol in patients with chronic hepatitis C might enhance liver disease. Consequently, an HCV-infected patient identified by the proposed ''lookback'' program could minimize liver damage associated with alcohol consumption by restricting his or her intake.

Next, while other percutaneous exposures currently represent the most common means of infection, some case-control studies have also reported a positive association with sexual contact with a person with a history of hepatitis and acquiring hepatitis C. In fact, 15 to 20 percent of the acute hepatitis C patients reported to CDC's sentinel counties surveillance system have a history of sexual exposure in the absence of other risk factors. Infected patients identified through the proposed ''lookback'' procedures could take steps to protect sexual partners from the risk of infection.

Next, it is important to note that identified infected patients would benefit from treatment with available therapies. Studies of patient characteristics and responsiveness to therapy indicate that best results are achieved if treatment is initiated earlier in the disease, when patients are younger and have not yet developed cirrhosis (Ref. 10). For example, Bennett et al. estimated the cost effectiveness of a single course (6 months) of treatment with alfa interferon and found that patients at age 20 experience an average of 3.1 years of life gained at $500 per year of life extended (YLE); 30-year-old patients have an average gain of 1.9 years of life, at $7,100/YLE; patients starting treatment at age 50 have 6 months of life gained at $7,100/YLE; and 70-year-old patients gain an average of 22 days at $62,000/YLE (Ref. 11).

Next, care providers for the identified infected patient would be aware of the infection and could use additional precautions to avoid the risk of exposure to blood or wounds when providing care to the patient. Finally, identified infected patients would be informed that they must not donate blood.

Currently, the primary treatment for chronic hepatitis C is alfa interferon therapy (Ref. 12). On average, of those patients who undergo interferon treatment, a reported 10 to 20 percent show a sustained response after 6 months of therapy, and 20 to 30 percent a sustained response if therapy is continued for 12 months. Although alfa interferon produces a wide array of adverse side effects (Ref. 13), and some patients experience a relapse of HCV infection despite therapy, the benefits for patients identified for treatment through HCV ''lookback'' are likely to continue to increase as improved therapies are developed. In particular, combination therapy using alfa interferon plus ribavirin has been reported to result in an improved outcome (Ref. 13).

In addition to the ''lookback'' costs discussed previously, the overall cost-effectiveness of the proposed regulation will vary with the cost and effectiveness (i.e., cure rate) of therapy for hepatitis C, and the cost of treatment for chronic liver disease and its sequelae in the absence of, or with failure of treatment for hepatitis C. A single course of alfa interferon therapy has been estimated to cost $2,300 (Ref. 9), but hepatitis C therapy is a rapidly changing area of clinical practice and the cost-effectiveness of treatment can shift dramatically with the introduction of new drugs and the age distribution and the comorbidities of the population receiving treatment. An illustrative example, however, can demonstrate the potential benefits of the increased therapies that might result from this

regulation. Although FDA cannot precisely determine the number of HCV positive individuals that would respond to the notification and seek medical consultation, a projection derived largely from interim findings of the CDC survey indicates that retrospective notification activities might identify about 3,764 cases of previously unidentified chronic HCV. This projection assumes that about 22.4 percent of 258,551 potential recipients are notified, about 13 percent of those notified test positive for HCV, 66.7 percent of the HCV cases are not currently known, and 75 percent of the HCV cases are chronic. Kim et al. (Ref. 9) found that, on average, patients with chronic HCV gain 0.25 discounted (3 percent) quality adjusted life-years (QALY's) from 6 months of interferon-2b treatment. (The authors do not provide estimates for any other discount rates.) On this basis, the above assumptions imply that retrospective ''lookback'' would gain a total of 941 QALY's, at a cost of about $88,573 per QALY.

There is no generally accepted means of valuing life-years saved, although a number of empirical studies indicate a societal willingness-to-pay of from $1.6 million to $11.6 million to avoid a statistical death. Assuming a mid-range estimate of $5 million and annualizing over a 35-year period at 3 percent yields an annual value of $233,000. The above assumptions imply that providing 6 months of interferon- 2b therapy to an additional 3,764 HCV-positive individuals could produce societal willingness-to-pay benefits of $219 million. The additional discounted (3 percent) incremental cost of providing such therapy was estimated by Kim et al. to be about $1,000 per patient, which implies an additional treatment cost of only $3,764,000 (3,764 patients x $1,000). Thus, by this measure, the individual benefits of retrospective HCV ''lookback'' easily exceed their incremental costs.

The benefits of the prospective ''lookback'' provisions can be similarly analyzed. Based on the CDC interim findings, FDA assumed that prospective ''lookback'' notifications would be initiated for 10,894 transfused recipients, of which 48 percent would be successful, 5.4 percent of those who are notified would test positive for HCV, 66.7 percent would be previously unknown, and 75 percent chronic. Thus, 123 patients could potentially gain 0.25 QALY's per year at a cost of roughly $217,011 per QALY. According to the monetization values described above, these health gains could generate annual benefits of $7.2 million, or roughly the level of the prospective ''lookback'' costs.

The agency recognizes the substantial uncertainty that surrounds such estimates. For example, medical cost-effectiveness studies sometimes assume a maximum societal value of about $50,000 per QALY. This modification would imply one-time retrospective ''lookback'' benefits of about $47 million and annual prospective ''lookback'' benefits of about $1.5 million, which would cover over half of the estimated initial costs of compliance. In addition, the figures assume that the distribution of recipient ages would reasonably match those of the Kim et al. study. Other studies of HCV treatment outcomes may project differently. FDA seeks public comment on the above assumptions and estimates.

2. Societal Benefits of HCV ''lookback''

In addition to the direct benefits of medical treatment, the proposed ''lookback'' program will help to boost confidence and trust in the national blood supply. Thus, HCV ''lookback'' will generate societal benefits that are incremental to the health benefits discussed above. Recent public reviews of blood supply issues have recognized the importance of assuring both safety and the perception of safety. For example, reviews suggest that the public trust in the blood supply system was severely shaken by the transmission of HIV by blood products. This effect was exacerbated by the perceived failure of blood collection centers, public health agencies, and health care providers to take timely action to prevent or minimize patient risk. The failure to institute an HIV ''lookback'' program at an early date resulted in a number of cases in which transfusion recipients were unaware of their infection, failed to seek treatment and subsequently infected others (Refs. 13 and 14).

Now that information is available to identify and to offer counseling and treatment options for those confirmed HCV-positive, FDA believes that the public trust demands the timely communication of relevant risk information. Although the agency cannot accurately assess the dollar value of this public trust or the potential impact of its loss, the following discussion, considers the cost of unfavorable shifts in public perception to be a potential indicator of the value of stabilizing public trust in the U.S. blood system. The purpose of the discussion is to provide an order-of-magnitude value assessment to which the estimated costs of HCV ''lookback'' can be compared.

Potential indicator of yearly cost: Changes in the blood donation patterns. The impact of the AIDS epidemic on the perceived safety of the nation's blood supply is believed to have contributed to the reduction in volunteer blood donations and to the dramatic increase in autologous and directed blood donation in subsequent years. The IOM discussion of bioethical issues in risk communication regarding the blood supply describes blood services as special because ''Trust is perhaps uniquely important. You know pretty fast if you have lost the public trust because people stop showing up to donate'' (Ref. 17). This comment suggests two measures of the loss of public trust in the blood supply in the wake of the HIV/AIDS transfusions of the 1980's: The reduction in the volume of allogeneic blood donations and the substantial increase in the volume of autologous blood collections. These shifts have associated opportunity costs and inefficiency costs. Part of the observed changes in blood donation reflect tighter donor screening and more efficient use of the patient's own blood in scheduled surgery. But some of the shift is believed to reflect a distrust of the blood supply not warranted based on objective measures of disease risk. FDA reviewed the extent of the blood donation decline that might be attributable to AIDS-related public mistrust and asked whether a similar round of impacts might result if risk communication about known HCV exposures were perceived as inadequate by the general public.

CDC estimates that the number of donations per donor has dropped from five as recently as 1992 to 1993, to two donations per donor in the period 1996 to 1998. This trend was already apparent in the survey findings of Wallace et al. published in 1995. Their survey compared blood collections in 1989 with collections in 1992, and found that 904,000 fewer allogeneic units and 462,000 more autologous units of blood were collected in 1992 compared with 1989. At an estimated average price of $103 per unit[1], the reduction in (allogeneic) donations represents an annual loss to the nation's blood supply valued at $93.11 million. If the allogeneic donations yielded more than one product per unit donation, the loss of potential supply would be greater.

[1] The estimates of $103 per allogeneic unit and $137 per autologous unit represent midpoint values in the range of blood costs reported by S. L. Lee in ''Patients' Willingness to pay for Autologous Blood Donation'' in *Risk in Perspective*, Harvard Center for Risk Analysis, vol. 6, No. 6, June 1988.

Autologous blood collection presents less risk of infectious disease, but it is not generally considered to be cost-effective, since much of the collected product is ultimately discarded because the patient does not require it. Of the estimated 1,117,000 autologous units collected in 1992, a total of 546,000 was reported as discarded. At an estimated average cost of $137 per unit, this represents an annual loss valued at $74.80 million. These discarded autologous units represent a real cost incurred by either the hospital or other blood establishment (if unrecoverable), by the third-party payer, or by the patient for a product that provided no therapeutic value. The most recent data suggest that the volume of unnecessary autologous collections is starting to decline, with clinical practice changes and regained public trust in the blood supply. Although the shifting patterns of blood collections may largely reflect appropriate responses to actual blood safety risks, if even a fraction of the shifts result from misperceptions, due to perceived failures in government and industry risk communication, then avoidable opportunity and inefficiency costs will be incurred.

FDA cannot assume that the failure to require notification of known exposures to hepatitis C among transfusion recipients would produce a similar second round of blood supply shifts and costs. However, hepatitis C has been characterized in the media, which influences public perception, as being as lethal as AIDS (Ref. 18) and its prevalence is much greater. If timely communication and support for patients, after inadvertent exposure to hepatitis C, were to eliminate as little as 15 percent of the yearly costs associated with the supply shifts described previously, this annual saving of over $25 million would exceed the $19 million in total annualized compliance costs estimated to be imposed by this regulation (calculated over 10 years at 7 percent).

3. Alternatives Considered for HCV ''Lookback''

FDA finds that the targeted ''lookback'' approach proposed is the most effective of several alternatives when evaluated in terms of ethical, cost, and effectiveness criteria. The following provides a discussion of the alternatives that have been considered.

a. *Alternative:* Publication of FDA guidance but no regulatory requirement for ''lookback''. One alternative to regulation involves FDA taking no further action, as the agency has already issued industry guidance concerning HCV ''lookback''. The principle advantage of this approach would be the elimination of FDA expenses related to issuing and later enforcing the rule. However, although the ''lookback'' process described in the guidance is much the same as that required under the proposed rule, the approach would be less effective in achieving the desired benefits. Because FDA would only recommend a process and timeframe, but have no basis for enforcing it, some in industry may elect a more extended timeframe for performing the ''lookback'' based on the review of historical testing records in order to spread the costs of this effort. Such delay, however, would increase each recipient's risk of serious disease complications and speed the spread of infection.

For blood establishments, a potential cost of such delay would be the risk of litigation by blood recipients who discover through other means that they have contracted hepatitis C through transfusion. The risk of litigation, however, appears relatively small. Blood-product related injuries have been removed from the scope of strict liability law by blood shield laws in 47 of the 51 jurisdictions in this country. Although these laws may protect society's interest in assuring an adequate blood supply by shielding providers and manufacturers from liability claims in instances where due care is taken, they have also made it difficult and often impossible for individuals to obtain compensation for infections acquired from blood or blood products. A review of transfusion associated AIDS litigation for the period 1984 through 1993 (Ref. 20) reports only a handful of cases based on failure of a blood establishment to perform ''lookback'' and none were reported won by a plaintiff on this basis. The adoption of an approach involving agency informal action based on the expectation of industry self-regulation to solve problems has been strongly criticized in the IOM review as inadequate to protect the public in the context of HIV/AIDS. FDA believes this view is similiarly applicable to HCV.

b. *Alternative:* Use of general ''lookback.''. An alternative to targeted ''lookback'' is an approach referred to as ''general lookback.'' This approach would be implemented through the general broadcast and other public media and regional medical organizations. The program would be aimed at all patients who received blood before the onset of screening, with the recommendation that they be tested for evidence of infection. Physicians participate in the program by recommending that previously transfused patients be tested for HCV. The program often includes a letter campaign to all previously transfused patients (regardless of the HCV status of the blood donors) from hospitals and other blood consignees who performed the transfusion service.

The cost and ultimate effectiveness of general ''lookback'' would vary depending on the program structure. All of the general ''lookback'' approaches involve reduced costs for blood collection centers, because the identification of infected donors would no longer be required. Nevertheless, if the general ''lookback'' involves a consignee letter campaign, the record review needed to identify current addresses for all transfusion recipients could be as great or greater than that required to identify only those recipients of blood products who are at higher risk of HCV.

A recent Canadian effort involving general letter ''lookback'' is estimated to have cost $1,654 per identified and confirmed positive recipient ($2,123 including HCV testing) (Ref. 7). Another Canadian hospital had completed a general letter ''lookback'' for HCV when the Canadian Red Cross Society began targeted ''lookback'' in 1995. By April of 1998, at least 13 new seropositive recipients had been identified by targeted ''lookback'' who were missed by general ''lookback.'' As a result, targeted ''lookback'' raised the number of HCV-positive recipients tested at that hospital by at least 9 percent over general ''lookback.''

A general approach without letter notification can be less costly. A 1990 electronic media program in Cincinnati, for example, was estimated to have cost the blood center only $13,370, or $209 per identified positive recipient; although the authors note that ''costs to the notified recipients may far exceed those of the Center'' (Ref. 19). Despite the vigorous public information campaign, less than 5 percent of these recipients sought testing (Ref. 24). The CDC also is undertaking a program of general ''lookback'' media activities, but evidence of effectiveness is not yet available.

At this time, FDA believes that although general ''lookback'' may be less costly, it is unlikely to communicate the relevant risk message to the majority of affected transfusion recipients. The effectiveness of a general ''lookback'' program requires that patients: (1) Be reached by the program, (2) be aware of the transfusion episode, and (3) seek testing even though the average risk per recipient is small. Experience suggests that a substantial share of patients and families are not

aware of earlier transfusions. A review of general ''lookback'' efforts in Canada, for example, found that 25 to 32 percent of pediatric patients and their families were unaware of an earlier transfusion. FDA agrees that general ''lookback'' activities can be important, particularly by reaching the population at risk due to parenteral drug use or other risk behaviors not involving blood transfusion. General ''lookback'' activities can also reinforce the effectiveness of targeted ''lookback.'' The agency believes, however, that by itself, general ''lookback'' does not adequately inform all affected recipients of blood transfusions.

c. *Proposed: Use of targeted ''lookback.''* The ''lookback'' provisions of the proposed rule can be characterized as a ''targeted lookback'' program, meaning that the notification of infection risk is limited to or targeted at individuals identified as recipients of blood from donors subsequently found to be infected with HCV. Targeted ''lookback'' requires that the transfusion service be aware that the donor subsequently tested positive, donor and product disposition records be available to link blood components with the identified donors, and the physician or transfusion service know the recipient's current whereabouts. Blood consignees would locate recipient records for all transfused units from an affected donor, and have current recipient or physician address information available so that notifications can be delivered. Ideally, the recipient will still be alive and be able to receive testing and treatment, if appropriate.

Recent experiences among Canadian facilities implementing HCV ''lookback'' suggest that the effectiveness of targeted ''lookback'' may vary, depending on the extent to which these conditions for success hold true within a community. For example, a Canadian Red Cross Center in Toronto reported that although able to identify 5,301 affected components, trace 3,209 of those to hospitals, obtain responses for 2,807 (87 percent) of the units, and identify 2,437 as having been transfused, the establishment found that 45 percent of the transfused patients had already died. Of those remaining, only 184 patients (8 percent of the transfused) were finally tested as a result of the ''lookback'' effort, although as many as 68 percent of those tested were found to be HCV positive (Ref. 21).

Despite the difficulties of implementing targeted ''lookback,'' FDA concludes that it remains a valuable means of reaching patients at high risk for HCV. As noted previously, a comparison of Canadian efforts in targeted ''lookback'' versus general ''lookback'' through physician and public education found that a large number of targeted patients and families were unaware of the transfusion episode. These recipients would not have been reached through the general ''lookback'' effort (Ref. 7). Similar experiences have occurred with HIV ''lookback'' efforts (Ref. 22).

C. Small Business Impact

Because of the lack of information to characterize the relevant volumes of affected blood and plasma products, the impact on those establishments and consignees that might qualify as small entities is uncertain. The FDA has therefore prepared an Initial Regulatory Flexibility Analysis. The blood establishments and blood product consignees affected by the proposed rule are included under the major SIC (standard industrialization classification) group 80 for providers of Health Services. According to Section 601 of the Regulatory Flexibility Act of 1980, the term ''small entity'' encompasses the terms ''small business,'' ''small organization'' and ''small governmental jurisdiction.'' According to the Small Business Administration (SBA), a small business within the blood industry is an enterprise with less than $5 million in annual receipts. A small organization is a not-for-profit enterprise which is independently owned and operated and is not dominant in its field. A ''small governmental jurisdiction'' generally means governments of cities, counties, towns, townships, villages, school districts, or special districts, with a population of less than 50,000.

The FDA registry of blood establishments does not provide an indication of the size of the registered entities. Although uncertain, it is likely that some smaller facilities may experience significant costs as a result of compliance with the proposed rule. According to the 1996 directory of the American Association of Blood Banks (AABB), only 34 regional and community blood centers have annual revenues of less than $5 million and each collect no more than 30,000 donations per year. Based on their survey of the blood industry in 1992, Wallace et al. (Ref. 3) estimate an annual total of 12,035,000 units of allogeneic blood were collected by blood establishments. Each small blood center would therefore account for approximately 0.2 percent (30,000/12,035,000) of all collections. Assuming that the one-time and annual costs of HCV ''lookback'' for blood collection facilities (see table 1 of section IV of this document) will be proportionate to the volume of collections, this implies that the small centers would each experience a one-time cost of approximately $72,229 ($36,114,442 x 0.002) and yearly costs of approximately $9,117 ($4,558,442 x 0.002). Based on an estimated average price of $103 per allogeneic unit (see footnote 1) this one-time cost would represent approximately 2 percent ($72,229/($103 x 30,000)) of annual average revenues. The yearly costs of on-going prospective ''lookback'' would represent approximately 0.3 percent of average annual revenues ($9,117/($103 x 30,000)).

Hospitals are expected to be the primary entity affected by the proposed requirements for transfusion services, but the extent of the small business impact is uncertain. Although the details of transfusion activities at hospitals are not available, FDA examined other data to develop a preliminary assessment of small business impact. The size of U.S. hospitals varies substantially. The 1998 American Hospital Association (AHA) survey data indicate a total of 5,134 U.S. registered community hospitals grouped into eight bed size categories. The average annual revenues for facilities in these bed size categories range from approximately $5.5 million to $513 million. However, since many hospitals are not-for-profit or are operated by state and local governments, the SBA annual receipts criteria for small businesses would not apply to these facilities. Of the 5,134 U.S. community hospitals included in the AHA report 1,330 are under the control of State and local government, 3,045 are nonprofit institutions and the remaining 759 are reported to be investor-owned.

The number of hospitals that would meet at least one of the various SBA definitions for small entities is uncertain. According to the AHA statistics for 1998, the smallest reported hospital size category includes 262 hospitals with 6 to 24 beds, and total gross revenues of $1.43 billion, yielding average revenues of $5.46 million. FDA assumes that the 11 facilities reported to be investor-owned within this bed size category could qualify as small entities. Although it is possible that all nonprofit hospitals may qualify as small entities, it appears that a number of facilities might be excluded from that definition because they are reported to be hospitals in a system. According to the AHA survey definition, ''hospitals in a system'' refer to those ''hospitals belonging to a corporate body that owns and/or manages health provider facilities or health-related subsidiaries;

the system may also own non-health-related facilities'' (Ref. 23). The AHA currently has record of 1,592 hospitals that are non-Federal and nonprofit (including State and local government controlled) that are hospitals in a system. If these facilities were excluded, FDA estimates that 2,783 (1,330 State and local + 3,045 nonprofit − 1,592 in-a-system) non-Federal, nonprofit hospitals may qualify as small entities. Thus, a total of 2,794 (2,783 + 11) hospitals might qualify as small entities.

The agency does not know how many of the estimated affected transfusion recipients received their transfusion as part of care provided at a hospital qualifying as a ''small entity.'' The following analysis of potential impact by size of hospital suggests that, regardless of hospital size, the cost impact may be limited if the number of affected transfusion recipients is proportionate to the number of inpatient surgeries performed by hospitals in different size categories. Table 3 of this document estimates the percentage of all inpatient hospital surgeries, based on the number of inpatient surgeries reported to AHA as performed by hospitals in different bed size categories. This percentage is used to estimate a share of the total 303,676 retrospective recipient notification activities initiated by hospitals in each category. The number of transfusion recipients to be contacted per hospital within a bed size category is based on the total estimated recipients per bed size category divided by the number of hospitals reported for each category. These estimates are presented in the right-most column of table 3. (Note that estimated values are rounded).

TABLE 3.—ESTIMATED NUMBER OF AFFECTED BLOOD RECIPIENTS PER HOSPITAL, BASED ON ESTIMATED NUMBER OF FACILITIES AND DISTRIBUTION OF IMPORTANT SURGERIES BY HOSPITAL SIZE CATEGORY (RETROSPECTIVE REVIEW)

Bed Size Category	Non-Federal Hospitals	Estimated Percent Inpatient Surgeries	Estimated Share of Recipients	Estimated Recipients per Hospital
6 to 24	262	0.21	627	2
25 to 49	906	2.02	6,121	7
50 to 99	1,128	6.03	18,315	16

Table 4 presents estimates of the cost per hospital, which are derived from estimates of the number of transfusion recipients per hospital (as shown in table 3) and the estimated notification cost of $165 per recipient. To provide additional perspective on relative impact, table 4 includes the notification cost shown as a percentage of average annual gross revenues per hospital. The notification cost is estimated to be approximately 0.01 percent of the average annual gross revenues for every size category.

TABLE 4.—ESTIMATED NOTIFICATION COST AS A PERCENT OF GROSS ANNUAL REVENUE, BASED ON ESTIMATES OF AVERAGE ANNUAL HOSPITAL REVENUE

Bed Size Category	Cost per Hospital for Retrospective Notification	Gross Annual Revenue per Hospital	Notification Cost as Percent of Gross Annual Revenue
6 to 24	$395	$5.459 million	0.01 percent
25 to 49	$1,115	$12.606 million	0.01 percent
50 to 99	$2,679	$27.711 million	0.01 percent
100 to 199	$7,256	$74.803 million	0.01 percent

A similar analysis of the yearly cost impact of prospective on-going notification, that would involve an estimated 12,816 affected components distributed across all hospitals, produces costs per hospital per year ranging from $17 per facility for the smallest hospital size category, to approximately $1,936 per facility for hospitals in the 500 + bed size category. For all bed size categories, the estimated yearly costs represent less than one-thousandth of a percent of average annual revenues.

These findings of the Initial Regulatory Flexibility Analysis suggests that the relative cost impact may be fairly consistent across hospitals of different sizes, if the number of affected transfusion recipients per hospital is proportionate to the number of inpatient surgeries performed by hospitals in different size categories. However, the distribution of affected transfusion recipients across hospitals of different size and types of ownership is currently unknown. Because this information is essential for the estimation of the economic impact on small entities, FDA requests industry comment on the anticipated numbers of affected transfusion recipients, the ability to trace transfused products, and the volume of transfused products handled by consignees, particularly those that can be classified as small entities.

In general, it is expected that the regulatory costs for blood establishments will be a function of the volume of donors, the number of donations testing repeatedly reactive in a screening test for evidence of HCV infection, the volume of donor blood components that must be traced, the quality of facility recordkeeping and the number of different consignees to which the collection facility distributes blood products. These factors are likely to be larger and generate higher potential costs for larger blood establishments. Yet careful screening is already in place in most facilities, which will minimize the number of affected units over time. It is similarly expected that transfusing facilities will already have recordkeeping systems and SOP's in place that can be readily adapted to HCV ''lookback.'' Also, recordkeeping and procedures to support targeted ''lookback'' for HIV are expected to provide a ready capability to trace donations and components affected by the proposed rule. FDA anticipates therefore that most of the information infrastructure needed for HCV ''lookback'' will already be in place for both blood establishments and blood transfusion services. For both types of establishments, the cost of compliance will primarily involve additional staff time.

As described earlier, FDA has considered several alternatives, and considers that a targeted ''lookback'' will be the most effective approach to contacting affected recipients of HCV-infected blood products. However, within that approach the agency allows for flexibility in the facility's individual approach to compliance, to help minimize the resource impact. For example, the particular design and systems for record-keeping and standard operating procedures developed in response to the proposed rule are under the control of the facility, as is the approach taken to notification. This will enable each facility to develop procedures that are most appropriate and cost-effective given the resources available. In addition, the agency has specified a limited time frame for notification, and a maximum required number of attempts, in order to provide a clear endpoint to facility efforts related to the ''lookback.''

Although FDA has obtained initial estimates of the number of blood centers that would be classified as small entities, the agency currently does not have data on the distribution of repeat donors, donations testing repeatedly reactive in a screening test for evidence of HCV infection, and affected blood components, for those establishments that would qualify as small business entities. Because this information is essential for the estimation of the economic impact on small businesses, FDA requests industry comment on the current recordkeeping, the ability to trace products, and the volumes of donation units and components handled by these facilities.

V. The Paperwork Reduction Act of 1995

This proposed rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (the PRA) (44 U.S.C. 3501–3520). The title, description, and respondent description of the information collection provisions are shown in section V of this document with an estimate of the annual reporting and recordkeeping burden. Included in this estimate is the time for reviewing the procedures, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

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

Title: Reporting and recordkeeping requirements within Current Good Manufacturing Practices for Blood and Blood Components: Notification of Consignees and Transfusion Recipients Receiving Blood and Blood Components at Increased Risk for Transmitting HCV Infection (''lookback'').

Description: This proposed rule would require that blood establishments prepare and follow written procedures when the blood establishments have collected Whole Blood, blood components, Source Plasma, and Source Leukocytes later determined to be at risk for transmitting HCV infections. Under the proposed rule, blood establishments would be required to include procedures that are similar to procedures now in effect for HIV ''lookback'' (§§ 610.46 and 610.47), for clarifying the status of the donor who later tests repeatedly reactive in a licensed screening test for HCV, quarantining prior collections from such donors, and notifying transfusion recipients, as appropriate, based on further testing of the donor. When a donor who previously donated blood is tested in accordance with § 610.40 on a later donation, and tests repeatedly reactive for antibody to HCV, the blood establishment would be required to perform a supplemental test using a licensed test, and notify consignees who received Whole Blood, blood components, Source Plasma, and Source Leukocytes from prior collections so that appropriate action is taken. Blood establishments and consignees would be required to quarantine previously collected Whole Blood, blood components, Source Plasma and Source Leukocytes from such donors (some exemptions apply), and where appropriate, consignees would notify transfusion recipients.

Under the proposed rule, blood establishments additionally would be required to perform a one-time retrospective review of historical HCV testing records that will identify prior collections from donors at increased risk for transmitting HCV. The retrospective review of HCV testing records would be limited to a period of time that is 12 months prior to the last negative licensed multiantigen screening test, whenever there is a record of such a prior test. Blood establishments would be required to notify consignees of the risk of HCV transmission that exists for prior collections based on the retrospective review of HCV testing records and the results of the supplemental HCV testing performed before or as a result of the retrospective review of testing records. Blood establishments would notify consignees of the risk of HCV transmission that exists for prior collections from a donor who tested repeatedly reactive on a screening test for HCV and for whom the blood establishment has no record of further testing and further testing is impractical or infeasible (an exception may apply). Under this proposal, consignees would notify the transfusion recipients.

FDA is also proposing conforming amendments to certain provisions of §§ 610.46 and 610.47, the HIV ''lookback'' regulations (61 FR 47413, September 9, 1996). The proposed revisions to §§ 610.46 and 610.47, discussed under the corresponding sections of this proposal, are intended to clarify and provide consistency between the HIV and HCV ''lookback'' requirements but do not include a requirement for the retrospective review of historical HIV testing records. The agency is issuing this proposed rule to help ensure that the blood supply continues to be safe, that information is provided to users of blood and blood components, and that transfusion recipients of blood and blood components at risk for transmitting HCV will be notified, as appropriate.

Description of Respondents: Blood establishments (Business and Not-for-Profit) and consignees of blood establishments, including hospitals, transfusion services and physicians.

The total reporting and recordkeeping burden for the first year is estimated to be 492,148 hours. However, of this total approximately 470,237 hours would be expended on a one-time basis for establishing the written procedures and doing the one-time retrospective review of historical HCV testing records. Therefore, 21,911 hours is estimated as the ongoing annual burden related to this proposed regulation. The total ongoing annual burden for blood collection facilities under §§ 610.46(a), 610.46(b), 610.47(b) and 606.160(b)(1)(viii) for HIV ''lookback'' is estimated to be 1,843 hours. The total ongoing annual burden for blood collection facilities under §§ 610.48(a)(1)(ii), 610.48(b), 610.49(b), 610.49(c) and 606.160(b)(1)(viii) for

HCV ''lookback'' is estimated to be 20,698 hours.

Based on information previously discussed in section IV of this document, there are approximately 2,800 FDA registered blood establishments in the United States that collect approximately 12 million allogeneic donations annually. The CDC estimates there are approximately 9,628,000 donations from repeat donors per year. The following reporting and recordkeeping estimates are based on information provided by industry, and FDA experience.

1. HIV Reporting Burden

In table 5, it is estimated that approximately 3,500 repeat donors (an annual average of 1.25 repeat donors per establishment) will test repeatedly reactive on a screening test for HIV. Under proposed §§ 610.46(a) and (b), this estimate results in 3,500 notifications of the HIV screening test results to consignees by blood establishments for the purpose of quarantine of affected units, and another 3,500 notifications to consignees of subsequent test results. FDA estimates an average of 10 minutes per notification of consignees.

In addition, it is estimated that 180 transfusion services not subject to HCFA regulations will be required under § 610.47(b) to notify physicians, or in some cases recipients, an average of 0.14 times per year resulting in a total number of 25 notifications. The estimate of one-half hour for notifications under § 610.47(b) is based on the minimum requirement of three attempts to notify recipients by transfusion services. FDA estimates that each repeat donor has donated two previous times and two components were made from each donation. The estimates for HIV ''lookback'' provided in the tables differ from the estimates for HIV ''lookback'' provided in a notice published in the **Federal Register** of November 4, 1999 (64 FR 60212) because FDA has new, updated information from industry representatives from which to base its estimates.

2. HCV Reporting Burden

Based on the interim results from a recent CDC survey (ref. 4), CDC estimates that 11,520 repeat donors per year would test repeatedly reactive for antibody to HCV. Under proposed §§ 610.48(a)(1)(ii) and 610.48(b), blood establishments would notify the consignee two times for each of the 12,816 components prepared from these donations, once for quarantine purposes and again with additional HCV test results for a total 25,632 notifications as an annual ongoing burden. Under proposed § 610.49(b) and (c), FDA estimates that approximately 6,200 transfusion services would notify two recipients annually.

A. HCV One-time Reporting Burden

Based on estimates from CDC, FDA expects that for the one-time retrospective review of historical testing records, as many as 303,676 blood components would be at increased risk for transmitting HCV. For each of these products, under §§ 610.48(e)(2), 610.48(f)(2), 610.48(h)(3)(i) and (ii), and 610.48(i)(3)(i) and (ii), blood establishments would notify consignees to quarantine these products and report additional HCV test results to consignees, and, under § 610.49(b) and (c), consignees would notify transfusion recipients or recipients' physicians of record. CDC estimated that there could be approximately 258,125 transfusion recipients that would be notified after a one-time retrospective review of historical test results for HCV screening. The numbers in the hours per response column are based on FDA's knowledge and experience regarding notification.

B. HCV Ongoing Annual Reporting Burden

Under § 610.49(b) and (c), it is estimated that transfusion services may be expected to notify approximately 10,894 transfusion recipients per year, as previously discussed. The estimated average 0.5 hours to complete notification under §§ 610.47(b), 610.49(b) and (c) is based on FDA's knowledge and experience. The estimates of 13 hours, 5,447 hours, and 129,063 hours, respectively, allow for a consignee to make up to three attempts to complete the notification process.

3. HIV and HCV Recordkeeping Burden

In the recordkeeping charts, the numbers in the hours per record column are based on FDA's estimate of the time to complete one record. FDA estimates that it will take blood collection facilities approximately 40 hours to establish the written procedures proposed under § 606.100(b)(19) and consignees approximately 16 hours to establish written procedures in accordance with proposed § 610.49(b) and (c). In table 7, the estimate of 154 recordkeepers and 175 total annual records are based on the estimate that the HIV ''lookback'' requirements of § 610.47(b) are already implemented voluntarily by more than 95 percent of the facilities, which collect 98 percent of the Nation's blood supply. FDA estimates that it takes transfusion services approximately 10 minutes to document and maintain the records to relate the donor with the unit number of each previous donation. The time required for recordkeeping under § 606.160(b)(1)(viii) is estimated to be approximately 10 minutes for each HIV or HCV repeatedly reactive donation record and approximately 10 minutes per transfusion recipient record required under §§ 610.47(b) and 610.49(b) and (c).

FDA estimates the burden for this collection of information as follows:

TABLE 5.—ESTIMATED ANNUAL REPORTING BURDEN[1]

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
610.46(a)	2,800	1.25	3,500	.17	600
610.46(b)	2,800	1.25	3,500	.17	600
610.47(b)	180	0.14	25	.50	13
610.48(a)(i)(ii)	2,800	4.6	12,816	.17	2,179
610.48(b)	2,800	4.6	12,816	.17	2,179
610.49(b)and (c)	6,200	2	10,894	.50	5,447
Total					11,018

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

TABLE 6.—ESTIMATED ONE-TIME REPORTING BURDEN[1]

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Respondents	Hours per Response	Total Hours
610.48(e)(2)	2,800	41	115,228	.1	11,523
610.48(f)(2)	2,800	67	188,448	.1	18,845
610.48(h)(3)(i) and (h)(3)(ii)	2,800	41	115,228	.1	11,523
610.48(i)(3)(i) and (i)(3)(ii)	2,800	67	188,448	.1	18,845
610.49(b) and (c)	6,200	42	258,125	.5	129,063
Total					189,799

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

TABLE 7.—ESTIMATED ANNUAL RECORDKEEPING BURDEN[1]

21 CFR Section	No. of Recordkeepers	Annual Frequency of Recordkeeping	Total Annual Records	Hours per Record	Total Hours
606.160(b)(1)(viii)					
HIV	154	1.14	175	.17	30
HIV	2,800	1.25	3,500	.17	600
HCV	2,800	9	25,632	.17	4,357
606.160(b)(1)(viii)	6,200	4	25,632	.17	4,357
610.49(b) and (c)	6,200	2	12,816	.17	2,179
Total					11,523

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

TABLE 8.—ESTIMATED ONE-TIME RECORDKEEPING BURDEN[1]

21 CFR Section	No. of Recordkeepers	Frequency of Recordkeeping	Total Records	Hours per Record	Total Hours
606.100(b)(19)	2,800	1	2,800	40	112,000
606.100(b)(19)	6,200	1	6,200	16	99,200
606.160(b)(1)(viii)	2,800	108	303,676	0.08	24,294
606.160(b)(1)(viii)	6,200	49	303,676	0.08	24,294
610.49(b) and (c)	6,200	42	258,125	0.08	20,650
Total					280,438

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

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

In compliance with the Paperwork Reduction Act of 1995 (44 U.S.C. 3507(d)), the agency has submitted the information collection provisions of this proposed rule to OMB for review. Interested persons are requested to submit written comments regarding information collection by December 18, 2000, to the Office of Information and Regulatory Affairs, OMB (address above), Attention: Wendy Taylor, Desk Officer for FDA.

VI. Request for Comments

Interested persons may submit to the Dockets Management Branch (address above) written comments regarding this proposed rule by February 14, 2001. 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.

VII. Proposed Effective Date

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

VIII. References

The following references have been placed on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Alter, M., ''Epidemiology of Hepatitis C,'' *Hepatology*, 26:62S–65S, 1997.

2. Alter, M., ''Epidemiology of Hepatitis C,'' *Hepatology*, 26:62S–65S, 1997.

3. Wallace, E. L., W. H. Churchill, D. M. Surgenor, J. An, G. Cho, S. McGurk, and L. Murphy, ''Collection and Transfusion of Blood and Blood Components in the United States, 1992,'' *Transfusion*, 35: 802–812, 1995.

4. Alter, M., CDC Survey Interim Results.

5. MacPherson, J., America's Blood Centers, ''Advisory Committee on Blood Safety and Availability'' Tenth Meeting, vol. II, p. 7.

6. Quattrocchi, R., Home Access Health Corp.

7. Goldman, M., S. Juodvalkis, P. Gill, and G. Spurll, ''Hepatitis C Lookback,'' *Transfusion Medicine Review*, vol. 12, No. 2: 84–93, 1998.

8. U.S. Department of Health and Human Services, Center for Disease Control and Prevention, ''Recommendations for Prevention and Control of Hepatitis C Virus (HCV) Infection and HCV–Related Chronic Disease,'' *Morbidity and Mortality Weekly Report*, vol. 47, No. RR–19, October 16, 1998.

9. Kim, W. R., J. J. Poterucha, J. E. Hermans, T. M. Therneau, E. R. Dickson, R. W. Evans, and J. B. Gross, ''Cost-Effectiveness of 6 and 12 Months of Interferon-alfa Therapy for Chronic Hepatitis C,'' *Annals of Internal Medicine*, vol. 127, No. 10, November 1997.

10. Davis, G. L., and J. Y. N. Lau, ''Factors Predictive of a Beneficial Response to Therapy of Hepatitis C,'' *Hepatology*, vol. 26, No. 3, Suppl.1: 122s–126s.

11. Bennett, W. G., Y. Inoue, J. R. Beck, J. B Wong, S. G. Pauker, and G. L. Davis, ''Estimates of the Cost-Effectiveness of a Single Course of Interferon-alfa2b in Patients with Histologically Mild Chronic Hepatitis C,'' *Annals of Internal Medicine*, vol. 127, No. 10, November 1997.

12. National Institutes of Health (NIH) Consensus Development Conference Panel Statement: Management of Hepatitis C,

Hepatology, vol. 26, No. 3, Suppl. 1:2s–10s, 1997.

13. Dusheiko, G., ''Side Effects of Alpha Interferon in Chronic Hepatitis C,'' *Hepatology*, vol. 26, No. 3, Suppl. 1:112s–119s, 1997.

14. J. G. McHutchison et al., *New England Journal of Medicine*, 339: 1485, 1998.

15. Leveton, L. B., H. C. Sox, Jr., and M. A. Stoto, editors, *HIV and the Blood Supply: An Analysis of Crisis Decisionmaking*, Chapter 7, Institute of Medicine, National Academy Press, Washington, DC, 1995.

16. Ottosen, J. S., *The Blood Conspiracy: How to Avoid Getting AIDS and Hepatitis in a Transfusion*, Aspen Leaf Press, Woodland Park, CO, 1993.

17. Moreno, J. D., ''Attitudes Toward Risk: The Right to Know and the Right to Give Informed Consent'' in *Blood and Blood Products: Safety and Risk*, Institute of Medicine, National Academy Press, Washington, DC, 1996.

18. Groopman, J., ''The Shadow Epidemic'' *The New Yorker*, May 11, 1998.

19. Zuck, T. F., G. A. Rose, U. J. Dumaswala, N. J. Geer, ''Experience with a Transfusion Recipient Education Program about Hepatitis C,'' *Transfusion*, vol. 30, No. 8, 761, 1990.

20. Kern, J. M., and B. B. Croy, ''A Review of Transfusion-Associated AIDS Litigation: 1984 Through 1993,'' *Transfusion*, vol. 34, No. 6, 1994.

21. Wall, A., W. Lau, J. Lewis, J. A. Chiavetta, S. Mohammad, and R. Herst, ''Hepatitis C Virus (HCV) Targeted Lookback Program,'' *Transfusion*, vol. 37 Suppl. s392, 1997.

22. Gill, M. J., D. Towns, S. Allaire, and G. Meyers, ''Transmission of Human Immunodeficiency Virus Through Blood Transfusion: The Use of Lookback and Traceback Approaches to Optimize Recipient Identification in a Regional Population,'' *Transfusion*, vol. 37, 513–516, 1997.

23. Healthcare InfoSource, Inc., a subsidiary of the American Hospital Association, *Hospital Statistics*, 1998 ed., Chicago IL.

24. AuBuchon, J., ''Public Health, Public Trust, and Public Decision Making: Making Hepatitis C Virus Lookback Work,'' *Transfusion*, vol. 39, p. 124, 1999.

List of Subjects

21 CFR Part 606

Blood, Labeling, Laboratories, Reporting and recordkeeping requirements.

21 CFR Part 610

Biologics, Labeling, Reporting and recordkeeping requirements.

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

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

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

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

2. Section 606.100 is amended by revising paragraph (b)(19) to read as follows:

§ 606.100 Standard operating procedures.

* * * * *

(b) * * *

(19) Procedures in accordance with §§ 610.46 and 610.48 of this chapter to look at prior donations of blood and blood components from a donor who has donated blood and subsequently tests repeatedly reactive for evidence of human immunodeficiency virus (HIV) infection or hepatitis C virus (HCV) infection when tested in accordance with § 610.40 of this chapter or when a blood establishment has been made aware of other test results indicating evidence of HIV or HCV infection. Procedures to quarantine in-date blood and blood components, intended for further manufacture into injectable products that were obtained from such donors; procedures to notify consignees regarding the need to quarantine such products; procedures to determine the suitability for release of such products; procedures to notify consignees of blood and blood components from such donors of the results of the HIV and HCV testing performed on such donors; procedures in accordance with §§ 610.47 and 610.49 of this chapter to notify physician of record so that recipients of transfusion with blood or blood components are informed that they may have received blood or blood components at increased risk of transmitting HIV and HCV, respectively.

* * * * *

3. Section 606.160 is amended by revising paragraph (b)(1)(viii) and the second sentence of paragraph (d) to read as follows:

§ 606.160 Records.

* * * * *

(b) * * *

(1) * * *

(viii) Records of quarantine, consignee notification, further testing, transfusion recipient notification, and disposition performed under §§ 610.46, 610.47, 610.48, and 610.49 of this chapter.

* * * * *

(d) * * * The retention period shall be no less than 10 years after the records of processing have been completed or 6 months after the latest expiration date for the individual product, whichever is the later date. * * *

* * * * *

PART 610—GENERAL BIOLOGICAL PRODUCTS STANDARDS

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

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

5. Section 610.40 is amended by adding paragraph (g) to read as follows:

§ 610.40 Test for hepatitis B surface antigen.

* * * * *

(g) For a donor whose test result for HIV or HCV is repeatedly reactive when tested in accordance with paragraphs (a), (c), and (d) of this section, or when a blood establishment has been made aware of other test results indicating evidence of HIV or HCV infection, the blood establishment shall comply, as applicable, with §§ 610.46, 610.47, 610.48, and 610.49.

6. Section 610.46 is amended by revising the section heading and paragraph (a), the heading for paragraph (b), the first sentence of paragraphs (b) and (c), and paragraph (d); by redesignating paragraph (e) as paragraph (f); by revising newly redesignated paragraph (f); and by adding new paragraph (e) to read as follows:

§ 610.46 Human Immunodeficiency Virus (HIV) ''Lookback;'' quarantine, consignee notification and further testing.

(a) *Quarantine and consignee notification.* (1) All blood and plasma establishments shall take appropriate action when a donor of blood or blood components tests repeatedly reactive for evidence of HIV infection on a screening test in accordance with § 610.40(a), or when the blood establishment has been made aware of other test results indicating evidence of HIV infection, provided the testing was performed by a laboratory certified under the Clinical Laboratory Improvement Amendments of 1988, using a test approved by FDA. For blood and blood components collected from that donor at any time prior to the repeatedly reactive test, whenever records are available, if intended for transfusion or for further manufacture into injectable products, except those products exempt from quarantine in accordance with paragraph (c) of this section, the blood establishment shall, within 3-calendar days after the date on which the donor tested repeatedly reactive for evidence of HIV infection or after the date on which the blood establishment was made aware of other test results

indicating evidence of HIV infections, identify the prior collections from that donor and:

(i) Quarantine all such prior collections of blood and blood components; and

(ii) Notify consignees of the repeatedly reactive HIV screening test result so that the consignee may quarantine all such prior collections of blood and blood components.

(2) Consignees notified in accordance with paragraph (a)(1)(ii) of this section shall quarantine all such prior collections of blood and blood components held at that establishment, except as provided in paragraph (c) of this section.

(b) *Further testing and consignee notification of results.* Blood establishments shall perform further testing on the donor's blood, as specified in § 610.40(c), and shall notify the consignee(s) of the results of this test within 45-calendar days after the date on which the donor tested repeatedly reactive for evidence of HIV infection on a screening test. * * *

(c) *Exemption from quarantine.* Prior collections otherwise subject to quarantine under paragraph (a) of this section need not be held in quarantine if a determination has been made that the blood or blood component was collected more than 12 months prior to the donor's most recent negative screening test when tested for HIV in accordance with § 610.40(a). * * *

(d) *Release from quarantine.* Prior collections of blood and blood components intended for transfusion or further manufacture into injectable products which have been quarantined under paragraph (a) of this section may be released if the donor's current repeatedly reactive sample is subsequently tested for antibody to HIV as provided in paragraph (b) of this section and the test result is negative, absent other informative test results.

(e) *Destruction or labeling of prior collections held in quarantine.* Blood establishments and consignees shall destroy or appropriately label for in vitro use prior collections of blood and blood components otherwise subject to quarantine in accordance with paragraphs (a) and (d) of this section, unless such prior collections are determined to be exempt from quarantine in accordance with paragraph (c) of this section or subject to release from quarantine in accordance with paragraph (d) of this section. Quarantined prior collections made available for in vitro use shall be appropriately relabeled consistent with §§ 606.121 and 640.70 of this chapter. In addition, these units must be relabeled as ''Biohazard'' with the cautionary statement as follows:

''Collected from a donor who subsequently tested positive for anti-HIV. An increased risk for transmission of human immunodeficiency virus is present;'' in addition, the label must contain one of the following cautionary statements, as appropriate: ''Caution: For Further Manufacturing Into In Vitro Diagnostic Reagents For Which There Are No Alternative Sources.'' or ''For Laboratory Research Use Only.''

(f) *Actions under this section.* Actions under this section do not constitute a recall as defined in § 7.3 of this chapter.

7. Section 610.47 is revised to read as follows:

§ 610.47 Human Immunodeficiency Virus (HIV) ''Lookback;'' notification of transfusion recipients.

(a) *Appropriate actions following further testing.* Transfusion services that are not subject to the Health Care Financing Administration's regulations on conditions of Medicare participation for hospitals (42 CFR part 482) are required to take appropriate action in accordance with paragraphs (b) and (c) of this section when a recipient has received prior collections of blood or blood components from a donor later determined to be unsuitable when tested for evidence of infection due to HIV and the result of the additional tests as provided for in § 610.46(b) are positive.

(b) *Notification of recipients of prior transfusion.* If the transfusion service has administered blood or blood components as described in paragraph (a) of this section, the transfusion service shall either notify the recipient directly or notify the recipient's physician of record (i.e., physician of record or physician who ordered the blood or blood component) and ask him or her to inform the recipient of the need for HIV testing and counseling. If the physician is not available or declines to notify the recipient, the transfusion service shall notify the recipient and inform the recipient of the need for HIV testing and counseling. The notification process shall include a minimum of three attempts to notify the recipient, or the recipient's physician, and be completed within a maximum of 12 weeks of receipt of the result of the licensed, more specific test for HIV from the blood establishment. The transfusion service is responsible for notification, including basic explanations to the recipient and referral for counseling and further testing, and shall document the notification and the result of attempts to notify the recipient and the recipient's physician of record, if contacted, under § 606.160 of this chapter.

(c) *Notification of legal representative or relative.* If the transfusion recipient has been adjudged incompetent by a State court, the legal representative, designated in accordance with State law, shall be notified. If the transfusion recipient is competent, but State law permits a legal representative or relative to receive the information on the recipient's behalf, the transfusion service or the physician who agreed to perform the notification on behalf of the transfusion service shall notify the recipient or his or her legal representative or relative. If the transfusion recipient is a minor at the time of notification, the transfusion service or physician, as described in this paragraph, shall notify the recipient's legal representative or relative. If the transfusion recipient is deceased, the transfusion service or physician, as described in this paragraph, shall continue the notification process and inform the deceased recipient's legal representative or relative. The transfusion service is responsible for notification, including basic explanations to the recipient's legal representative or relative and referral for counseling and further testing of the recipient, and shall document the notification and the result of attempts to notify the recipient's legal representative or relative and the recipient's physician of record, if contacted, under § 606.160 of this chapter. Reasons for notifying the recipient's relative or legal representative on his or her behalf shall be documented under § 606.160 of this chapter.

8. Section 610.48 is added to subpart E to read as follows:

§ 610.48 Hepatitis C Virus (HCV) ''Lookback;'' quarantine, consignee notification and further testing.

(a) *Quarantine and consignee notification.* (1) *Repeatedly reactive screening test.* All blood and plasma establishments shall take appropriate action when a donor of blood or blood components tests repeatedly reactive for evidence of HCV infection on a screening test, in accordance with § 610.40(a), or when the blood establishment has been made aware of other test results indicating evidence of HCV infection, provided the testing was performed by a laboratory certified under the Clinical Laboratory Improvement Amendments of 1988, using a test approved by FDA. For in-date blood and blood components collected from that donor at any time prior to the repeatedly reactive test,

whenever records are available, if intended for transfusion, or if intended for further manufacture into injectable products, except those products exempt from quarantine in accordance with paragraph (g)(1) of this section, the blood establishment shall, within 3-calendar days after the date on which the donor tested repeatedly reactive for evidence of HCV infection or after the date on which the blood establishment was made aware of other test results indicating evidence of HCV infection, identify the prior collections from that donor and:

(i) Quarantine all such prior collections of blood and blood components; and

(ii) Notify consignees of the repeatedly reactive HCV screening test result so that the consignee may quarantine all such prior collections of blood and blood components.

(2) *Quarantine by consignee*. Consignees notified in accordance with paragraph (a)(1)(ii) of this section shall quarantine all such prior collections of blood and blood components held at that establishment, except as provided in paragraph (g)(1) of this section.

(b) *Further testing and consignee notification of results*. In the case of a donor with a repeatedly reactive screening test for HCV, blood establishments shall perform further testing on the donor's blood, as specified in § 610.40(c). Where prior collections from the same donor were distributed, blood establishments shall notify the consignee(s) of the results of this test within 45-calendar days after the date on which the donor tested repeatedly reactive for evidence of HCV infection on a screening test.

(c) *Review of historical testing records and identification of donors tested using a multiantigen screening test prior to* [*the effective date of the final rule*]. Blood establishments shall review records of donor testing completed prior to [the effective date of the final rule] in order to identify donors who tested repeatedly reactive for evidence of HCV infection on a multiantigen screening test for HCV and to identify prior collections from such donors. Blood establishments shall, by (date 1 year from the effective date of the final rule), identify previously distributed blood and blood components from such donors, based on available required records maintained in accordance with § 606.160 of this chapter, dating back indefinitely for computerized electronic records and to January 1, 1988, for other readily retrievable records, or to the date 12 months prior to the donor's most recent negative multiantigen screening test for antibody to HCV, whichever is the lesser period. Blood establishments shall identify previously distributed blood and blood components from such donors in any of the following instances:

(1) *First instance*. Where the donor tested repeatedly reactive for evidence of HCV infection on the multiantigen screening test and positive on a supplemental test for HCV performed on the repeatedly reactive sample;

(2) *Second instance*. Where the donor tested repeatedly reactive for evidence of HCV infection on the multiantigen screening test and indeterminate on a supplemental test for HCV performed on the repeatedly reactive sample;

(3) *Third instance*. Where the donor tested repeatedly reactive for evidence of HCV infection on an HCV EIA 3.0 multiantigen screening test and negative on a HCV 2.0 strip immunoblot assay (HCV RIBA 2.0 supplemental test) with no record of a negative licensed HCV 3.0 strip immunoblot assay (RIBA 3.0 supplemental test) performed on the repeatedly reactive sample or a later sample from the same donor.

(4) *Fourth instance*. Where the donor tested repeatedly reactive for evidence of HCV infection on a licensed HCV EIA 2.0 screening test with no record of a supplemental test for HCV performed on the repeatedly reactive sample or on a later sample from the same donor and no record of a negative licensed HCV EIA 3.0 screening test performed on the repeatedly reactive sample or a later sample from the same donor; or

(5) *Fifth instance*. Where the donor tested repeatedly reactive for evidence of HCV infection on a licensed HCV EIA 3.0 screening test with no record of a supplemental test for HCV performed on the repeatedly reactive sample or on a later sample from the same donor.

(d) *Review of historical testing records and identification of donors tested using a single antigen screening test prior to [the effective date of the final rule]*. Blood establishments shall review records of donor testing completed prior to [the effective date of the final rule] in order to identify donors who tested repeatedly reactive for evidence of HCV infection on a single antigen screening test for HCV and to identify prior collections from such donors. Blood establishments shall, by (date 1 year from the effective date of the final rule), identify previously distributed blood and blood components from such donors, based on available required records maintained in accordance with § 606.160 of this chapter, dating back indefinitely for computerized electronic records and to January 1, 1988, for other readily retrievable records, or to the date 12 months prior to the donor's most recent negative multiantigen screening test for antibody to HCV, whichever is the lesser period, in any of the following instances:

(1) *First instance*. Where the donor tested repeatedly reactive for evidence of HCV infection on the single antigen screening test and repeatedly reactive on an HCV EIA 2.0 or HCV EIA 3.0 screening test performed on the repeatedly reactive sample or a fresh sample from the same donor;

(2) *Second instance*. Where the donor tested repeatedly reactive for evidence of HCV infection on the single antigen screening test and either positive or indeterminate on an HCV 2.0 or HCV 3.0 strip immunoblot assay (HCV RIBA 2.0 or HCV RIBA 3.0, respectively) supplemental test for HCV performed on the repeatedly reactive sample or a fresh sample from the same donor;

(3) *Third instance*. Where the donor tested repeatedly reactive for evidence of HCV infection on an HCV EIA 1.0 screening test, with a signal to cutoff (S/CO) value less than 2.5 for at least two out of the three EIA tests (i.e., the initial EIA screening test and the duplicate retests), with no record of a supplemental test or multiantigen screening test for HCV performed on the repeatedly reactive sample or on a later sample from the same donor; or

(4) *Fourth instance*. Where the donor tested repeatedly reactive for evidence of HCV infection on an HCV EIA 1.0 screening test, with a S/CO value equal to or greater than 2.5 for at least two out of the three EIA tests (i.e., the initial EIA screening test and the duplicate retests) or with no determination of S/CO value for all three EIA tests, and with no record of a supplemental test or multiantigen screening test for HCV performed on the repeatedly reactive sample or on a later sample from the same donor.

(e) *Quarantine and consignee notification following the review of historical testing records based on screening performed using a multiantigen screening test*. Blood establishments shall, by (date 1 year from the effective date of the final rule), complete all quarantine and consignee notification requirements for prior collections from donors identified in the review of historical testing records in accordance with paragraph (c) of this section as follows:

(1) *Quarantine*. Blood establishments shall, within 3-calendar days of the date of the identification of the donor's repeatedly reactive multiantigen screening test for HCV, quarantine all in-date prior collections of blood and blood components collected from such a donor at any time prior to the

repeatedly reactive multiantigen screening test and identified in accordance with paragraph (c) of this section, if intended for transfusion, or if intended for further manufacture into injectable products, except those products exempt from quarantine in accordance with paragraph (g)(2) of this section.

(2) *Consignee notification.* Blood establishments shall, within 3-calendar days of the date of identification of the donor's repeatedly reactive multiantigen screening test for HCV, notify consignees of the donor's test results, including the supplemental test results, if available, so that consignees may quarantine all in-date prior collections of blood and blood components subject to quarantine under paragraph (e)(1) of this section.

(3) *Quarantine by consignees.* Consignees notified in accordance with paragraph (e)(2) of this section shall quarantine all in-date prior collections of blood and blood components subject to quarantine under paragraph (e)(1) of this section, except as provided in paragraph (g)(2) of this section.

(f) *Quarantine and consignee notification following the review of historical testing records based on screening performed using a single antigen screening test.* (1) *Quarantine.* Blood establishments shall, by (date 1 year from the effective date of the final rule) and within 3-calendar days of the date of the identification of the donor's repeatedly reactive single antigen screening test for HCV, quarantine all in-date prior collections of blood and blood components collected from such a donor at any time prior to the repeatedly reactive single antigen screening test and identified in accordance with paragraph (d) of this section, if intended for transfusion, or if intended for further manufacture into injectable products, except those products exempt from quarantine in accordance with paragraph (g)(3) of this section.

(2) *Consignee notification.* Blood establishments shall, within 3-calendar days of the date of identification of the donor's repeatedly reactive single antigen screening test for HCV, notify consignees of the donor's test results, including the supplemental test results, if available, so that consignees may quarantine all in-date prior collections of blood and blood components subject to quarantine under paragraph (f)(1) of this section.

(3) *Quarantine by consignees.* Consignees notified in accordance with paragraph (f)(2) of this section shall quarantine all in-date prior collections of blood and blood components subject to quarantine under paragraph (f)(1) of this section, except as provided in paragraph (g)(3) of this section.

(g) *Exemption from quarantine.* As used in § 610.48, an appropriately chosen licensed supplemental test is one which includes all antigens contained in the screening test that was performed.

(1) *Prior collections subject to quarantine under paragraph (a) of this section.* Prior collections otherwise subject to quarantine under paragraph (a) of this section need not be placed in quarantine if a determination has been made that:

(i) The blood or blood component was collected more than 12 months prior to the donor's most recent negative multiantigen screening test when tested for HCV in accordance with § 610.40(a); or

(ii) An appropriately chosen licensed supplemental test for HCV, performed in accordance with paragraph (b) of this section has been completed within 3-calendar days of the date of the donor's repeatedly reactive screening test and the result is negative.

(2) *Prior collections subject to quarantine under paragraph (e)(1) of this section.* Prior collections otherwise subject to quarantine under paragraph (e)(1) of this section need not be placed in quarantine if a determination has been made that:

(i) The blood or blood component was collected more than 12 months prior to the donor's most recent negative multiantigen screening test for HCV that preceded the repeatedly reactive screening test; or

(ii)(A) The repeatedly reactive screening test result was obtained using an HCV EIA 2.0 screening test, and either the original sample or a later sample from the same donor was tested and found negative using an HCV RIBA 2.0 or HCV RIBA 3.0 supplemental test or an HCV EIA 3.0 screening test; or

(B) The repeatedly reactive screening test result was obtained using an HCV EIA 3.0 screening test, and either the original sample or a later sample from the same donor was tested and found negative using an HCV RIBA 3.0 supplemental test;

(3) *Prior collections subject to quarantine under paragraph (f)(1) of this section.* Prior collections otherwise subject to quarantine under paragraph (f)(1) of this section need not be placed in quarantine if the donor's testing records show that:

(i) The repeatedly reactive screening test result was obtained using an HCV EIA 1.0 screening test, and either the original sample or a later sample from the same donor was further tested and found negative using an HCV EIA 2.0 or 3.0; or

(ii) The repeatedly reactive screening test result was obtained using an HCV EIA 1.0 screening test, and either the original sample or a later sample from the same donor was tested and found negative using an HCV RIBA 2.0 or HCV RIBA 3.0 supplemental test ; or

(iii)(A) The donor, identified in accordance with paragraph (d)(1) of this section, as testing repeatedly reactive on an HCV EIA 2.0, was further tested using a HCV RIBA 2.0 or HCV RIBA 3.0 supplemental test, on a fresh sample, or frozen sample from the repeatedly reactive donation and the result was negative; or

(B) The donor, identified in accordance with paragraph (d)(1) of this section, as testing repeatedly reactive on an HCV EIA 3.0, was further tested using an HCV RIBA 3.0 supplemental test, on a fresh sample, or frozen sample from the repeatedly reactive donation and the result was negative; or

(iv) The donor identified in accordance with paragraph (d)(2) of this section, as testing indeterminate on a HCV RIBA 2.0 supplemental test, was further tested using either an HCV EIA 3.0 or a HCV RIBA 3.0 supplemental test on a fresh sample, or frozen sample from the repeatedly reactive donation and the result was negative.

(h) *Further testing following review of historical testing records and consignee notification based on screening performed using a multiantigen screening test.* (1) *Further testing.* Blood establishments that have performed the review of records and identified prior collections in accordance with paragraphs (c)(4) and (c)(5) of this section shall, by (date 1 year from the effective date of the final rule):

(i)(A) If the repeatedly reactive test result was obtained using a HCV EIA 2.0 screening test, perform a licensed supplemental test for HCV on a frozen sample from the repeatedly reactive donation, if available; or if such a frozen sample is not available, obtain a fresh sample from such a donor and perform a licensed supplemental test for HCV; or

(B) If the repeatedly reactive test result was obtained using a HCV EIA 2.0 screening test, perform a licensed HCV EIA 3.0 screening test on a frozen sample, if available, or on a fresh sample from such a donor and perform a licensed supplemental test if the HCV EIA 3.0 screening test is repeatedly reactive; or

(ii) If the repeatedly reactive test result was obtained using a HCV EIA 3.0 screening test, perform a licensed supplemental test for HCV on a frozen

sample, if available, or on a fresh sample from such a donor; or

(iii) Make a determination that neither a frozen sample from the repeatedly reactive donation nor a fresh sample from the donor is available for further testing.

(2) *Options for further testing.* Blood establishments that have performed the review of records and identified certain prior collections in accordance with paragraphs (c)(2) or (c)(3) of this section, and as described in paragraphs (h)(2)(i) through (h)(2)(iv) of this section may further test a frozen sample from the repeatedly reactive donation or a fresh sample from the same donor by (date 1 year from the effective date of the final rule), as follows:

(i) Donors identified in accordance with paragraph (c)(2) of this section as testing repeatedly reactive using an HCV EIA 2.0 screening test, and indeterminate on an HCV RIBA 2.0 supplemental test, may be further tested using either a licensed HCV EIA 3.0 screening test or a currently available licensed supplemental test for HCV;

(ii) Donors identified in accordance with paragraph (c)(2) of this section as testing repeatedly reactive using an HCV EIA 2.0 screening test, indeterminate on a HCV RIBA 2.0 supplemental test, and repeatedly reactive on an HCV EIA 3.0 screening test, performed in accordance with paragraph (h)(2)(i) of this section, may be further tested using an appropriately chosen licensed supplemental test for HCV;

(iii) Donors identified in accordance with paragraph (c)(2) of this section as testing repeatedly reactive using an HCV EIA 3.0 screening test, and indeterminate on a HCV RIBA 2.0 supplemental test, may be further tested using an appropriately chosen licensed supplemental test for HCV;

(iv) Donors identified in accordance with paragraph (c)(3) of this section as testing repeatedly reactive using an HCV EIA 3.0 screening test, and negative on a HCV RIBA 2.0 supplemental test with no record of a negative HCV RIBA 3.0 supplemental test, may be further tested using an appropriately chosen licensed supplemental test for HCV.

(3) *Consignee notification.* Except for blood and blood components exempt from quarantine in accordance with paragraph (g)(2) of this section, blood establishments shall:

(i) Within 45 days following completion of additional testing and prior to (date 1 year from the effective date of the final rule), notify consignees of the results of the additional licensed screening test and/or the licensed, supplemental test performed in accordance with paragraphs (h)(1) and (h)(2) of this section; or

(ii) Prior to (date 1 year from the effective date of the final rule), notify consignees of the test results for a donor who was identified in the review of historical testing records, in accordance with paragraphs (c)(1) through (c)(5) of this section.

(i) *Further testing following review of historical testing records and consignee notification based on screening performed using a single antigen screening test.* (1) *Further testing.* Blood establishments that have performed the review of records and identified prior collections in accordance with paragraph (d)(4) of this section shall, by (date 1 year from the effective date of the final rule):

(i) Perform a licensed, supplemental test for HCV on a frozen sample from the repeatedly reactive donation, if available; or if such a frozen sample is not available, obtain a fresh sample from such a donor and perform a licensed supplemental test for HCV; or

(ii) Make a determination that neither a frozen sample from the repeatedly reactive donation nor a fresh sample from the donor is available for further testing.

(2) *Options for further testing.* Blood establishments that have performed the review of records and identified certain prior collections in accordance with paragraphs (d)(1) or (d)(2) of this section and described in paragraphs (i)(2)(i) through (i)(2)(iii) of this section may further test a frozen sample from the repeatedly reactive donation or a fresh sample from the same donor, by (date 1 year from the effective date of the final rule), as follows:

(i) Donors identified in accordance with paragraph (d)(1) of this section as testing repeatedly reactive on an HCV EIA 1.0 screening test and repeatedly reactive on either an HCV EIA 2.0 or HCV EIA 3.0 screening test may be further tested using an appropriately chosen licensed supplemental test for HCV; or

(ii) Donors identified in accordance with paragraph (d)(2) of this section as testing repeatedly reactive on an HCV EIA 1.0 screening test with an indeterminate test result obtained using an HCV RIBA 2.0 supplemental test, may be further tested using a currently available licensed supplemental test for HCV or an HCV EIA 3.0. If such optional further testing is performed using an HCV EIA 3.0 and the result is repeatedly reactive, blood establishments may perform further testing using an appropriately chosen licensed supplemental test for HCV.

(iii) Donors identified in accordance with paragraph (d)(3) of this section as testing repeatedly reactive on an HCV EIA 1.0 screening test with a S/CO value less than 2.5 for at least two out of the three EIA tests, and with no record of a supplemental test or multiantigen screening test for HCV performed on the repeatedly reactive sample or on a later sample from the same donor, may be further tested using a licensed multiantigen screening test for HCV or a licensed supplemental test for HCV.

(3) *Consignee notification.* Except for blood and blood components exempt from quarantine in accordance with paragraph (g)(3) of this section, blood establishments shall:

(i) Within 45 days following completion of additional testing and prior to (date 1 year from the effective date of the final rule), notify consignees of the results of the additional licensed screening test and/or the licensed, supplemental test performed in accordance with paragraphs (i)(1) and (i)(2) of this section; or

(ii) Prior to (date 1 year from the effective date of the final rule), notify consignees of the test results for a donor who was identified in the review of historical testing records in accordance with paragraphs (d)(1) through (d)(4) of this section.

(j) *Release from quarantine.* (1) *Prior collections subject to quarantine under paragraph (a) of this section.* Prior collections of blood and blood components intended for transfusion or further manufacture into injectable products which are subject to quarantined under paragraph (a) of this section may be released if the donor's current, repeatedly reactive sample is subsequently tested using a licensed, supplemental test for HCV as provided in paragraph (b) of this section and the result is negative.

(2) *Prior collections subject to quarantine under paragraph (e)(1) of this section.* Prior collections of blood and blood components, which are not exempt from quarantine under paragraph (g)(2) of this section, and are otherwise subject to quarantine under paragraph (e)(1) of this section may be released from quarantine if:

(i)(A) The donor's testing records meet the conditions specified in paragraph (c)(4) of this section and further testing was performed in accordance with paragraph (h)(1)(i)(A) of this section on a frozen sample from the repeatedly reactive donation or a fresh sample from the same donor using a licensed supplemental test for HCV, and the result of the licensed supplemental test for HCV is negative; or

(B) The donor's testing records meet the conditions specified in paragraph (c)(4) of this section and further testing was performed in accordance with paragraph (h)(1)(i)(B) of this section on a frozen sample from the repeatedly reactive donation or a fresh sample from the same donor using a licensed, HCV EIA 3.0 screening test and the result is negative, or using a licensed, supplemental test if the HCV EIA 3.0 screening test is repeatedly reactive and the result of the licensed, supplemental test is negative; or

(ii) The donor's testing records meet the conditions specified in paragraph (c)(5) of this section and further testing was performed in accordance with paragraph (h)(1)(ii) of this section on a frozen sample or a fresh sample from the same donor using a licensed, supplemental test for HCV and the result is negative; or

(iii) The donor's testing records meet the conditions specified in paragraph (c)(2) of this section and further testing was performed, in accordance with paragraph (h)(2) of this section, as follows:

(A) The repeatedly reactive sample (test performed using an HCV EIA 2.0 screening test), or a later sample from the donor was further tested in accordance with paragraph (h)(2)(i) of this section using either a licensed HCV EIA 3.0 screening test or a licensed supplemental test for HCV and the result is negative; or

(B) The repeatedly reactive sample (test performed using an HCV EIA 2.0 screening test) or a later sample from the donor was further tested in accordance with paragraph (h)(2)(ii) of this section using an licensed supplemental test for HCV and the result is negative; or

(C) The repeatedly reactive sample (test performed using an HCV EIA 3.0 screening test) or a later sample from the donor was further tested in accordance with paragraph (h)(2)(iii) of this section using a licensed supplemental test for HCV and the result is negative; or

(iv) The donor's testing records meet the conditions specified in paragraph (c)(3) of this section and further testing was performed in accordance with paragraph (h)(2)(iv) of this section on a frozen sample or a fresh sample from the same donor using a licensed supplemental test for HCV and the result is negative.

(3) *Prior collections subject to quarantine under paragraph (f)(1) of this section.* Prior collections of blood and blood components, which are not exempt from quarantine under paragraph (g)(3) of this section, and are otherwise subject to quarantine under paragraph (f)(1) of this section may be released from quarantine if:

(i) The donor's testing records meet the conditions specified in paragraph (d)(4) of this section and further testing was performed in accordance with paragraph (i)(1)(i) of this section on a fresh sample, or frozen sample from the repeatedly reactive donation using a licensed supplemental test for HCV and the result is negative; or

(ii) The donor's testing records meet the conditions specified in paragraph (d)(1) of this section and further testing was performed in accordance with paragraph (i)(2)(i) of this section on a fresh sample, or frozen sample from the repeatedly reactive donation and the result of the an appropriately chosen licensed supplemental test for HCV is negative; or

(iii) The donor's testing records meet the conditions specified in paragraph (d)(2) of this section and further testing was performed in accordance with paragraph (i)(2)(ii) of this section on a fresh sample, or frozen sample from the repeatedly reactive donation and the result when further tested using either a licensed HCV EIA 3.0 screening test or a licensed supplemental test for HCV is negative;

(iv) The donor's testing records meet the conditions specified in paragraph (d)(3) of this section and further testing was performed in accordance with paragraph (i)(2)(iii) of this section on a fresh sample, or frozen sample from the repeatedly reactive donation and the result when further tested using a licensed multiantigen screening test for HCV or a licensed supplemental test for HCV is negative.

(k) *Destruction or labeling of prior collections held in quarantine.* Blood establishments and consignees shall destroy or appropriately label for in vitro use prior collections of blood and blood components otherwise subject to quarantine in accordance with paragraphs (a), (e), and (f) of this section, unless such prior collections are determined to be exempt from quarantine in accordance with paragraph (g) of this section or subject to release from quarantine in accordance with paragraph (j) of this section. Quarantined prior collections made available for in vitro use shall be appropriately relabeled consistent with §§ 606.121 and 640.70 of this chapter. In addition, these units must be relabeled as ''Biohazard'' with the cautionary statement as follows:

''Collected from a donor who subsequently tested reactive for anti-HCV. An increased risk of transmission of hepatitis C virus is present.''; in addition, the label must contain one of the following cautionary statements as appropriate: ''Caution: For Further Manufacturing Into In-Vitro Diagnostic Reagents For Which There Are No Alternative Sources'' or ''For Laboratory Research Use Only.''

(l) *Recalls.* Actions under this section do not constitute a recall as defined in § 7.3 of this chapter.

9. Section 610.49 is added to subpart E to read as follows:

§ 610.49 Hepatitis C Virus (HCV) ''Lookback;'' notification of transfusion recipients.

(a) *Appropriate actions following further testing.* Transfusion services are required to take appropriate action in accordance with paragraphs (b) and (c) of this section when a recipient has received prior collections of blood or blood components from a donor later determined to be at increased risk of transmitting HCV infection when tested for evidence of infection due to HCV and:

(1) The result of the licensed, supplemental test, performed as prescribed in § 610.48(b) and in accordance with the testing requirements specified in § 610.40(c), is positive;

(2) The result of the supplemental test identified in the review of historical testing records is positive, as specified in § 610.48(c)(1);

(3) The result of the supplemental test identified in the review of historical testing records in accordance with § 610.48(c)(2) is indeterminate, unless:

(i) The review of historical testing records shows the supplemental test was performed using an HCV RIBA 3.0 supplemental test; or

(ii) Any of the conditions for exemption from quarantine specified in § 610.48(g)(2) have been met; or

(iii) The donor was further tested in accordance with § 610.48(h)(2)(i), (h)(2)(ii), or (h)(2)(iii) and any of the conditions for release from quarantine specified in § 610.48(j)(2)(iii) have been met; or

(iv) The donor was further tested in accordance with § 610.48(h)(2)(ii) or (h)(2)(iii) using a supplemental test for HCV and the result is indeterminate;

(4) The result of the licensed supplemental test performed in accordance with § 610.48(h)(1)(i)(A), (h)(1)(i)(B), or (h)(1)(ii) is positive for a donor identified in the review of historical testing records in accordance with § 610.48(c)(4) and (c)(5), as testing repeatedly reactive on a multiantigen screening test in the past with no record of further testing;

(5) No record of further testing is available for a donor identified in the

review of historical testing records, in accordance with § 610.48(c)(4) and (c)(5), and no fresh or frozen sample is available for further testing, as specified in § 610.48(h)(1)(iii);

(6) The result of the additional test using HCV EIA 2.0 or 3.0 identified in the review of historical testing records is repeatedly reactive, as specified in § 610.48(d)(1), unless:

(i) Any of the conditions for exemption from quarantine specified in § 610.48(g)(3) have been met; or

(ii) The donor was further tested in accordance with § 610.48(i)(2)(i) and any of the conditions for release from quarantine specified in § 610.48(j)(3) have been met; or

(iii) The donor was further tested in accordance with § 610.48(i)(2)(i) using an appropriately chosen licensed supplemental test for HCV and the result is indeterminate; or

(7) The result of the supplemental test performed using an HCV RIBA 2.0 or HCV RIBA 3.0 is positive for a donor identified in the review of historical testing records in accordance with § 610.48(d)(2);

(8) The result of the supplemental test performed using an HCV RIBA 2.0 is indeterminate, for a donor identified in the review of historical testing records in accordance with § 610.48(d)(2), unless:

(i) Any of the conditions for exemption from quarantine specified in § 610.48(g)(3) have been met; or

(ii) The donor was further tested in accordance with § 610.48(i)(2)(ii) and any of the conditions for release from quarantine specified in § 610.48(j)(3) have been met; or

(iii) The donor was further tested in accordance with § 610.48(i)(2)(ii) using a licensed supplemental test for HCV and the result is indeterminate; or

(9) The result of the licensed, supplemental test for HCV or a licensed multiantigen screening test performed in accordance with § 610.48(i)(2)(iii) is positive for a donor identified in the review of historical testing records, in accordance with § 610.48(d)(3); or

(10) The result of the licensed, supplemental test for HCV performed in accordance with § 610.48(i)(1) is positive for a donor identified in the review of historical testing records, in accordance with § 610.48(d)(4), as testing repeatedly reactive on a single antigen screening test with a S/CO value equal to or greater than 2.5 for at least two of the three EIA tests, or the S/CO value can not be calculated, and with no record of further testing; or

(11) No record of further testing is available for a donor identified in the review of historical testing records, in accordance with § 610.48(d)(4), and no fresh or frozen sample is available for further testing, as specified in § 610.48(i)(1)(ii).

(b) *Notification of recipients of prior transfusion*. If the transfusion service has administered blood or blood components later determined to be at increased risk of transmitting HCV infection, as described in paragraph (a) of this section, the transfusion service shall either notify the recipient directly or notify the recipient's physician of record (i.e., physician of record or physician who ordered the blood or blood component) and ask him or her to inform the recipient of the need for HCV testing and counseling. If the physician is not available or declines to notify the recipient, the transfusion service shall notify the recipient and inform the recipient of the need for HCV testing and counseling. The notification of transfusion recipients based on donor testing completed after (the effective date of the final rule) shall include a minimum of three attempts to notify the recipient or the recipient's physician of record and be completed within a maximum of 12 weeks of receipt of the result of the supplemental test for HCV from the blood establishment. The notification of transfusion recipients based on donor testing completed prior to (the effective date of the final rule) shall include a minimum of three attempts to notify the recipient or the recipient's physician of record and be completed within 1 year of the date on which the transfusion service received notification from the blood establishment. The transfusion service is responsible for notification, including basic explanations to the recipient and referral for counseling and further testing, and shall document the notification and the result of attempts to notify the recipient and the recipient's physician of record, if contacted, under § 606.160 of this chapter.

(c) *Notification of legal representative or relative*. If the transfusion recipient has been adjudged incompetent by a State court, the legal representative, designated in accordance with State law, shall be notified. If the transfusion recipient is competent, but State law permits a legal representative or relative to receive the information on the recipient's behalf, the transfusion service or the physician who agreed to perform the notification on behalf of the transfusion service shall notify the recipient or his or her legal representative or relative. If the transfusion recipient is a minor at the time of notification, the transfusion service or physician, as described in this paragraph, shall notify the recipient's legal representative or relative. If the transfusion recipient is deceased, the transfusion service or physician, as described in this paragraph, may discontinue the notification process. The transfusion service is responsible for notification, including basic explanations to the recipient's legal representative or relative and referral for counseling and further testing of the recipient, and shall document the notification and the result of attempts to notify the recipient's legal representative or relative and the recipient's physician of record, if contacted, under § 606.160 of this chapter. Reasons for notifying the recipient's relative or legal representative on his or her behalf shall be documented under § 606.160 of this chapter.

(d) *Reference tables*. Tables 1 through 4 of this paragraph show the various tests performed for HCV (including both current donor testing shown in table 1 of this paragraph and tests identified in the review of historical testing records in tables 2 through 4 of this paragraph), steps of the ''lookback'' process, and applicable provisions of §§ 610.48 and 610.49. Based on the initial screening test select the appropriate table from the following:

TABLE 1.—OUTLINE OF PROVISIONS OF § 610.48 FOR HEPATITIS C VIRUS (HCV) ''LOOKBACK'' BASED ON CURRENT DONOR TESTING

Actions to be taken	Applicable section(s):
Identify prior collections	610.48(a)(1)
Quarantine prior in-date collections	610.48(a)(1)(i)
Notify consignees to quarantine	610.48(a)(1)(ii)
Consignees perform quarantine of prior collections	610.48(a)(2)
Exemptions from quarantine	610.48(g)(1)(i) 610.48(g)(1)(ii)
Perform further testing	610.48(b)
Notify consignees of test results	610.48(b)
Release prior collections from quarantine	610.48(j)(1)[1]
Destroy or label prior collections	610.48(k)
Notify transfusion recipients	610.49(a)(1)[2]

[1] If the licensed supplemental test for HCV is negative.
[2] If the licensed supplemental test for HCV is positive.

TABLE 2.—OUTLINE OF PROVISIONS OF § 610.48 FOR HEPATITIS C VIRUS (HCV) ''LOOKBACK'' BASED ON REVIEW OF HISTORICAL TESTING RECORDS AND IDENTIFICATION OF DONORS TESTING REPEATEDLY REACTIVE USING AN HCV EIA[1] 3.0 SCREENING TEST

Results of Further Testing:	RIBA 2.0[2] Positive or RIBA 3.0[3] Positive	RIBA 2.0 Negative	RIBA 2.0 Indeterminate	RIBA 3.0 Negative	RIBA 3.0 Indeterminate	No Supplemental Test Done	
Actions To Be Taken:	Applicable Sections						
Identify prior collections	610.48(c)(1)	610.48(c)(3)	610.48(c)(2)		610.48(c)(2)	610.48(c)(5)	
Quarantine prior in-date collections	610.48(e)(1), (e)(2), (e)(3)	610.48(e)(1), (e)(2), (e)(3)	610.48(e)(1), (e)(2), (e)(3)		610.48(e)(1), (e)(2), (e)(3)	610.48(e)(1), (e)(2), (e)(3)	
Notify consignees to quarantine							
Consignees perform quarantine of prior collections							
Exemptions from quarantine	610.48(g)(2)(i)	610.48(g)(2)(i)	610.48(g)(2)(i)	610.48(g)(2)(ii)(B)	610.48(g)(2)(i)	610.48(g)(2)(i)	
Perform further testing						610.48(h)(1)(ii)[4]	610.48(h)(1)(iii)[6]
Perform optional further testing		610.48(h)(2)(iv)[4]	610.48(h)(2)(iii)[4]				
Notify consignees of test results	610.48(h)(3)(ii)	610.48(h)(3)(i) 610.48(h)(3)(ii)	610.48(h)(3)(i) 610.48(h)(3)(ii)		610.48(h)(3)(ii)	610.48(h)(3)(i) 610.48(h)(3)(ii)	610.48(h)(3)(i) 610.48(h)(3)(ii)
Release prior collections from quarantine		610.48(j)(2)(iv)[5]	610.48(j)(2)(iii)(C)[5]			610.48(j)(2)(ii)[5]	
Destroy or label prior collections	610.48(k)	610.48(k)	610.48(k)		610.48(k)	610.48(k)	610.48(k)
Notify transfusion recipients	610.49(a)(2)		610.49(a)(3)			610.49(a)(4)[7]	610.49(a)(5)

[1] ''EIA'' means enzyme linked immunosorbant assay.
[2] ''RIBA 2.0'' means HCV 2.0 strip immunoblot assay.
[3] ''RIBA 3.0'' means HCV 3.0 strip immunoblot assay.
[4] Using a licensed supplemental test for HCV.
[5] If the licensed supplemental test for HCV is negative.
[6] No frozen or fresh sample is available for further testing.
[7] If the licensed supplemental test for HCV is positive.

TABLE 3.—OUTLINE OF PROVISIONS OF § 610.48 FOR HEPATITIS C VIRUS (HCV) ''LOOKBACK'' BASED ON REVIEW OF HISTORICAL TESTING RECORDS AND IDENTIFICATION OF DONORS TESTING REPEATEDLY REACTIVE USING AN HCV EIA[1] 2.0 SCREENING TEST

Results of Further Testing:	RIBA 2.0[2] Positive or RIBA 3.0[3] Positive	RIBA 2.0 Negative	RIBA 2.0 Indeterminate		RIBA 3.0 Negative	RIBA 3.0 Indeterminate	No Supplemental Test Done		
Actions to be Taken:	Applicable Sections								
Identify prior collections	610.48(c)(1)		610.48(c)(2)			610.48(c)(2)	610.48(c)(4)		
Quarantine prior in-date collections	610.48(e)(1), (e)(2), (e)(3)		610.48(e)(1), (e)(2), (e)(3)			610.48(e)(1), (e)(2), (e)(3)	610.48(e)(1), (e)(2), (e)(3)		
Notify consignees to quarantine									
Consignees perform quarantine of prior collections									
Exemptions from quarantine	610.48(g)(2)(i)	610.48(g)(2)(ii)(A)	610.48(g)(2)(i)		610.48(g)(2)(ii)(A)	610.48(g)(2)(i)	610.48(g)(2)(i)		
Perform further testing							610.48(h)(1)(i)(A)[9]	610.48(h) (1)(i)(B)[10]	610.48(h) (1)(iii)[11]
Perform optional further testing			610.48(h) (2)(i)[4] 610.48(h)(2)(ii)[5]	610.48(h) (2)(i)[6]					
Notify consignees of test results	610.48(h)(3)(ii)		610.48(h)(3)(i) 610.48(h) (3)(ii)	610.48(h)(3)(i) 610.48(h) (3)(ii)		610.48(h) (3)(ii)	610.48(h)(3)(i) 610.48(h)(3)(ii)	610.48(h)(3)(i) 610.48(h)(3)(ii)	610.48(h)(3)(i) 610.48(h)(3)(ii)
Release prior collections from quarantine			610.48(j)(2)(iii)(A)[7] 610.48(j)(2)(iii)(B)[8]	610.48(j) (2)(iii)(A)[8]			610.48(j)(2)(i)(A)[12]	610.48(j)(2) (i)(B)[13]	
Destroy or label prior collections	610.48(k)		610.48(k)	610.48(k)		610.48(k)	610.48(k)	610.48(k)	610.48(k)
Notify transfusion recipients	610.49(a)(2)		610.49(a)(3)	610.49(a)(3)			610.49(a)(4)[14]	610.49(a)(4)[14]	610.49(a)(5)

[1] ''EIA'' means enzyme linked immunosorbant assay.
[2] ''RIBA 2.0'' means HCV 2.0 strip immunoblot assay.
[3] ''RIBA 3.0'' means HCV 3.0 strip immunoblot assay.
[4] Using an HCV EIA 3.0 screening test.
[5] If the HCV EIA 3.0 screening test is repeatedly reactive, may perform a licensed supplemental test for HCV.
[6] Using a licensed supplemental test for HCV.
[7] If the HCV EIA 3.0 screening test is negative.
[8] If the licensed supplemental test for HCV is negative.
[9] Perform a licensed supplemental test for HCV.
[10] Perform an HCV EIA 3.0 screening test and perform a licensed supplemental test for HCV if the HCV EIA 3.0 screening test is repeatedly reactive.
[11] No frozen or fresh sample is available for further testing.
[12] If the licensed supplemental test for HCV is negative.
[13] If the HCV EIA 3.0 screening is negative; or, if it is repeatedly reactive, the licensed supplemental test for HCV is negative.
[14] If the licensed supplemental test for HCV is positive.

TABLE 4.—OUTLINE OF PROVISIONS OF § 610.48 FOR HEPATITIS C VIRUS (HCV) ''LOOKBACK'' BASED ON REVIEW OF HISTORICAL TESTING RECORDS AND IDENTIFICATION OF DONORS TESTING REPEATEDLY REACTIVE USING AN HCV EIA [1] 1.0 SCREENING TEST

RESULTS OF FURTHER TESTING:	EIA 2.0[2] Repeatedly Reactive	EIA 3.0[3] Repeatedly Reactive	EIA 2.0 Negative or EIA 3.0 Negative	RIBA 2.0 Positive or RIBA 3.0 Positive	RIBA 2.0 Indeterminate	RIBA 3.0 Indeterminate	RIBA 2.0 Negative or RIBA 3.0 Negative	S/CO[4] < 2.5	S/CO >2.5 or No Determination of S/CO	
ACTIONS TO BE TAKEN:	Applicable Sections									
Identify prior collections	610.48(d)(1)	610.48(d)(1)		610.48(d)(2)	610.48(d)(2)	610.48(d)(2)		610.48(d)(3)	610.48(d)(4)	
Quarantine prior in-date collections	610.48(f)(1), (f)(2), (f)(3)	610.48(f)(1), (f)(2), (f)(3)		610.48(f)(1), (f)(2), (f)(3)	610.48(f)(1), (f)(2), (f)(3)	610.48(f)(1), (f)(2), (f)(3)		610.48(f)(1), (f)(2), (f)(3)	610.48(f)(1), (f)(2), (f)(3)	
Notify consignees to quarantine										
Consignees perform quarantine of prior collections										
Exemptions from quarantine	610.48(g)(3)(iii)[5]	610.48(g)(3)(iii)[5]	610.48(g)(3)(i)		610.48(g)(3)(iv)[7]		610.48(g)(3)(ii)			
Perform further testing									610.48(i)(1)(i)[13]	610.48(i)(1)(ii)[14]
Perform optional further testing	610.48(i)(2)(i)[6]	610.48(i)(2)(i)[6]			610.48(i)(2)(ii)[8]			610.48(i) (2)(iii)[10]		
Notify consignees of test results	610.48(i)(3)(i) 610.48(i)(3)(ii)	610.48(i)(3)(i) 610.48(i)(3)(ii)		610.48(i)(3)(ii)	610.48(i)(3)(i) 610.48(i)(3)(ii)	610.48(i)(3)(ii)		610.48(i)(3)(i) 610.48(i)(3)(ii)	610.48(i)(3)(i) 610.48(i)(3)(ii)	610.48(i)(3)(i) 610.48(i)(3)(ii)
Release prior collections from quarantine	610.48(j)(3)(ii)[5]	610.48(j)(3)(ii)[5]			610.48(j)(3)(iii)[9]			610.48(j)(3)(iv)[11]	610.48(j)(3)(i)[15]	
Destroy or label prior collections	610.48(k)	610.48(k)		610.48(k)	610.48(k)	610.48(k)		610.48(k)	610.48(k)	610.48(k)
Notify transfusion recipients	610.49(a)(6)	610.49(a)(6)		610.49(a)(7)	610.49(a)(8)			610.49(a)(9)[12]	610.49(a)(10)[16]	610.49(a)(11)

[1] ''EIA'' means enzyme linked immunosorbant assay.
[2] ''RIBA 2.0'' means HCV 2.0 strip immunoblot assay.
[3] ''RIBA 3.0'' means HCV 3.0 strip immunoblot assay.
[4] ''S/CO'' means ''Signal to cut off.''
[5] If further testing using an appropriately chosen supplemental test for HCV was performed and the result was negative.
[6] May perform further testing using an appropriately chosen licensed supplemental test for HCV.
[7] If further testing using an HCV EIA 3.0 screening test or an HCV RIBA 3.0 supplemental test was performed and the result was negative.
[8] May perform further testing using an HCV EIA 3.0 screening test or a licensed supplemental test for HCV. If an HCV EIA 3.0 screening test is performed and is repeatedly reactive, may perform further testing using a licensed supplemental test for HCV.
[9] If further testing using an HCV EIA 3.0 screening test or a licensed supplemental test for HCV was performed and the result was negative.
[10] May perform further testing using a licensed multiantigen screening test for HCV or a licensed supplemental test for HCV.
[11] If further testing using a licensed multiantigen screening test for HCV or a licensed supplemental test for HCV was performed and the result was negative.
[12] If further testing using a licensed multiantigen screening test for HCV or a licensed supplemental test for HCV was performed and the result was positive.
[13] Using a licensed supplemental test for HCV.
[14] No frozen or fresh sample is available for further testing.
[15] If the licensed supplemental test for HCV is negative.
[16] If the licensed supplemental test for HCV is positive.

Dated: December 3, 1999.

Jane E. Henney,

Commissioner of Food and Drugs.

Donna E. Shalala,

Secretary of Health and Human Services.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Health Care Financing Administration

42 CFR Part 482

[HCFA–3014–P]

RIN 0938–AJ29

Medicare and Medicaid Programs; Hospital Conditions of Participation: Laboratory Services

AGENCY: Health Care Financing Administration (HCFA), HHS.

ACTION: Proposed rule.

SUMMARY: This proposed rule would require hospitals that transfuse blood and blood products to prepare and follow written procedures for appropriate action when it is determined that blood and blood products the hospitals received and transfused are at increased risk for transmitting hepatitis C virus (HCV); quarantine prior collections from a donor who is at increased risk for transmitting HCV infection; notify transfusion recipients, as appropriate, of the need for HCV testing and counseling; and extend the records retention period to 10 years.

These changes are based on recommendations by the Secretary's Advisory Committee on Blood Safety and Availability. The intent is to aid in the prevention of HCV infection and to create opportunities for disease prevention many years after recipient exposure to a donor.

DATES: We will consider written comments if we receive them at the appropriate address, as provided below, no later than 5 p.m. on or before January 16, 2001.

ADDRESSES: Mail written comments (one original and three copies) to the following address: Health Care Financing Administration, U.S. Department of Health and Human Services, P.O. Box 8010, Attention: HCFA–3014–P, 7500 Security Boulevard, Baltimore, Maryland 21244–8010.

If you prefer, you may deliver your written comments (one original and three copies) to one of the following addresses:

Room 443–G, Hubert H. Humphrey Building, 200 Independence Avenue, SW., Washington, DC 20201, or,

Room C5–09–26, 7500 Security Boulevard, Baltimore, Maryland 21244–1850.

Because of staffing and resource limitations, we cannot accept audio, visual, or facsimile (FAX) copies of comments. In commenting, please refer to file code HCFA–3014–P. Comments received timely will be available for public inspection as they are received, generally beginning approximately 3 weeks after publication of a document, in room 443–G of the Department's offices at 200 Independence Avenue, SW., Washington, DC, on Monday through Friday of each week from 8:30 a.m. to 5 p.m. (phone: (202) 690–7890).

FOR FURTHER INFORMATION CONTACT: Mary Collins, (410) 786–3189.

SUPPLEMENTARY INFORMATION:

I. Background

In accordance with section 1861(e) of the Social Security Act (the Act), hospitals must meet certain conditions in order to participate in the Medicare program. These conditions are intended to protect patient health and safety and ensure that high-quality care is provided. Hospitals receiving payment under Medicaid must meet the Medicare conditions of participation.

Regulations containing the Medicare conditions of participation for hospitals are located in the Code of Federal Regulations at 42 CFR part 482. The condition of participation for hospital laboratory services at § 482.27 (c) currently specifies the steps hospitals must take when they become aware they have administered potentially human immunodeficiency virus (HIV) infectious blood or blood products to a patient. The more detailed requirements for laboratories appear in 42 CFR part 493, which sets forth requirements for all laboratories participating in the Medicare, Medicaid, and Clinical Laboratory Improvement Amendments (CLIA) programs.

The Health Care Financing Administration (HCFA) and the Food and Drug Administration (FDA) are responsible for ensuring the safety of blood and blood products.

Blood banks (referred to as blood establishments in FDA regulations) are subject to the FDA regulations for current good manufacturing practices and additional standards for the manufacture of blood and blood components under 21 CFR parts 211, 600, 601, 606, 610, and 640. Laboratories that provide transfusion services are subject to CLIA requirements for quality control and health and safety standards (42 CFR part 493, subpart K). Laboratories in hospitals are also subject to the hospital conditions of participation for adequacy of laboratory services (42 CFR 482.27). HCFA coordinates inspections of hospital-based blood banks with the FDA to minimize duplication of effort and reduce the burden on affected facilities.

Hepatitis C virus (HCV) was first discovered and established as a causative agent of transfusion-associated hepatitis in the late 1980s. In October 1989, FDA's Blood Products Advisory Committee (BPAC) first discussed steps to identify and quarantine potentially HCV infectious blood and blood products remaining in storage and notify recipients of the blood. (These steps are known as ''lookback.'') BPAC advised that there was insufficient information available concerning HCV infection to propose either product quarantine or notification of recipients transfused with products prepared from prior collections from donors later determined to be at increased risk for transmitting HCV.

In 1996, the Tenth Report of the U.S. House of Representatives Committee on Government Reform and Oversight (H. Rpt. No. 104–746) focused attention on the significant public health problem that HCV infections pose for the nation. HCV infection is the most common blood-borne infection in the United States. The Centers for Disease Control and Prevention (CDC) estimate that during the 1980s, as many as 180,000 new HCV infections occurred each year. Since 1989, the annual number of new infections has declined by 80 percent. Currently approximately 4 million individuals in the United States are believed to be chronically infected with HCV.

In 1996, however, data from the Third National Health and Nutritional Examination Survey conducted from 1988 to 1994 indicated that chronically infected persons may not be aware of their infection. Despite progression of the disease, HCV infection is usually asymptomatic for about 20 years, but in many cases causes serious liver injury that is thought to be the leading cause of late stage liver failure and cirrhosis in the United States. HCV is also thought to play a significant role in the development of liver cancer. Between 8,000 and 12,000 deaths annually result from HCV-related chronic liver disease.

HCV can be transmitted in a number of ways, including sharing of drug use equipment among injection drug users, blood transfusion and solid organ

transplants from infectious donors, hemodialysis, occupational exposure to blood, perinatal exposure of infants to infected mothers, and unprotected sex.

In response to scientific data that show that HCV is transmissible through infectious blood and blood products, FDA has implemented an extensive system of donor screening and testing procedures performed before, during, and after a donation takes place to help prevent the transfusion of blood and blood products that are infected with HCV.

Blood establishments are currently testing each donation of blood and blood components for the antibody to HCV. FDA restricts the use, for transfusion or further manufacture, of donations testing repeatedly reactive for the antibody to HCV. Repeatedly reactive means that the initial HCV antibody screening test is reactive (in which case it is retested in duplicate), and that one or both of the duplicate tests are reactive.

As a result of the FDA blood donor screening and testing procedures, the risk of transmitting HCV infections through blood transfusion is very low. Despite the best practices of blood establishments, however, a person may donate blood early in the infection process when the antibody to HCV is not detectable by the screening test but is nevertheless present in the donor's blood (a so-called ''window'' period). If the donor attempts to donate blood at a later date, the test for the antibody to HCV may at that time be repeatedly reactive. Under these circumstances, previously collected blood and blood products would be at increased risk for transmitting HCV, and a recipient of a blood product collected during the window period would not know whether the donor was infected with HCV at the time of the previous donations. Approximately 7 percent of the 3.9 million Americans believed to be chronically infected with HCV were infected as a result of transfusion of blood components before the availability of donor screening tests or due to past use of non-viral-inactivated plasma derivative products. [1]

As a result of advances in identifying the presence of HCV, the window period continues to shrink. The FDA proposed rule titled ''Current Good Manufacturing Practice for Blood and Blood Components: Notification of Consignees and Transfusion Recipients Receiving Blood and Blood Components at Increased Risk of Transmitting HCV Infection ('Lookback'),'' published elsewhere in this issue of the **Federal Register,** provides more information on the length of the window period and discusses various diagnostic modalities for HCV infection.

The incidence of transfusion-transmitted HCV infection has decreased markedly since the implementation of donor screening for HCV and viral inactivation of clotting factors and intravenous immune globulins. Blood establishments implemented donor screening tests after a single antigen, enzyme linked immunosorbent assay (EIA) for antibody to HCV (HCV EIA 1.0 screening test) was licensed in May 1990. FDA issued a memorandum to all registered blood establishments in November 1990, ''Testing for Antibody to Hepatitis C Virus Encoded Antigen (Anti-HCV),'' recommending use of approved donor screening tests for antibody to HCV. A lookback program was not recommended because: (1) Screening tests available at the time could not distinguish between on-going infection and recovery, thus rendering unclear the meaning of a reactive test for any one individual; (2) donor screening for antibody to HCV did not include confirmatory testing, and most notification would have been based on false positive donor test results; (3) there was limited knowledge of routes of transmission for HCV other than parenteral; and (4) no potential long-term benefits of therapy were known.

A significantly more sensitive multiantigen screening test (HCV EIA 2.0 screening test) was licensed in March 1992. In June 1993, FDA licensed an HCV 2.0 strip immunoblot assay (HCV RIBA 2.0), also known as recombinant immunoblot assay (RIBA), a supplemental test for antibody to HCV. Supplemental tests for antibody to HCV are used to distinguish false positive test results from true repeatedly reactive screening test results. Following the December 1993 BPAC meeting, BPAC recommended product quarantine of prior collections from a donor who later tests repeatedly reactive for the antibody to HCV and tests positive or indeterminate on a supplemental test; however, BPAC only marginally endorsed consignee notification for the purpose of transfusion recipient notification because the public health benefit of the notification was not clear.

The Public Health Service Advisory Committee on Blood Safety and Availability (PHS Advisory Committee) discussed improvements in the treatment and management of HCV infection and improvements in testing for the antibody to HCV at public meetings held on April 24, 1997 and on August 11 and 12, 1997. The PHS Advisory Committee also discussed the public health benefits of notifying transfusion recipients receiving prior collections from a donor who subsequently tests repeatedly reactive for evidence of HCV infection. Following the Department of Health and Human Services' acceptance of recommendations from the PHS Advisory Committee, the FDA developed guidance, published in March 1998, regarding procedures for testing blood for HCV, quarantining blood and blood products, and notifying patients who may have received HCV-infected blood and blood products.

At public meetings on November 24, 1998 and January 28, 1999, the PHS Advisory Committee reconsidered the issue of recipient notification related to repeatedly reactive results on the single antigen screening test. The PHS Advisory Committee recommended that targeted lookback should be initiated based on a repeatedly reactive HCV EIA 1.0 screening test result on a repeat donor unless a supplemental test was performed and the result did not indicate increased risk of HCV infection, or, in the absence of a supplemental test result, unless the signal to cut off value of the repeatedly reactive HCV EIA 1.0 screening test was less than 2.5 or follow-up testing of the donor was negative.

FDA published a notice in the **Federal Register** on June 22, 1999 (64 FR 33309) announcing the availability of a draft guidance titled ''Guidance for Industry: Current Good Manufacturing Practice for Blood and Blood Components: (1) Quarantine and Disposition of Prior Collections from Donors with Repeatedly Reactive Screening Tests for Hepatitis C Virus (HCV); (2) Supplemental Testing, and the Notification of Consignees and Transfusion Recipients of Donor Test Results for Antibody to HCV (Anti-HCV).'' Consistent with the recommendations of the PHS Advisory Committee, this revised draft guidance addressed lookback actions related to donor screening by HCV EIA 1.0 and also recommended that the search of historical testing records of prior donations from donors with repeatedly reactive EIA 1.0, EIA 2.0, or EIA 3.0 screening tests for HCV should extend back indefinitely to the extent that electronic or other retrievable records exist.

In the proposed rule titled ''Medicare and Medicaid Programs; Hospital Conditions of Participation; Provider Agreements and Supplier Approval'' (HCFA–3745–P), published on

[1] M.J. Alter, ''Epidemiology of Hepatitis C,'' Hepatology 26.3 (1997): 62s–65s.

December 19, 1997 in the **Federal Register** (62 FR 66726), we proposed to revise the hospital conditions of participation to focus on patient care outcomes, reflect a cross-functional view of the hospitals' organization and patient treatment, encourage flexibility in meeting quality standards, and eliminate outdated and redundant evaluation criteria. The lookback requirement for HIV infectious blood and blood products was the only lookback under this proposed condition. The HIV requirement was restated without change in the existing § 482.27(c). This requirement would merely be redesignated under this proposed rule. We are still in the process of analyzing comments we received on the December 19, 1997 proposed rule as we develop the final rule.

Should the restructuring of part 482 in the December 19, 1997 proposed rule become final before we publish this proposed rule (HCFA–3014–P) as a final rule, the provisions dealing with potentially HCV infectious blood and blood products would be set forth in the final rule (HCFA–3014–F) as a revision to § 482.145.

II. Provisions of This Proposed Rule

In order to have consistent industry standards for potentially infectious blood and blood products, we propose to adopt as our requirements for hospitals the procedures for HIV and HCV proposed by the FDA published elsewhere in this issue of the **Federal Register**. Since our proposed rule is in concert with the FDA's proposed rule, we will consider comments we receive in conjunction with the FDA. We specifically request comments on the reasonableness of our adopting the FDA requirements.

The FDA proposed rule for HCV lookback would require the search of historical testing records of prior donations from donors with repeatedly reactive EIA 1.0, EIA 2.0, or EIA 3.0 screening tests for HCV to extend back indefinitely for computerized electronic records and to January 1, 1998 for other retrievable records. Under the FDA rule, the blood establishment would notify the hospital if it supplied the hospital with potentially HIV or HCV infectious blood.

Our proposed rule would amend the hospital conditions of participation to require a hospital to develop agreements with outside blood banks under which the blood bank would notify the hospital when it has supplied the hospital with potentially HCV infectious blood and blood products. This proposed rule would establish a lookback, similar to that now in effect for HIV, requiring hospitals, when notified by blood banks, to quarantine prior collections from a donor who later tests repeatedly reactive for evidence of HCV infection, and to notify transfusion recipients based on further testing of such a donor, as appropriate.

In existing § 482.27, we propose to remove the designation for paragraph (a) and redesignate paragraphs (b) and (c) as (a) and (b), respectively. In addition, we would add a definition of potentially HCV infectious blood and blood products as prior collections from a donor who tested repeatedly reactive for evidence of HCV infection on a single antigen screening test with a signal to cut off value equal to or greater than 2.5 for at least two of the three EIA tests, or the signal to cut off value cannot be calculated, and with no record of further testing; who tests or tested repeatedly reactive for evidence of HCV infection and positive on a multiantigen supplemental test licensed at an earlier or later date by FDA; who tested repeatedly reactive for evidence of HCV infection and indeterminate on a supplemental test for HCV, unless an indeterminate RIBA 3.0 supplemental test result was obtained or a negative EIA 3.0 or negative RIBA 3.0 test result was subsequently obtained; who tested repeatedly reactive for evidence of HCV infection on a multiantigen screening test with no record of further testing; or who tested repeatedly reactive for evidence of HCV infection on a single antigen screening test and repeatedly reactive on a subsequent multiantigen screening test, unless a negative supplemental test result or an indeterminate RIBA 3.0 supplemental test result was obtained. (See proposed § 482.27(b)(2).)

Our regulations currently require that a hospital that regularly uses the services of an outside blood bank have an agreement with the blood bank that requires the blood bank to notify the hospital if the blood bank has supplied the hospital with potentially HIV infectious blood. This proposed rule would amend that provision to also require notification in the case of potentially HCV infectious blood. (See proposed § 482.27(b)(3).) In addition, we would revise our regulations to include HCV-relevant testing required by FDA. (See proposed § 482.27(b)(3)(ii).)

As a new provision, we would require hospitals to include in agreements with blood banks that the blood bank notify the hospital under FDA's proposed 21 CFR 610.48(h)(3)(i) and (h)(3)(ii), and (i)(3)(i) and (i)(3)(ii). The FDA's proposed rule would require hospitals to perform a lookback of blood or blood products collected from a donor extending back indefinitely for computerized electronic records and to January 1, 1998 for other retrievable records, or to the date 12 months before the donor's most recent negative multiantigen screening test for the antibody to HCV, whichever is the later date. (See proposed § 482.27(b)(3)(ii) and (b)(3)(iii).)

We would also revise our regulations to apply the provisions regarding the quarantine of potentially HIV infectious blood and blood products currently set forth at § 482.27(c)(3) to potentially HCV infectious blood and blood products. In addition, we would require hospitals to destroy or label prior collections of blood or blood products held in quarantine as set forth in FDA's proposed 21 CFR 610.48(k). (See proposed § 482.27(b)(4).)

Hospitals are currently required to maintain clinical records on all patients for 5 years. We would add a new provision requiring hospitals to maintain adequate records of the source and disposition of all units of blood and blood products for at least 10 years from the date of disposition. Hospitals would be required to increase the record retention period yearly until 10 years of records from the date of disposition have accrued. (For example, the first year after the effective date of this regulation, hospitals would have 6 years of records, the second year after the effective date, 7 years, etc., until 10 years have been reached.) Hospitals would then be able and expected to maintain 10 years of patient records. (See proposed § 482.27(b)(5).) This is necessary to increase opportunities for disease prevention or treatment years after a recipient has been exposed to a donor later determined to be at risk of transmitting a disease through transfusion.

The FDA has proposed changes in its requirement for patient notification to allow transfusion services to make three attempts to either notify patients directly or notify the attending physician or the physician who ordered the blood. We are proposing that hospitals follow the same notification procedures with regard to potentially HIV and HCV infectious blood and blood products. For consistency, we are also proposing that the HIV lookback requirements be changed to conform to the requirements for HCV lookback. (See proposed § 482.27(b)(6).)

We propose to add a new paragraph (c) requiring hospitals to comply with FDA regulations pertaining to the appropriate testing and quarantining of infectious blood and blood products and to the notification and counseling of

recipients that may have received infectious blood and blood products.

Note that our Medicaid regulations at § 441.17 (''Laboratory services'') provide that the State plan must pay for laboratory services furnished by a hospital-based laboratory meeting the requirements for Medicare participation set forth in § 482.27. Therefore, the provisions of this proposed rule would also affect the Medicaid program. That is, in order for the laboratory services furnished by a hospital-based laboratory under Medicaid to be covered under the State plan, the hospital would have to meet the new requirements set forth in this proposed rule.

III. Collection of Information Requirements

Under the Paperwork Reduction Act of 1995, agencies are required to provide a 60-day notice in the **Federal Register** and solicit public comment before a collection of information requirement is submitted to the Office of Management and Budget (OMB) for review and approval. In order to fairly evaluate whether an information collection should be approved by OMB, section 3506(c)(2)(A) of the Paperwork Reduction Act of 1995 (44 U.S.C. 3506(c)(2)(A)) requires that we solicit comment on the following issues:

- Whether the information collection is necessary and useful to carry out the proper functions of the agency;
- The accuracy of the agency's estimate of the information collection burden;
- The quality, utility, and clarity of the information to be collected; and
- Recommendations to minimize the information collection burden on the affected public, including automated collection techniques.

Therefore, we are soliciting public comment on each of these issues for the provisions summarized below that contain information collection requirements:

Section 482.27 Condition of participation: Laboratory services

In summary, § 482.27(b)(3) requires a hospital that regularly uses the services of an outside blood bank to establish and maintain a written agreement with the blood bank that governs the procurement, transfer, and availability of blood and blood products. This section also requires the blood bank to notify the hospital within 3 calendar days after the date on which the donor tested repeatedly reactive for evidence of HCV infection or after the date on which the blood establishment was made aware of other test results indicating evidence of HCV infection, as outlined in (i) through (iii).

In summary, § 482.27(b)(5) requires a hospital to maintain, in a manner that permits prompt retrieval, adequate records of the source and disposition of all units of blood and blood products for at least 10 years from the date of disposition. In addition, this section requires a hospital to maintain a fully funded and documented plan that demonstrates how the hospital will transfer these records to another hospital or other entity if the former hospital ceases operation for any reason.

In summary, § 482.27(b)(6) requires a hospital that has administered potentially HIV or HCV infectious blood or blood products (either directly through its own blood bank or under an agreement), or released the blood or blood products to another entity or individual, to make at least three attempts to notify the patient, or to notify the attending physician or the physician who ordered the blood or blood product and ask the physician to notify the patient, that potentially HIV or HCV infectious blood or blood products were transfused to the patient. Time frame and notification requirements are outlined in §§ 482.27(b)(6), (b)(7), and (b)(8).

In summary, § 482.27(b)(9) requires a hospital to maintain policies and procedures for notification and documentation that conform to Federal, State, and local laws, including requirements for confidentiality and medical records.

In summary, § 482.27(b)(10) requires a physician or hospital, if the patient has been adjudged incompetent by a State court, to notify a legal representative designated in accordance with State law. If the patient is competent, but State law permits a legal representative or relative to receive the information on the patient's behalf, the physician or hospital must notify the patient or his or her legal representative or relative. If the patient is deceased, the physician or hospital must continue the notification process and inform the deceased patient's legal representative or relative. If the patient is a minor, the legal guardian must be notified.

While all of the information collection requirements referenced above are subject to the Paperwork Reduction Act, the burden associated with these requirements is captured and discussed in the FDA's proposed regulation titled ''Current Good Manufacturing Practice for Blood and Blood Components: Notification of Consignees and Transfusion Recipients Receiving Blood and Blood Components at Increased Risk of Transmitting HCV Infection ('Lookback'),'' Docket No. 98N–0609. Therefore, we are assigning 1 token hour of burden to these requirements.

The FDA's rule assigns a one-time burden of 16 hours for hospitals to develop procedures to conduct lookback activities. HCFA also requires hospitals that currently receive blood from an outside blood bank to have an agreement with the blood bank that governs the procurement, transfer, and availability of blood and blood products for HIV. Our proposed rule would require those hospitals to modify their current agreements to include HCV. Although the FDA does not require hospitals to have this agreement, we believe that the time necessary to perform this task would be minimal and is already captured in the 16 hours allotted in the FDA rule.

We have submitted a copy of this proposed rule to OMB for its review of the information collection requirement. These requirements are not effective until they have been approved by OMB. A notice will be published in the **Federal Register** when approval is obtained.

If you comment on any of these information collection and record keeping requirements, please mail copies directly to the following:

Health Care Financing Administration, Office of Information Services, Security and Standards Group, Division of HCFA Enterprise Standards, Room N2–14–26, 7500 Security Boulevard, Baltimore, MD 21244–1850. Attn: John Burke, HCFA–3014–P, Fax number: (410) 786–0262,

and,

Office of Information and Regulatory Affairs, Office of Management and Budget, Room 10235, New Executive Office Building, Washington, DC 20503. Attn.: Allison Herron Eydt, HCFA Desk Officer, Fax numbers: (202) 395–6974 or (202) 395–5167.

IV. Response to Comments

Because of the large number of items of correspondence we normally receive on **Federal Register** documents published for comment, we are not able to acknowledge or respond to them individually. We will consider all comments we receive by the date and time specified in the **DATES** section of this preamble, and, if we proceed with a subsequent document, we will respond to the comments in the preamble to that document.

V. Regulatory Impact Analysis

A. Overall Impact

We have examined the impacts of the proposed rule as required by Executive Order 12866 and the Regulatory Flexibility Act (RFA) (Pub. L. 96–354). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, if regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety effects, distributive impacts, and equity). A regulatory impact analysis (RIA) must be prepared for major rules with economically significant effects ($100 million or more annually). Because the projected cost of this proposed rule falls below the threshold for a major rule, we have determined that this proposed rule is not a major rule.

The RFA requires agencies to analyze options for regulatory relief of small businesses. For purposes of the RFA, small entities include small businesses, nonprofit organizations, and government agencies. Most hospitals and most other providers and suppliers are small entities, either by nonprofit status or by having revenues of $5 million or less annually. Individuals and States are not included in the definition of a small entity.

In addition, section 1102(b) of the Act requires us to prepare an RIA if a rule may have a significant impact on the operations of a substantial number of small rural hospitals. This analysis must conform to the provisions of section 603 of the RFA. For purposes of section 1102(b) of the Act, we define a small rural hospital as a hospital that is located outside of a Metropolitan Statistical Area and has fewer than 50 beds.

Section 202 of the Unfunded Mandates Reform Act of 1995 (Pub. L. 104–4) also requires that agencies assess anticipated costs and benefits before issuing any rule that may result in an expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100 million in any one year. We believe that this proposed rule is not an economically significant rule as described in the Executive Order, nor a significant action as defined in the Unfunded Mandates Reform Act. Aggregate impacts of the rule, and aggregate expenditures caused by the rule, would not reach $100 million for either the public or the private sector. As discussed in the following paragraphs, because of the lack of information to characterize the number and volumes of affected blood and blood products in hospitals that might qualify as small business entities, the impact on small business establishments is uncertain.

It is clear that a number of hospitals that provide blood transfusions will be affected by the implementation of this proposed rule and that a substantial number of those entities will be required to make changes in their operations. For these reasons, we have prepared the following voluntary analysis. This analysis, in combination with the rest of the preamble, is consistent with the analysis set forth by the RFA.

B. Anticipated Effects

1. Effects on Hospitals

This proposed rule would require hospitals that transfuse blood and blood products to (1) prepare and follow written procedures for appropriate action when it is determined that blood and blood products the hospitals received and transfused are at increased risk for transmitting HCV; (2) quarantine prior collections from a donor who is at increased risk for transmitting HCV infection; (3) notify transfusion recipients, as appropriate, of the need for HCV testing and counseling; and (4) extend the records retention period to 10 years.

The proposed rule would affect hospitals that transfuse blood and blood components. We estimate that there are approximately 6,200 Medicare- and Medicaid-participating hospitals. The CDC estimates that 303,676 recipients may need to be notified due to the historical review.

As indicated previously, the proposed rule would require hospitals to notify transfusion recipients who received prior collections from a donor at increased risk for transmitting HCV. The hospital may notify the attending physician or notify the recipient directly. If the transfusion recipient is a minor or adjudged incompetent by a State court, the hospital or physician would be required to notify the recipient's legal representative. The proposed rule is expected to generate one-time costs and some additional annual costs for hospitals. One-time costs include the development of procedures and policies for recipient notification and the agreement a hospital should have with a blood bank if it uses the services of an outside bank. We assume that these tasks will involve a review of current procedures and policies (for example, for HIV lookback) and the adaptation or modification of current procedures and policies to address the provisions of this rule, and we estimate, in consultation with the FDA, that the tasks will require an average of 16 hours per facility. The Bureau of Labor Statistics estimates that the total hourly compensation in 1997 for a staff medical technologist performing the review would be $25.67. Thus, we estimate the total one-time cost for all 6,200 hospitals to develop HCV lookback procedures to be $2,546,464 (16 x $25.67 x 6,200). (See Table in this section.)

For notifications resulting from donors tested on or after the effective date of the final rule under FDA's proposed § 610.48(a)(b), the hospital's required notification effort must include a minimum of three attempts to notify the transfusion recipient, and the hospital must complete the process within a maximum of 12 weeks from the time it receives from the blood establishment the results of the donor's supplemental test for HCV. The following estimated cost for compliance with provisions concerning the prospective review and recipient notification is based on: (1) FDA's estimation of the number of recipient notification multiplied by the unit cost of each notification. First, the number of annual affected blood donations was calculated as the product of 12 million donations, an 80 percent donor rate, and a 12 percent HCV positive donor rate. (2) The resulting 11,520 figure was then adjusted upward to 12,816 to reflect the difference found between the number of donors triggering lookback and the component notifications reported as interim results from a recent survey conducted by the Centers for Disease Control and prevention (CDC). (3) The cost per attempted notification is estimated at $165, which reflects the average cost quoted by a third party contractor for matching, notifying, testing, counseling, and documenting lookback efforts for over 100 hospitals.[2] Although the proposed rule does not specifically require hospitals to perform testing and counseling services many do. These assumptions yield an annual cost of $2,114,640 (12,816 × $165) for hospitals to conduct prospective lookback activities. (See Table in this section.)

For notifications resulting from donors tested before the effective date of the final rule under FDA's proposed § 610.48(c)(d), the hospital must complete the notification effort within 1 year from the time it receives notification from the blood establishment. The recipient notification provided by the hospital

[2] Richard Quattrocchi, Home Access Health Corporation.

must include a basic explanation to the recipient, referral for counseling and further testing, and documentation of the notification or attempts to notify the attending physician or recipient. Notification resulting from the review of historical testing records and the identification of prior collections are to be completed by the hospital within one year of receipt of notification from the blood establishment. The recipient notification provided by the hospital would include a basic explanation to the recipient, referral for counseling and further testing and documentation of the notification or attempts to notify the physician of record or recipient. The estimated one-time cost of recipient notification associated with the review of historical testing records is $50,106,540. This is based on the CDC estimate of blood components of about 303,676 recipients identified for notification produced from donations (188,448 from 1990 to mid-1992 and 115,228 from 1990 to mid-1992), and the average cost of $165 of staff time per component for recipient notification. Thus, the total one-time cost to hospitals for conducting the historical ''lookback'' efforts is estimated to be $52,653,004 ($2,546,464 to develop procedures and $50,106,540 for recipient notification). (See Table in this section.)

SUMMARY OF ESTIMATED COST OF PROPOSED RULE

Type of cost	Total one-time cost	Total annual cost
Development of HCV Lookback Procedures	[1] $2,546,464.00	
Prospective Review		[3] $2,114,640.00
Historical Review	[2] 50,106,540.00	
Total	52,653,004.00	2,114,640.00

[1] Based on 6,200 hospitals.
[2] Based on the CDC estimate of the total number of blood products (303,676).
[3] Based on the CDC estimate of 12,816 repeat-donor repeatedly reactive donations per year.

2. Effects on Beneficiaries

Timely notification of HCV infection benefits beneficiaries, both directly and indirectly, in several important ways. First, although factors predicting the severity of liver disease due to HCV have not been well defined, recent data indicate that increased alcohol intake is associated with more severe liver disease. According to CDC, even moderate amounts of alcohol in patients with chronic HCV might exacerbate liver disease. Consequently, an HCV-infected patient identified by the proposed lookback program could minimize liver damage associated with alcohol consumption by restricting his or her intake.

Furthermore, while other percutaneous exposures currently represent the most common means of infection, some case-control studies have also reported that HCV can be transmitted through sexual contact. In fact, 15 to 25 percent of the acute HCV patients who were reported to CDC's sentinel counties surveillance system have a history of sexual exposure in the absence of other risk factors. Infected patients identified through the proposed lookback procedures could take steps to protect sexual partners from the risk of infection.

It is also important to note that identified infected patients would benefit from counseling and treatment with available therapies. Studies of patient characteristics and responsiveness to therapy indicate that best results are achieved if treatment is initiated earlier in the disease, when patients are younger and have not yet developed cirrhosis.[3] For example, Bennett et al. estimated the cost effectiveness of a single course (6 months) of treatment with interferon alfa and found that patients at age 20 gained an average of 3.1 years of life, at $500 per year of life extended (YLE); 30-year-old patients gained an average of 1.9 years of life, at $1200/YLE; patients starting treatment at age 50 gained 6 months of life, at $2900/YLE; and 70-year-old patients gained an average of 22 days, at $62,000/YLE.[4]

Another benefit of timely notification is that care providers for the infected patient would be aware of the infection and could use additional precautions to avoid the risk of exposure to blood or wounds when providing care.

Finally, infected patients would be informed that they must not donate blood. The proposed lookback program would, therefore, help to ensure the safety and continued availability of the national blood supply.

3. Effects on Medicaid and Medicare Programs

We expect this proposed rule to generate a one-time cost to develop procedures for recipient notification. We estimate that this cost will be less than $5 million. Finally, the total one-time cost for the development of HCV lookback procedures and for recipient notification associated with the review of historical testing records is estimated to be $52,653,004 ($2,546,464 + $50,106,540). These one-time costs would likely be distributed among health programs as follows: Medicare, 33.3 percent; private health insurance, 30.5 percent; Federal Medicaid, 9.8 percent; State Medicaid, 5.8 percent; other private funds, 7.9 percent; other Federal funds, 6.9 percent; and other State and local funds, 5.7 percent. The total Federal distribution would be 50 percent; that is, 33.3 percent for Medicare, 9.8 percent for Medicaid, and 6.9 percent for other Federal sources. The degree to which the Federal programs fund these amounts will vary: Medicaid providers may be able to pass on costs through the States depending on the method of payment the State Medicaid program has adopted, while Medicare payments could be limited because of the hospital outpatient prospective payment system and increase only in accordance with specific rules regarding coverage of HCV testing for patients who have been exposed to HCV-infected blood, including those identified through the FDA lookback process.

It is important to note that, although this proposed rule presents the costs that would be imposed on all payers of hospital services, including the Medicare and Medicaid programs, it merely conforms to the FDA's proposed rule and has no additional economic impact. It simply repeats the analysis performed in the FDA companion rule

[3] G.L. Davis and J.Y.N. Lau, ''Factors Predictive of a Beneficial Response to Therapy of Hepatitis C,'' Hepatology 26.3 (1997): 122s–126s.

[4] W.G. Bennett et al., ''Estimates of the Cost-Effectiveness of a Single Course of Interferon-alfa2b in Patients with Histologically Mild Chronic Hepatitis C,'' Annals of Internal Medicine, 127.10 (1997): 855–865.

and presents the same total costs to hospitals.

C. Alternatives Considered

The PHS Advisory Committee discussed improvements in the treatment and management of HCV infection and improvements in testing for the HCV antibody at public meetings held in April and August 1997. The Advisory Committee recommended that blood establishments and hospitals notify previous recipients of blood components from donors who tested positive for HCV upon a subsequent donation.

Following the Department of Health and Human Services' acceptance of recommendations from the PHS Advisory Committee, FDA developed industry guidelines for testing blood for HCV, quarantining blood and blood products, and notifying patients who may have received HCV-infected blood and blood products. We explored the possibility of using a program memorandum to notify hospitals that they are required to follow FDA guidelines. We believe, however, that we should promulgate an enforceable regulation.

The following discussion considers some key elements of successful lookback efforts, describes certain challenges identified in lookback programs already in operation, and reviews the value of targeted recipient notification and treatment efforts.

The lookback provisions of the proposed rule can be characterized as a ''targeted lookback'' program, meaning that the notification of infection risk is limited to, or targeted at, individuals identified as recipients of blood from donors subsequently found to be infected with HCV. This program is distinct from ''general lookback'' programs, which are aimed at all patients who received blood before the onset of screening and which include the recommendation that the patients be tested for evidence of infection. General and targeted lookback programs may be complementary. General lookback can be conducted in a variety of ways, including use of the broadcast media, education, and letter campaigns addressed to physicians or patients. By contrast, targeted lookback can only be performed successfully if the transfusion service is aware that the donor subsequently tested positive, if donor and product disposition records are available to link blood components with the identified donors, and if the physician or hospital knows the recipient's current whereabouts. Hospitals would locate recipient records for all transfused units from an affected donor and would have current recipient or physician address information available so that the hospitals could deliver notifications. Ideally, the recipient would still be alive and would respond to the notification for testing and treatment, if appropriate.

However, recent experiences among Canadian facilities implementing HCV lookback suggest that the effectiveness of targeted lookback may vary depending on the extent to which conditions for success exist within a community. For example, an analysis of targeted lookback in Quebec province found that, because the records were inadequate or the whereabouts of recipients were unknown, hospitals could provide information on only approximately 50 percent of the components involved.[5] A Canadian Red Cross Center in Toronto reported on another lookback challenge. Although the establishment was able to identify 5,301 affected components, trace 3,209 of those to hospitals, obtain responses for 2,807 (87 percent) of the units, and identify 2,437 as having been transfused, 45 percent of the transfused patients had already died. Of those remaining, the Canadian facilities finally tested only 184 patients (8 percent of the transfused patients) as a result of the lookback effort although as many as 68 percent of those tested were found to be HCV positive.[6]

Despite the difficulties of implementing targeted lookback, it is considered a valuable means of reaching patients at high risk for HCV. For example, a comparison of Canadian efforts in targeted lookback with general lookback through physician and public education found that a large number of patients and families were unaware of the transfusion episode. These recipients would not have been reached through the general lookback effort.[7]

Timely notification is important because studies of patient characteristics and responsiveness to therapy indicate that the best results are achieved if patients receive treatment when they are younger and have not yet developed cirrhosis.[8] The primary treatment for chronic HCV is alfa interferon therapy.[9] Of those patients who undergo interferon treatment, a reported 10 to 20 percent show a sustained response (SR) after 6 months of therapy, and 20 to 30 percent show an SR if therapy is continued for 12 months. However, alfa interferon produces a wide array of adverse side effects,[10] and some patients experience a relapse after therapy. Still, the benefits for patients identified for treatment through HCV lookback are likely to continue to increase as improved therapies are developed. For example, recent reports based on pilot studies and completed randomized controlled trials indicate that the combination of interferon alfa and ribavirin leads to higher virological SR rates (40 to 50 percent) than interferon alfa alone, which was administered in 6-month clinical trials.[11] FDA has recently approved the use of this combination therapy for HCV patients who suffer a relapse after initial therapy with interferon alone.

As discussed in section I of this document, the BPAC and PHS Advisory Committee have met a number of times to discuss HCV testing and other issues related to ''HCV lookback.'' The PHS Advisory Committee made recommendations after considering alternative procedures to notify transfusion recipients. Alternative approaches for lookback are available but are not considered fully effective. Because of the importance of a safe national blood supply and because our mission is to protect the public health, we accepted the recommendations of the PHS Advisory Committee and did not select an alternative approach.

D. Conclusion

In addition to the prospective HIV lookback that hospitals are currently required to perform, hospitals would be required to conduct a lookback of transfusion recipients of potentially HCV-infected blood. This proposed rule would also require hospitals to have in their agreements with blood banks that blood banks notify hospitals after performing the FDA-mandated lookback. Therefore, we have prepared a voluntary analysis consistent with the analysis set forth by the RFA. We solicit public comments on the extent that any of the entities would be significantly economically affected by these provisions.

[5] M. Goldman *et al.*, ''Hepatitis C Lookback,'' Transfusion Medicine Review 12.2 (1998): 84–93.

[6] A. Wall *et al.*, ''Hepatitis C Virus (HCV) Targeted Lookback Program,'' Transfusion 37 (1997): 392s.

[7] M. Goldman *et al.*, ''Hepatitis C Lookback,'' Transfusion Medicine Review 12.2 (1998): 84–93.

[8] G.L. Davis and J.Y.N. Lau, ''Factors Predictive of a Beneficial Response to Therapy of Hepatitis C,'' Hepatology 26.3 (1997): 122s–126s.

[9] A. Wall *et al.*, ''Hepatitis C Virus (HCV) Targeted Lookback Program,'' Transfusion 37 (1997): 392s.

[10] G. Duscheiko, ''Side Effects of Alpha interferon in Chronic Hepatitis C,'' Hepatology 26.3 (1997): 112s–119s.

[11] National Institutes of Health (NIH) Consensus Development Conference Panel Statement: Management of Hepatitis C, Hepatology 26.3 (1997): 2s–10s.

In accordance with the provisions of Executive Order 12866, this proposed rule was reviewed by OMB.

We have reviewed this proposed rule under the threshold criteria of Executive Order 13132, Federalism. We have determined that it would not significantly affect the rights, roles, and responsibilities of States.

List of Subjects in 42 CFR Part 482

Grant programs—health, Hospitals, Medicaid, Medicare, Reporting and recordkeeping requirements.

Accordingly, for the reasons set forth in the preamble, 42 CFR part 482 would be amended as set forth below:

PART 482—CONDITIONS OF PARTICIPATION FOR HOSPITALS

1. The authority citation for part 482 continues to read as follows:

Authority: Secs. 1102 and 1871 of the Social Security Act (42 U.S.C. 1302 and 1395hh).

2. In § 482.27, the designation for paragraph (a) is removed; paragraphs (b) and (c) are redesignated as paragraphs (a) and (b), respectively; redesignated paragraph (b) is revised; and a new paragraph (c) is added to read as follows:

§ 482.27 Condition of participation: Laboratory services.

* * * * *

(b) *Standard: Potentially infectious blood and blood products*—(1) Definition. Potentially human immunodeficiency virus (HIV) infectious blood and blood products are prior collections from a donor—

(i) Who tested negative at the time of donation but tests repeatedly reactive for the antibody to HIV on a later donation;

(ii) Who tests positive on the FDA-licensed, more specific test or other followup testing required by FDA; and

(iii) For whom the timing of seroconversion cannot be precisely estimated.

(2) *Definition.* Potentially hepatitis C virus (HCV) infectious blood and blood products are prior collections from a donor—

(i) Who tested repeatedly reactive for evidence of HCV infection on a single antigen screening test with a signal to cut off value equal to or greater than 2.5 for at least two of the three enzyme linked immunosorbent assay (EIA) tests, or the signal to cut off value cannot be calculated, and with no record of further testing;

(ii) Who tests or tested repeatedly reactive for evidence of HCV infection and positive on a multiantigen supplemental test licensed at an earlier or later date by FDA;

(iii) Who tested repeatedly reactive for evidence of HCV infection and indeterminate on a supplemental test for HCV, unless an indeterminate recombinant immunoblot assay (RIBA) 3.0 supplemental test result was obtained or a negative EIA 3.0 or negative RIBA 3.0 test result was subsequently obtained;

(iv) Who tested repeatedly reactive for evidence of HCV infection on a multiantigen screening test with no record of further testing; or

(v) Who tested repeatedly reactive for evidence of HCV infection on a single antigen screening test and repeatedly reactive on a subsequent multiantigen screening test, unless a negative supplemental test result or an indeterminate RIBA 3.0 supplemental test result was obtained.

(3) *Services furnished by an outside blood bank.* If a hospital regularly uses the services of an outside blood bank, it must have an agreement with the blood bank that governs the procurement, transfer, and availability of blood and blood products. The agreement must require that the blood bank notify the hospital—

(i) Within 3 calendar days if the blood bank supplied blood and blood products collected from a donor who tested negative at the time of donation but tests repeatedly reactive for the antibody to HIV or HCV on a later donation or who is determined to be at increased risk for transmitting HIV or HCV infection;

(ii) Within 45 days of the test, of the results of the FDA-licensed, more specific test for HIV or HCV, as relevant, or other followup testing required by FDA; and

(iii) Within 3 calendar days if the blood bank supplied blood and blood products collected from a donor, whenever records are available, as set forth in FDA's 21 CFR 610.48(h)(3)(ii) and (i)(3)(ii), in instances in which the donor—

(A) Tested repeatedly reactive on the screening test and positive on a supplemental test for HCV performed on the repeatedly reactive sample;

(B) Tested repeatedly reactive on the screening test and indeterminate on a supplemental test for HCV; or

(C) Tests repeatedly reactive on the screening test with no record of a supplemental test for HCV performed on the repeatedly reactive sample and no record of a negative licensed screening test performed on the same donor.

(4) *Quarantine and disposition of blood and blood products pending completion of testing.* If the blood bank (either internal or under an agreement) notifies the hospital of the repeatedly reactive HIV or HCV screening test results, the hospital must determine the disposition of the blood or blood product and quarantine all blood and blood products from previous donations in inventory.

(i) If the blood bank notifies the hospital that the result of the FDA-licensed, more specific test or other followup testing required by FDA is negative, absent other informative test results, the hospital may release the blood and blood products from quarantine.

(ii) If the blood bank notifies the hospital that the result of the FDA-licensed, more specific test or other followup testing required by FDA is positive, the hospital must—

(A) Dispose of the blood and blood products; and

(B) Notify the transfusion recipients as set forth in paragraph (b)(6) of this section.

(iii) If the blood bank notifies the hospital that the result of the FDA-licensed, more specific test or other followup testing required by FDA is indeterminate, the hospital must destroy or label prior collections of blood or blood products held in quarantine as set forth in FDA's 21 CFR 610.48(k).

(5) *Recordkeeping by the hospital.* The hospital must maintain—

(i) Adequate records of the source and disposition of all units of blood and blood products for at least 10 years from the date of disposition;

(ii) The records in a manner that permits prompt retrieval; and

(iii) A fully funded plan to transfer these records to another hospital or other entity if the former hospital ceases operation for any reason.

(6) *Patient notification.* If the hospital has administered potentially HIV or HCV infectious blood or blood products (either directly through its own blood bank or under an agreement) or released the blood or blood products to another entity or individual, the hospital must take the following actions:

(i) Make at least three attempts to notify the patient, or to notify the attending physician or the physician who ordered the blood or blood product and ask the physician to notify the patient, that potentially HIV or HCV infectious blood or blood products were transfused to the patient.

(ii) Immediately notify the patient, or other individual as permitted under paragraph (b)(10) of this section, of the need for HIV or HCV testing and counseling.

(iii) If the physician is unavailable or declines to make the notification, make at least three attempts to give this

notification to the patient or other individual.

(iv) Document in the patient's medical record the notification or attempts to give the required notification.

(7) *Timeframe for notification.* (i) *For donors tested on or after [effective date of final regulation].* For notifications resulting from donors tested on or after [effective date of final regulation] as set forth in FDA's 21 CFR 610.48(a)(b), the notification effort begins when the blood bank notifies the hospital that it received potentially HIV or HCV infectious blood and blood products and continues for 12 weeks unless—

(A) The patient is located and notified; or

(B) The hospital is unable to locate the patient and documents in the patient's medical record the extenuating circumstances beyond the hospital's control that caused the notification timeframe to exceed 12 weeks.

(ii) *For donors tested before [effective date of final regulation].* For notifications resulting from donors tested before [effective date of final regulation] as set forth in FDA's 21 CFR 610.48(c)(d), the notification effort begins when the blood bank notifies the hospital that it received potentially HCV infectious blood and blood products. The hospital must make at least three attempts to give notification and must complete the actions within 1 year of the date on which the hospital received notification from the outside blood service.

(8) *Content of notification.* The notification must include the following information:

(i) A basic explanation of the need for HIV or HCV testing and counseling.

(ii) Enough oral or written information so that the transfused patient can make an informed decision about whether to obtain HIV or HCV testing and counseling.

(iii) A list of programs or places where the patient can obtain HIV or HCV testing and counseling, including any requirements or restrictions the program may impose.

(9) *Policies and procedures.* The hospital must establish policies and procedures for notification and documentation that conform to Federal, State, and local laws, including requirements for the confidentiality of medical records and other patient information.

(10) *Notification to legal representative or relative.* If the patient has been adjudged incompetent by a State court, the physician or hospital must notify a legal representative designated in accordance with State law. If the patient is competent, but State law permits a legal representative or relative to receive the information on the patient's behalf, the physician or hospital must notify the patient or his or her legal representative or relative. If the patient is deceased, the physician or hospital must continue the notification process and inform the deceased patient's legal representative or relative. If the patient is a minor, the legal guardian must be notified.

(c) *General blood safety issues.* Hospitals must comply with regulations of the FDA as they pertain to blood safety issues in the following areas:

(1) Appropriate testing and quarantining of infectious blood and blood products.

(2) Notification and counseling of recipients that may have received infectious blood and blood products.

Authority: Sections 1818(d)(2) and 1818A(d)(2) of the Social Security Act (42 U.S.C. 1395i–2(d)(2) and 1395i–2a(d)(2)).

(Catalog of Federal Domestic Assistance Program No. 93.773, Medicare—Hospital Insurance)

Dated: September 22, 1999.

Michael M. Hash,

Deputy Administrator, Health Care Financing Administration.

Dated: March 27, 2000.

Donna E. Shalala,

Secretary.

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