Guidance for Industry

"Lookback" for Hepatitis C Virus (HCV): Product Quarantine, Consignee Notification, Further Testing, Product Disposition, and Notification of Transfusion Recipients Based on Donor Test Results Indicating Infection with HCV

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (CBER)
August 2007
Updated December 2010

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NOTE: Changes have been made to update the guidance dated August 2007:

- Figure 1 and Table 1 of the guidance have been revised to reflect new technologies for anti-HCV testing, and corresponding changes have been made to the text.
- The guidance has been updated to note that Title 21 Code of Federal Regulations 610.48 (21 CFR 610.48) (historical lookback) requires blood establishments to have completed a number of actions by February 19, 2009, based on the review of historical testing records. Note that the recommendations for implementing historical lookback as reflected in Figures 2-4 and Tables 2-5 have been relocated to the new Appendix to this guidance.
- In section IV, "January 1, 1988" was revised to "February 20, 2008".
- The recommendation with respect to notification by transfusion services, as consignees, was expanded to include a recipient's physician of record, as appropriate, consistent with the regulations.
- The time frames in which blood establishments must perform appropriate procedures after a donor tests reactive for evidence of HCV infection were clarified.
- A number of nonsubstantive changes were made throughout the document for clarification purposes.

U.S. Department of Health and Human Services
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This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the appropriate FDA staff. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

Multiple layers of safeguards, including donor screening and testing, are used to reduce the risk of transmitting infection through blood transfusion. However, a person may donate blood early in infection, during the period when the viral marker is not detectable by a screening test, but the infectious agent is present in the donor's blood (the "window period"). For example, if an individual donates blood on a number of occasions and each donation tests nonreactive for antibody to HCV, but the donor returns and tests repeatedly reactive for antibody to HCV at a later date, prior collections from such a donor could be at increased risk for transmitting HCV. In addition, a recipient of a transfusion of blood or blood components collected during the "window period" from a donor who is now repeatedly reactive would not know that he or she might be at increased risk of infection with HCV through the transfusion, unless he or she is notified. Furthermore, untested collections from donors who later were found to be repeatedly reactive when tested for antibodies to HCV since 1990 (when antibody tests for HCV became available) might have been at increased risk for transmitting HCV due to a chronic infection in the donor.

Chronic hepatitis due to HCV is a major health problem in the U.S. The infection is usually clinically silent until the liver is seriously damaged. As a result, infected people usually are unaware of their disease. Although transfusion-transmitted infections account for only a very small proportion of HCV infections, it is possible to identify and "lookback" at prior donations that might have been collected during the "window period."

This guidance document provides recommendations for complying with 21 CFR 610.47 and 21 CFR 610.48[1] to (1) blood establishments that collect blood or blood components, including Source Plasma and Source Leukocytes, (2) hospitals, and (3) other consignees. This guidance does not apply to autologous donations, pooled blood components intended solely for further manufacturing into products that are manufactured using validated viral clearance procedures, and blood and blood components that were intended for manufacture into non-injectable products subject to the labeling described in Section VI.

This document supersedes the guidance document of the same title, dated August 2007. The August 2007 document superseded the HCV sections of the Food and Drug Administration (FDA) memorandum of July 19, 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 August 2007 guidance document also superseded the September 1998 guidance 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 Antibody to Hepatitis C Virus (Anti-HCV); (2) Supplemental Testing, and the Notification of Consignees and Blood Recipients of Donor Test Results for Anti-HCV." Additionally, the August 2007 guidance finalized FDA's draft guidance dated June 1999 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)."

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA's guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

Lookback related to HCV testing has been discussed at open public meetings, including meetings of FDA's Blood Products Advisory Committee (BPAC), on multiple occasions since October 1989. As a response to these discussions, FDA provided detailed guidance in the July 19, 1996, memorandum on the quarantine and disposition of certain prior collections of blood and blood components from donors who subsequently test repeatedly reactive for anti-HCV. The 1996 memorandum recommended that blood establishments notify consignees (such as the transfusion service, physician, or fractionator) for the purpose of quarantine and eventual disposition of products made from prior collections. Prior to recent advances in medical diagnosis and therapy,

[1] Section 610.48 (21 CFR 610.48) requires blood establishments to have completed a number of actions by February 19, 2009, based on the review of historical testing records. Recommendations for implementing historical lookback required under 21 CFR 610.48 are included in Figures 2-4 and Tables 2-5, located in the Appendix.

FDA did not recommend notification of recipients of blood from donors who subsequently test positive for anti-HCV because no clear consensus on the public health benefit (i.e., disease prevention and treatment) of such action had emerged.

Improvements in the management and treatment of chronic hepatitis C have occurred over time, and there is a strong correlation between a positive test for anti-HCV in a supplemental assay (e.g., the Chiron RIBA HCV 3.0 SIA[2]) and HCV infection (Refs. 1-4). Prior collections from donors later found to be repeatedly reactive for anti-HCV might also be at increased risk of transmitting HCV.

At public meetings on April 24 and 25, 1997, and August 11 and 12, 1997, the Public Health Service (PHS) Advisory Committee on Blood Safety and Availability recommended notification of recipients of transfused blood and blood components that are at increased risk of transmitting HCV infection based on donor screening with a licensed multiantigen screening test (Enzyme Immuno Assay (EIA) 2.0 or EIA 3.0) since 1992. Consistent with these recommendations, in March 1998, FDA issued guidance for implementation and public comment regarding recipient notification (63 FR 13675, March 20, 1998). In response to comments received, FDA issued a revised guidance for implementation in September 1998 (63 FR 56198, October 21, 1998).

At public meetings on November 24, 1998, and January 28, 1999, the PHS Advisory Committee on Blood Safety and Availability reconsidered the issue of recipient notification related to repeatedly reactive results on the single antigen (EIA 1.0) screening test that was licensed in 1990. The PHS Advisory Committee recommended the expansion of the targeted HCV lookback program to include recipients of blood and blood components from donors subsequently identified as repeatedly reactive by the EIA 1.0 screening test. In addition, the PHS Advisory Committee considered that, in cases where no supplemental test result is available, it is reasonable to perform lookback for EIA 1.0 based on a signal to cutoff ratio of the screening test of greater than 2.5 (S/CO > 2.5) to capture the vast majority of the true positives and minimize unnecessary recipient notifications based on false reactive screening test results.

In accordance with the recommendations from the PHS Advisory Committee, FDA issued a draft guidance on HCV Lookback dated June 1999 for public comment (64 FR 33309, June 22, 1999) and published a proposed rule entitled "Current Good Manufacturing Practice for Blood and Blood Components; Notification of Consignees and Transfusion Recipients Receiving Blood and Blood Components at Increased Risk of Transmitting HCV Infection ("Lookback") (65 FR 69378, November 16, 2000). In the *Federal Register* of August 24, 2007, (72 FR 48766), FDA published the final rule entitled "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 Hepatitis C Virus Infection ("Lookback")" and a companion guidance document, dated August 2007 (72 FR 48658). The August 2007 guidance provided recommendations for complying with 21 CFR 610.47 and 21 CFR 610.48.

[2] The Chiron Corporation (Emeryville, CA) RIBA HCV 3.0 SIA is a strip immunoblot assay based on recombinant antigens of HCV.

III. DEFINITIONS

Alternative Test: A licensed test for anti-HCV that is of equal or greater sensitivity in comparison to the licensed HCV EIA 3.0.

Blood and Blood Components: Whole Blood and blood components, including Source Plasma and Source Leukocytes.

Lookback:

- The identification of blood and blood components from prior collections from a donor with:
  1. a repeatedly reactive antibody screening test for anti-HCV; or
  2. a reactive NAT[3] for HCV; or
  3. other reliable test results or information indicating evidence of HCV infection (provided the testing was performed using a test approved by FDA by a laboratory compliant with the Clinical Laboratory Improvement Amendments of 1988, or has met equivalent requirements as determined by the Centers for Medicare and Medicaid Services in accordance with the provisions of 42 CFR part 493); and
- subsequent actions, such as:
  1. quarantine of such blood and blood components that are not expired;
  2. notification of consignees to quarantine such in-date blood products;
  3. further testing of the donor;
  4. destruction or relabeling of potentially infectious prior collections;
  5. release from quarantine of blood and blood components that do not present a greater risk of infection; and (if appropriate)
  6. notification of recipients of identified blood and blood components, or the recipient's physician of record.

Lookback Donations: Collectively, the blood and blood components from prior collections from the same donor.

Reactive NAT[3] for HCV: A result for an HCV RNA test that uses only one set of primers specific for HCV that is performed initially on an individual donation, or is performed as a discriminatory NAT subsequent to a reactive multiplex NAT, which tests for multiple viruses, including HCV RNA.

[3] This guidance does not address testing, product disposition, donor management, and lookback for individual donor samples that test reactive on a multiplex NAT or a minipool that test reactive on a multiplex NAT. In addition, under 21 CFR 610.47 and 610.48, lookback is required for individual donor samples that test reactive on a multiplex NAT but nonreactive for both HIV-1 and HCV when tested using discriminatory HIV-1 NAT and discriminatory HCV NAT. See "Guidance for Industry: Nucleic Acid Testing (NAT) for Human Immunodeficiency Virus Type 1 (HIV-1) and Hepatitis C Virus (HCV): Testing, Product Disposition, and Donor Deferral and Reentry" dated May 2010, for FDA recommendations in these circumstances. The document may be accessed at http://www.fda.gov/downloads/biologicsblood%20vaccines/guidancecomplianceregulatoryinformation/guidances/blood/ucm210270.pdf accessed December 20, 2010.

Repeatedly Reactive Screening Test: The result when an initially reactive screening test is repeated in duplicate samples on the same test run and one or both samples are reactive.

NOTE: In the HCV Lookback regulations, 21 CFR 610.47 and 610.48, we refer to screening tests as "reactive" instead of "repeatedly reactive" to accommodate the different testing algorithms established for NAT and other screening tests. However, in this guidance we refer to reactive antibody screening test results for anti-HCV as "repeatedly reactive" to accurately reflect the established testing algorithm for anti-HCV.

Transfusion Recipient Notification: The actions taken by a hospital, transfusion service, or recipient's physician of record to notify recipients that they received a transfusion of a Lookback Donation that is at increased risk of transmitting HCV infection.

IV. LOOKBACK REQUIREMENTS

In this guidance, FDA addresses lookback related to donor screening by a licensed anti-HCV test and NAT. Under 21 CFR 610.47 and 21 CFR 610.48, blood establishments must search records of prior collections from donors whose test results on current or historical review donations show evidence of infection with HCV (either repeatedly reactive on screening tests for anti-HCV or reactive on NAT for HCV RNA). Blood establishments must search their records to identify prior collections dating back 10 years (for **current** donations) or dating back to January 1, 1988 for **historical review** donations. If an establishment maintains computerized electronic records relating to collections made before February 20, 2008, the blood establishment must perform a **historical review** search of those records dating back indefinitely, as far back as they exist in computerized, electronic form (21 CFR 610.48(b)(1)(i)). The blood establishment must search records of prior collections, if available, back to the date 12 months prior to the donor's most recent nonreactive licensed multiantigen screening test for anti-HCV (if applicable), if that is a shorter period, since prior infection in the donor is highly unlikely based on the known duration of the window period (see 21 CFR 610.47(a)(1)(i) and 21 CFR 610.48(b)(1)(iii)(A)). FDA believes that this date (12 months prior to the last nonreactive multiantigen screening test for anti-HCV) will antedate the window period for infection in that donor.

FDA believes that results for NAT are of value in (1) lookback related to current collections when a NAT result exists and (2) in historical lookback, when a NAT result, including NAT performed under an Investigational New Drug Application (IND), exists in the record of the previous donation(s). Blood establishments should consider a reactive NAT result to be presumptive evidence of ongoing HCV infection. A reactive NAT must serve as a basis for initiating lookback (i.e., both quarantine and recipient notification) (21 CFR 610.47(a)(1)). Note that certain licensed HCV NAT have been labeled with a "limited supplemental claim." When current donor test results are repeatedly reactive on an anti-HCV screening test and reactive on HCV NAT, the reactive NAT acts as a positive supplemental test and it is not necessary to perform a licensed multiantigen supplemental test for anti-HCV. However, a nonreactive NAT should not be a reason for not performing lookback for a donation that is repeatedly reactive on

an anti-HCV screening test. This recommendation is based on current research that indicates that in about 15-25% of cases of HCV infection, viremia may be intermittently detectable (Ref. 5) or resolved (Ref. 6).

Blood establishments must initiate lookback based on a reactive NAT although a screening test or supplemental test for antibodies to HCV performed on the same collection is nonreactive (21 CFR 610.47(a)(1)). In this situation, blood establishments must search records of prior collections for the 12 months prior to the date of the NAT-reactive donation (21 CFR 610.47(a)(1)(ii) and 21 CFR 610.48(b)(1)(iii)(B)), since this configuration of test results is consistent with recent HCV infection in the donor (Ref. 7).

Blood establishments that collect blood or blood components, including Source Plasma and Source Leukocytes, must establish, maintain and follow appropriate procedures[4] for the following actions within specified timeframes after a donor tests reactive for evidence of HCV infection (21 CFR 610.47(a)); or during an historical record review, after identifying donors who tested reactive for evidence of HCV infection (21 CFR 610.48(b)):

- quarantine prior collections that remain in inventory;
- notify consignees to quarantine prior collections;
- further test the donor and notify consignee of test results; and
- destroy or relabel potentially infectious prior collections.

Under 21 CFR 610.47(b) and 21 CFR 610.48(c), transfusion services, as consignees, must establish, maintain and follow an appropriate system for the following actions within specified timeframes, when notified by the collecting establishment:

- quarantine prior collections that remain in inventory;
- destroy or relabel potentially infectious prior collections; and
- notify transfusion recipients who received blood or blood components from a donor who is later determined to be infected with HCV, if appropriate, or the recipient's physician of record, as appropriate.

NOTE: Recommendations for implementing historical lookback required under 21 CFR 610.48 are included in Figures 2-4 and Tables 2-5, located in the Appendix.

V. CURRENT RECOMMENDATIONS

Current lookback recommendations are provided in Figure 1 and Table 1 to assist blood establishments in complying with the regulations in 21 CFR 610.47.

[4] See 21 CFR 606.100(b)(19)(i) through (vi) and 606.160(b)(1)(viii) for requirements for standard operating procedures and records concerning the activities performed under 21 CFR 610.46, 610.47, and 610.48.

VI. BLOOD AND BLOOD COMPONENTS INTENDED FOR MANUFACTURE INTO NON-INJECTABLE PRODUCTS

There may be some limited uses for quarantined prior collections identified in the lookback either for current donations or for historical review donations that are not suitable for release from quarantine for their original intended use. We recommend that you do not use such prior collections for transfusion or for manufacturing into injectable products. You should destroy these prior collections as a general practice; however, in limited situations, release for research or for further manufacture is acceptable. If released for research or for further manufacture into in vitro diagnostic reagents, you must relabel the prior collections with a "BIOHAZARD" legend (21 CFR 610.40(h)(2)(ii)(B)). In addition, we recommend that you relabel the prior collections with two of the following statements:

- "Collected from a donor who subsequently tested reactive for anti-HCV or HCV RNA. An increased risk of transmission of HCV is present."

  and either

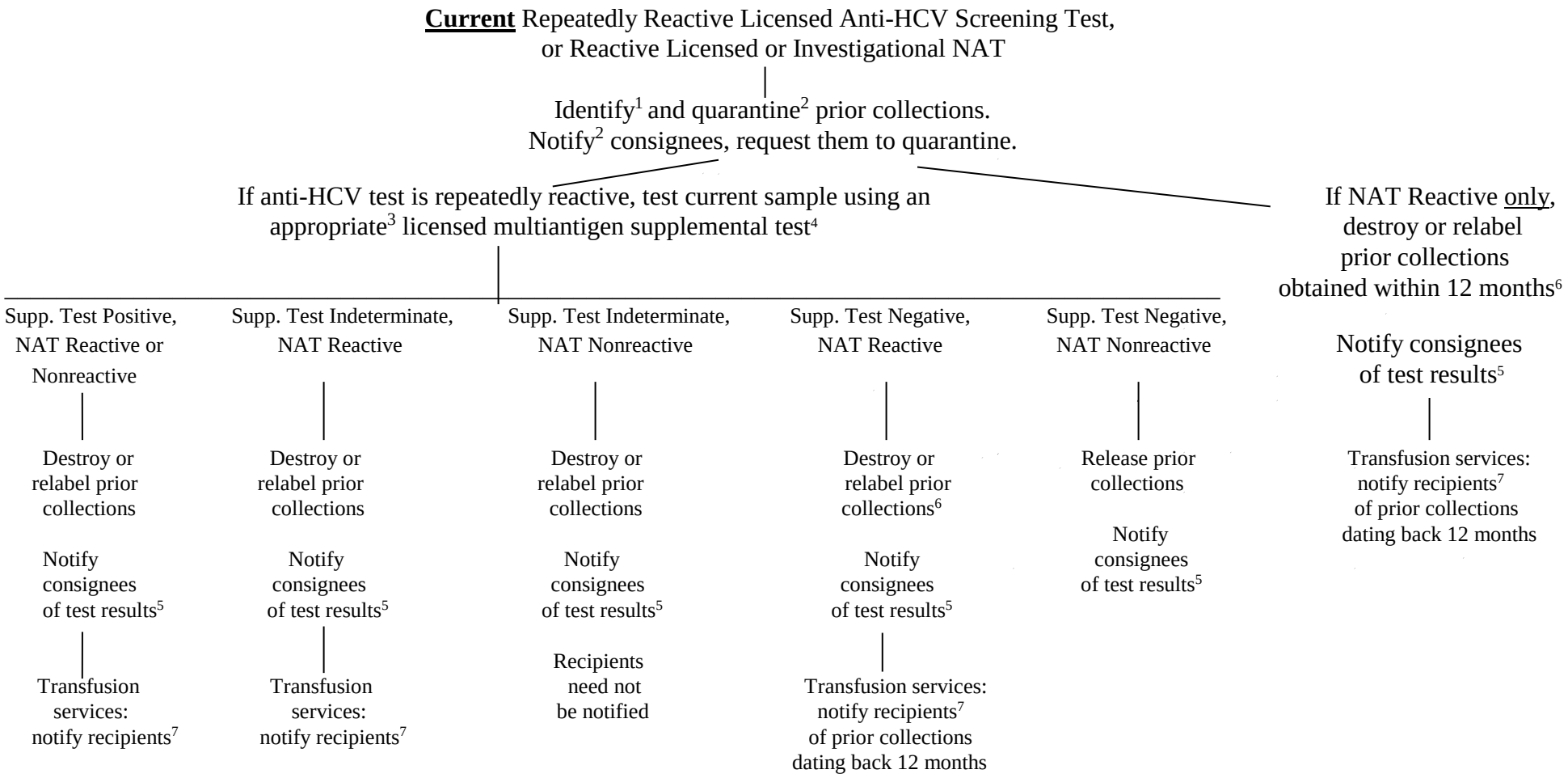
- "Caution: For Further Manufacturing Into In Vitro Diagnostic Reagents For Which There Are No Alternative Sources."

  or

- "Caution: For Laboratory Research Use Only."

If you release the units for further manufacture into injectable products, the units must include a statement on the container label indicating the exempted use specifically approved by FDA (21 CFR 610.40(h)(2)(ii)(D)).

Figure 1 Lookback for Hepatitis C Virus (HCV) Based on Current Donor Test Results Using a Licensed Screening Test for HCV Antibody or a Licensed or Investigational NAT for HCV RNA



[1] If repeatedly reactive for anti-HCV, prior collections should be identified from the same donor dating back to the date 12 months prior to the donor's most recent nonreactive licensed multiantigen screening test. If NAT-reactive only, prior collections should be identified from the same donor dating back 12 months prior to the reactive NAT.
[2] Within 3 calendar days after the day of obtaining the reactive NAT result or repeatedly reactive anti-HCV screening test result.
[3] An appropriate supplemental test is one that includes all the antigens contained in the screening test that was performed.
[4] Certain licensed HCV NAT have been labeled with a "limited supplemental claim." When current donor test results are repeatedly reactive on an anti-HCV screening test and reactive on HCV NAT, the reactive NAT acts as a positive supplemental test and it is not necessary to perform a licensed multiantigen supplemental test for anti-HCV.
[5] Notify consignees of all test results within 45 calendar days of the current repeatedly reactive anti-HCV or NAT-reactive test result.
[6] Prior collections obtained more than 12 months prior to the date of the NAT-reactive donation may be released.
[7] Transfusion services must identify and notify recipients of identified prior collections, or the recipient's physician of record, as appropriate.

Table 1 Current Review

You must take the following steps when donor test results for antibody to Hepatitis C Virus (anti-HCV) by **a licensed screening test** are **repeatedly reactive**, or a licensed or investigational HCV RNA **Nucleic Acid Test** (NAT) is **reactive**. You must identify and quarantine prior collections, notify the consignees and request them to quarantine prior collections. Then…

If the initial test is a licensed …		**And the additional testing[1] is a licensed or investigational …**		**Then …**			
				Notify Consignee of test result	Destroy/ Relabel prior collection	Transfusion services notify recipients or recipient's physician of record	Release prior collection
Anti-HCV	NR	NAT	Reactive	X	X[3]	X[3]	
Anti-HCV	RR	Appropriate Multiantigen Supplemental Test	Positive	X	X	X	
		NAT	Nonreactive				
Anti-HCV	RR	Appropriate Multiantigen Supplemental Test	Positive	X	X	X	
		NAT[2]	Reactive				
Anti-HCV	RR	Appropriate Multiantigen Supplemental Test	Indeterminate	X	X		
		NAT	Nonreactive				
Anti-HCV	RR	Appropriate Multiantigen Supplemental Test	Indeterminate	X	X	X	
		NAT[2]	Reactive				
Anti-HCV	RR	Appropriate Multiantigen Supplemental Test	Negative	X			X
		NAT	Nonreactive				
Anti-HCV	RR	Appropriate Multiantigen Supplemental Test	Negative	X	X[3]	X[3]	X[4]
		NAT[2]	Reactive				

[1]Appropriate additional testing includes all the antigens contained in the screening test that was performed
[2]Certain licensed HCV NAT have been labeled with a "limited supplemental claim." When current donor test results are repeatedly reactive on an anti-HCV screening test and reactive on HCV NAT, the reactive NAT acts as a positive supplemental test and it is not necessary to perform a licensed multiantigen supplemental test for anti-HCV.
[3]Collections during the 12 months prior to the date of the donation testing NAT reactive
[4]Release collections from more than 12 months prior to the date of the donation testing NAT reactive
NR means nonreactive
RR means repeatedly reactive

VII. REFERENCES

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3. Yun, Z. et al. Detection of Hepatitis C Virus (HCV) RNA by PCR Related to HCV Antibodies in Serum and Liver Histology in Swedish Blood Donors. *J Med Virol* 39:57-61 (1993).

4. Dow, B.C. et. al. Relevance of RIBA-3 Supplementary Test to HCV PCR Positivity and Genotypes for HCV Confirmation of Blood Donors. *J Med Virol* 49:132-136 (1996).

5. Alter, H.J. To C or Not to C: These Are the Questions. *Blood* 85:1681-1695 (1995).

6. CDC. Recommendations for Prevention and Control of Hepatitis C Virus (HCV) Infection and HCV-Related Chronic Disease. *MMWR Morb Mortal Wkly Rep* 47 (RR-19) (1998).

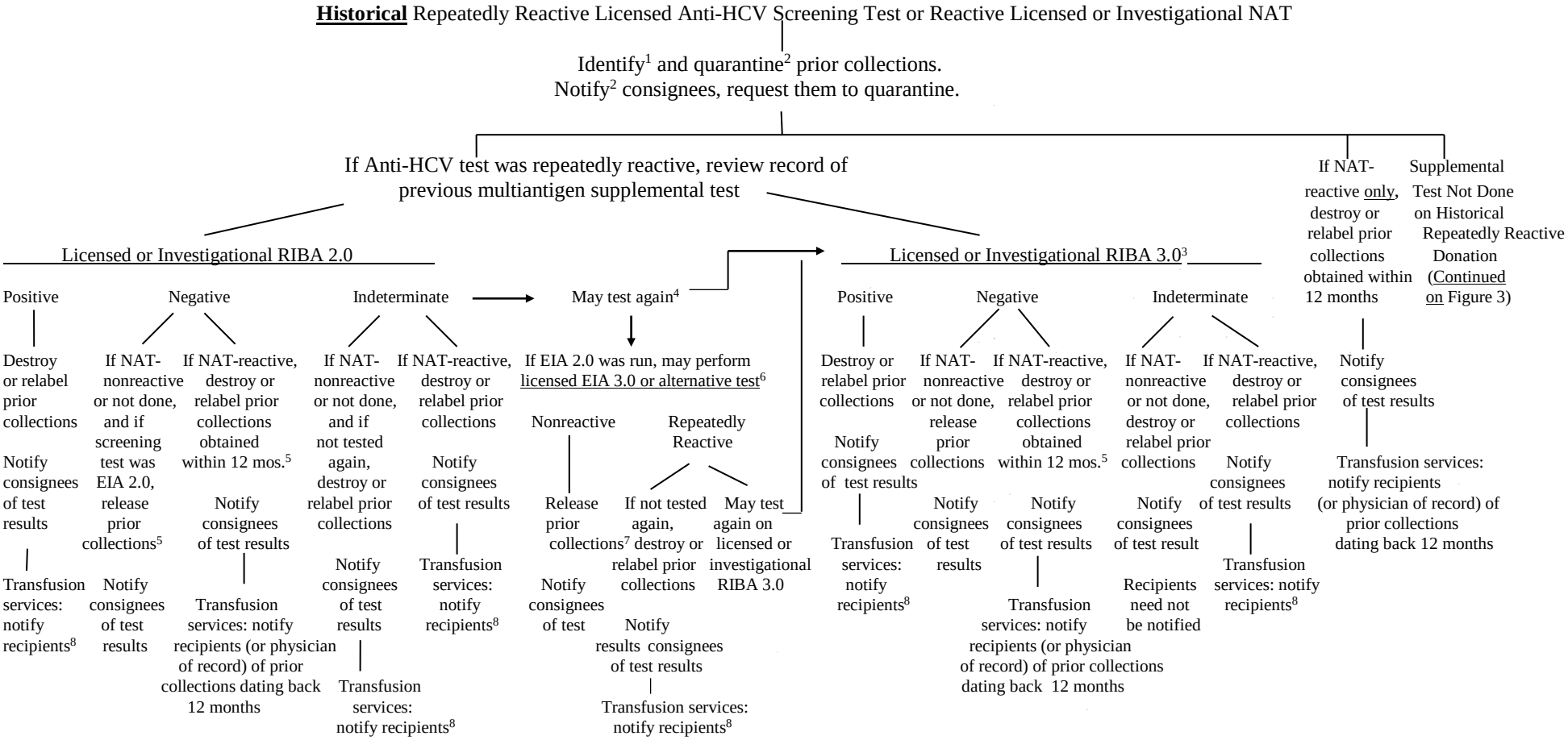
7. Schreiber, G.B. et al. The Risk of Transfusion-Transmitted Viral Infections. *N Engl J Med* 334:1685-1690 (1996).

APPENDIX

Recommendations for implementing historical lookback required under 21 CFR 610.48 are included in Figures 2-4 and Tables 2-5.

Contains Nonbinding Recommendations

Figure 2 Lookback for Hepatitis C Virus (HCV) Based on Historical Donor Test Results Using a Licensed Screening Test for HCV Antibody or a Licensed or Investigational NAT for HCV RNA



[1] If repeatedly reactive, prior collections should be identified from the same donor dating back to the date 12 months prior to the donor's most recent nonreactive licensed multiantigen screening test. If NAT-reactive only, prior collections should be identified from the same donor dating back 12 months prior to the date of the NAT-reactive donation.

[2] Within 3 calendar days after the day of identifying the reactive NAT result or repeatedly reactive anti-HCV screening test result.

[3] Testing already performed as an in-house service by Chiron Corp. using the Chiron RIBA HCV 3.0 SIA, or testing already performed using an investigational RIBA 3.0 in accordance with previous guidance, is also acceptable.

[4] A previously frozen serum or plasma sample from the repeatedly reactive/RIBA 2.0 indeterminate donation or a fresh sample from the same donor may be tested again. Notify consignees within 45 calendar days of completing the additional testing.

[5] If the repeatedly reactive screening test was EIA 3.0 and the negative supplemental test was RIBA 2.0, destroy or label prior collections and notify transfusion recipients. Alternatively, may test again using RIBA 3.0 (see outcomes at right). Notify consignees within 45 calendar days of completing the supplemental test result.

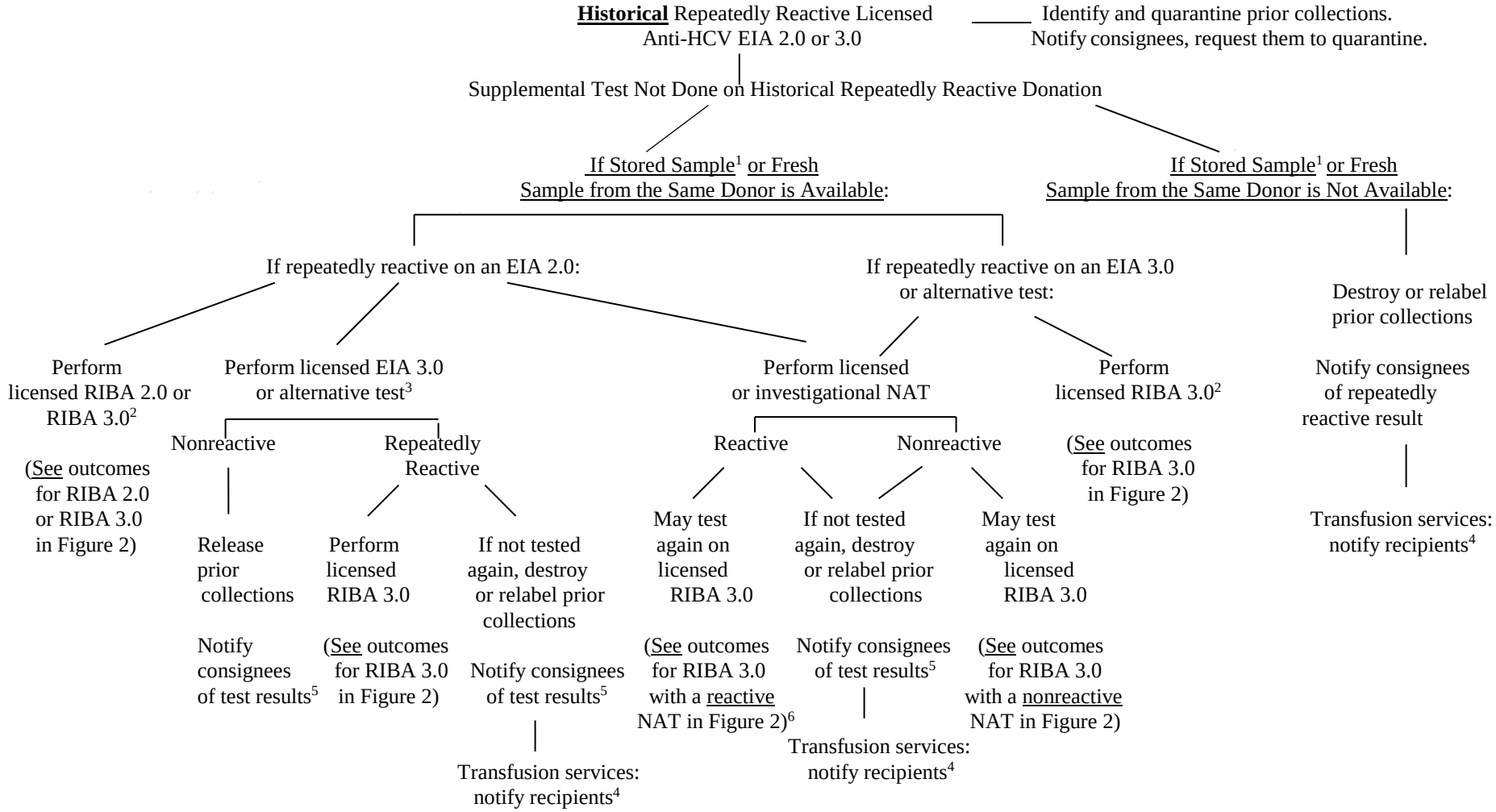
[6] An alternative test for anti-HCV is a test of equal or greater sensitivity in comparison to the licensed HCV EIA 3.0.

[7] If a RIBA 2.0 or RIBA 3.0 is negative, prior collections obtained more than 12 months prior to the date of the NAT-reactive donation may be released.

[8] Transfusion services must identify and notify recipients, or the recipient's physician of record, as appropriate, of identified prior collections dating back to the date 12 months prior to the donor's most recent nonreactive licensed multiantigen screening test for anti-HCV.

Contains Nonbinding Recommendations

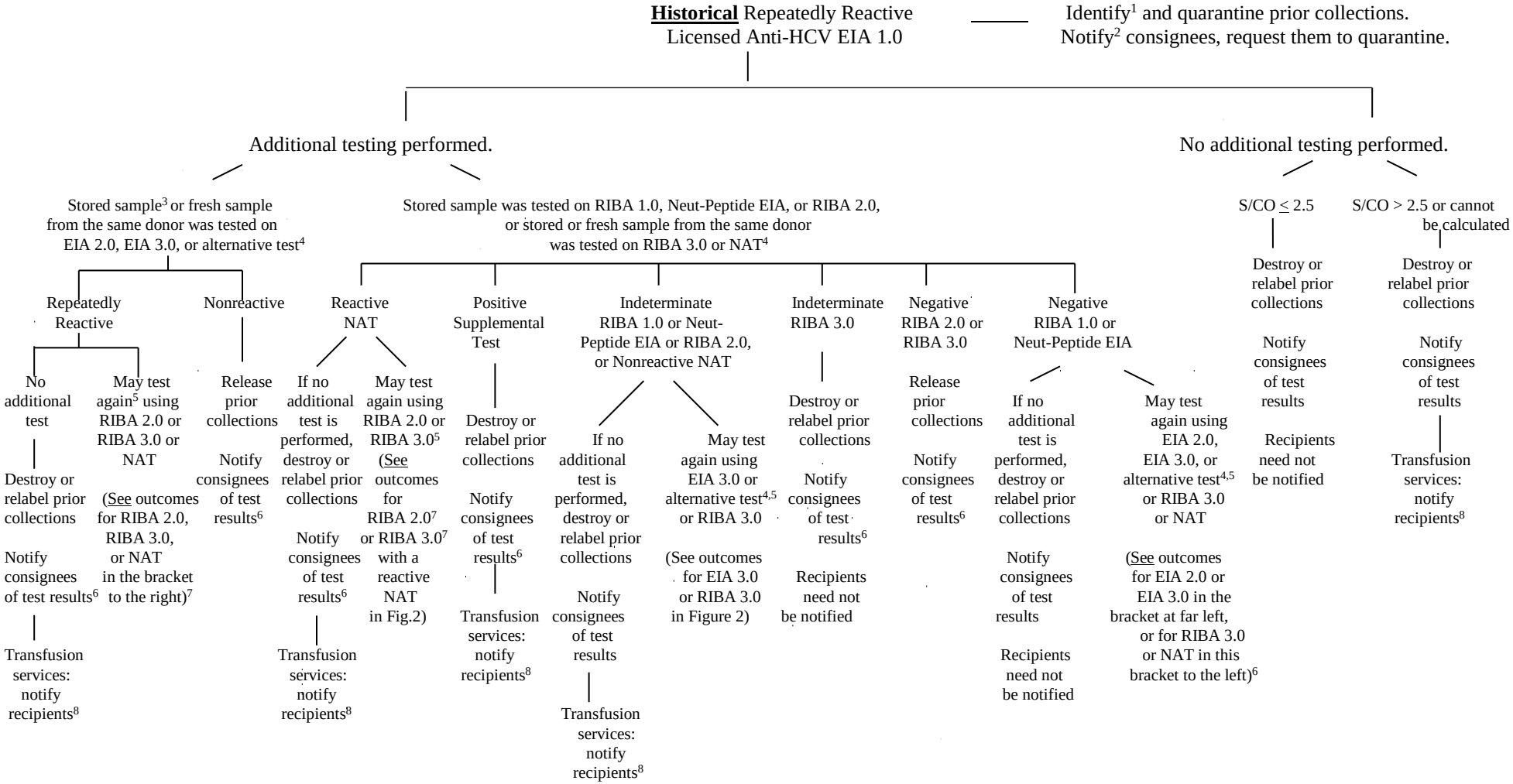
Figure 3 Lookback for Hepatitis C Virus (HCV) Based on Historical Donor Test Results Using a Licensed EIA 2.0 or EIA 3.0 Test for HCV Antibody or a Licensed or Investigational NAT for HCV RNA (Cont.)



[1] A previously frozen serum or plasma sample from the same repeatedly reactive donation.
[2] If a licensed RIBA 2.0 test or an investigational RIBA 3.0 test was performed consistent with previous guidance, refer to Figure 2 for outcomes.
[3] An alternative test for anti-HCV is a test of equal or greater sensitivity in comparison to the licensed HCV EIA 3.0.
[4] Transfusion services must identify and notify recipients, or the recipient's physician of record, of identified prior collections dating back to the date 12 months prior to the donor's most recent nonreactive licensed multiantigen screening test for anti-HCV.
[5] Notify consignees within 45 calendar days of completing the additional testing.
[6] If a NAT is reactive and further testing by RIBA 3.0 is negative or indeterminate, transfusion services should identify and notify recipients, or the recipient's physician of record, of identified prior collections dating back 12 months prior to the date of the NAT-reactive donation. If the RIBA 3.0 is negative, prior collections obtained more than 12 months prior to the date of the NAT-reactive donation may be released. If the RIBA 3.0 is indeterminate, prior collections should be destroyed or labeled consistent with section VI of this guidance. Note that a nonreactive NAT does not obviate lookback for a repeatedly reactive donation.

Contains Nonbinding Recommendations

Figure 4 **Lookback for Hepatitis C Virus (HCV) Based on Historical Donor Test Results Using an EIA 1.0 for HCV Antibody**



[1]Previously distributed units should be identified dating back 12 months prior to the donor's most recent nonreactive licensed screening test for anti-HCV.
[2]Within 3 calendar days after the day of identifying the repeatedly reactive anti-HCV screening test results.
[3] A previously frozen serum or plasma sample from the same repeatedly reactive donation.
[4] An alternative test for anti-HCV is a test of equal or greater sensitivity in comparison to the licensed HCV EIA 3.0.
[5] The supplemental test performed should include all the antigens contained in the screening test that was performed.
[6] Notify consignees within 45 calendar days of obtaining the supplemental or additional test result.
[7] If a NAT is reactive and further testing by RIBA 2.0 or RIBA 3.0 is negative, prior collections obtained more than 12 months prior to the date of the NAT-reactive donation may be released, and transfusion services must identify and notify recipients of prior collections dating back 12 months prior to the date of the NAT-reactive donation. If the RIBA 2.0 is indeterminate, destruction or labeling of prior collections and notification of recipients are not limited to collections within 12 months prior to the NAT-reactive donation. If the RIBA 3.0 is indeterminate, destruction or labeling of prior collections is not limited to collections within 12 months prior to the NAT-reactive donation, but notification of recipients should extend back only 12 months prior to the NAT-reactive donation. Note that a nonreactive NAT does not obviate lookback for a repeatedly reactive donation.
[8] Transfusion services must identify and notify recipients, or recipient's physician of record, as appropriate, of identified prior collections.

Table 2 Historical Review

You must take the following steps when donor test results for antibody to Hepatitis C Virus (anti-HCV) by **a licensed screening test** are **repeatedly reactive**, or a licensed or investigational HCV RNA **Nucleic Acid Test** (NAT) is **reactive**. You must identify and quarantine prior collections, notify the consignees and request them to quarantine prior collections. Then …							
If the historical initial test is a licensed …		**And the historical additional testing[1] is a licensed or investigational …**		**Then …**			
				Notify Consignee of test result	Destroy/ Relabel prior collection	Transfusion services notify recipients or recipient's physician of record	Release prior collection
EIA 2.0 or 3.0	RR	NFT	Sample available	See Table 4			
EIA 2.0 or 3.0	RR	RIBA 2.0 NAT	Positive Reactive, Nonreactive or NP	X	X	X	
EIA 2.0	RR	RIBA 2.0 NAT	Negative Nonreactive or NP	X			X
EIA 3.0	RR	RIBA 2.0 NAT	Negative Nonreactive or NP	X	X	X	
EIA 2.0	RR	RIBA 2.0 NAT	Negative Reactive	X	X[2]	X[2]	X[3]
EIA 3.0	RR	RIBA 2.0 NAT	Negative Reactive	X	X	X	
EIA 2.0 or 3.0	RR	RIBA 2.0 NAT	Indeterminate Nonreactive or NP	X	X	X	
EIA 2.0 or 3.0	RR	RIBA 2.0 NAT	Indeterminate Reactive	X	X	X	
EIA 2.0	RR	RIBA 2.0 (MTA) EIA 3.0 or alternative NAT	Indeterminate Nonreactive Nonreactive or NP	X			X
EIA 2.0	RR	RIBA 2.0 (MTA) EIA 3.0 or alternative NAT	Indeterminate Reactive Nonreactive or NP	X	X	X	
EIA 2.0 or 3.0	RR	RIBA 2.0 NAT RIBA 3.0	Indeterminate Nonreactive or NP	See Table 3			
EIA 2.0 or 3.0	NR	NAT only	Reactive	X	X[2]	X[2]	

[1]Appropriate additional testing includes all the antigens contained in the screening test that was performed
[2]Collections during the 12 months prior to the date of the donation testing NAT reactive
[3]Release collections more than 12 months prior to the date of the donation testing NAT reactive
NR means non-reactive
RR means repeatedly reactive
MTA means may test again
NFT means not further tested
NP means not performed

Table 3 Historical Review

You must take the following steps when donor test results for antibody to Hepatitis C Virus (anti-HCV) by **Licensed HCV EIA 2.0 or EIA 3.0** are **repeatedly reactive**, or a licensed or investigational HCV RNA **Nucleic Acid Test** (NAT) is **reactive**. You must identify and quarantine prior collections, notify the consignees and request them to quarantine prior collections. Then …							
If the historical initial test is a licensed …		**And the historical additional testing[1] is a licensed or investigational …**		**Then …**			
				Notify Consignee of test result	Destroy/ Relabel prior collection	Transfusion services notify recipients or recipient's physician of record	Release prior collection
EIA 2.0 or 3.0	RR	RIBA 3.0 NAT	Positive Reactive, Nonreactive or NP	X	X	X	
EIA 2.0 or 3.0	RR	RIBA 3.0 NAT	Negative Nonreactive or NP	X			X
EIA 2.0 or 3.0	RR	RIBA 3.0 NAT	Negative Reactive	X	X[2]	X[2]	X[3]
EIA 2.0 or 3.0	RR	RIBA 3.0 NAT	Indeterminate Nonreactive or NP	X	X		
EIA 2.0 or 3.0	RR	RIBA 3.0 NAT	Indeterminate Reactive	X	X	X	

[1]Appropriate additional testing includes all the antigens contained in the screening test that was performed
[2]Collections during the 12 months prior to the date of the donation testing NAT reactive
[3]Release collections more than 12 months prior to the date of the donation testing NAT reactive
RR means repeatedly reactive
NFT means not further tested
NP means not performed

Table 4 Historical Review

You must take the following steps when donor test results for antibody to Hepatitis C Virus (anti-HCV) by **Licensed HCV EIA 2.0 or EIA 3.0** are **repeatedly reactive**, or a licensed or investigational HCV RNA **Nucleic Acid Test** (NAT) is **reactive**. You must identify and quarantine prior collections, notify the consignees and request them to quarantine prior collections. Then …

If the historical initial test is a licensed …		**And the historical additional testing[1] is a licensed or investigational …**		**Then …**			
				Notify Consignee of test result	Destroy/ Relabel prior collection	Transfusion services notify recipients or recipient's physician of record	Release prior collection
EIA 2.0	RR	RIBA 2.0		See Table 2			
		RIBA 3.0		See Table 3			
EIA 2.0	RR	EIA 3.0 or alternative	Nonreactive	X			X
EIA 2.0	RR	EIA 3.0 or alternative	Reactive	X	X	X	
		(NFT)					
EIA 2.0	RR	EIA 3.0 or alternative	Reactive	See Table 3			
		RIBA 3.0					
EIA 3.0	RR	RIBA 3.0		See Table 3			
EIA 2.0 or 3.0	RR	NAT	Nonreactive	See Table 3			
		(MTA) RIBA 3.0					
EIA 2.0 or 3.0	RR	NAT	Nonreactive or Reactive	X	X[2]	X[2]	X[3]
		(NFT)					
EIA 2.0 or 3.0	RR	NAT	Reactive	See Table 3			
		(MTA) RIBA 3.0					
EIA 2.0 or 3.0	RR	(NFT)	No Sample Available	X	X	X	

[1]Appropriate additional testing includes all the antigens contained in the screening test that was performed
[2]Collections during the 12 months prior to the date of the donation testing NAT reactive
[3]Release collections more than 12 months prior to the date of the donation testing NAT reactive
RR means repeatedly reactive
MTA means may test again
NFT means not further tested

Table 5 Historical Review

You must take the following steps when donor test results for antibody to Hepatitis C Virus (anti-HCV) by **Licensed HCV EIA 1.0** are **repeatedly reactive**. You must identify and quarantine prior collections, notify the consignees and request them to quarantine prior collections. Then …

If the historical initial test is a licensed …		**And the additional testing[1] is a licensed or investigational …**		**Then …**			
				Notify Consignee of test result	Destroy/ Relabel prior collection	Transfusion services notify recipients or recipient's physician of record	Release prior collection
EIA 1.0	S/CO ≤ 2.5	(NFT)		X	X		
EIA 1.0	S/CO >2.5 or cannot be calculated	(NFT)		X	X	X	
EIA 1.0	RR	EIA 2.0 or 3.0 or alternative	Reactive	X	X	X	
		(NFT)					
EIA 1.0	RR	EIA 2.0 or 3.0 or alternative	Reactive	See Below			
		(MTA) RIBA 2.0 or 3.0 or NAT					
EIA 1.0	RR	EIA 2.0 or 3.0 or alternative	Nonreactive	X			X
EIA 1.0	RR	NAT	Reactive	X	X	X	
		(NFT)					
EIA 1.0	RR	NAT	Reactive				
		(MTA) RIBA 2.0	Negative	X	X[2]	X[2]	X[3]
			Indeterminate	X	X	X	
		(MTA) RIBA 3.0	Negative	X	X[2]	X[2]	X[3]
			Indeterminate	X	X	X[2]	
EIA 1.0	RR	RIBA 1.0, 2.0, or 3.0; or Neut-Peptide EIA	Positive	X	X	X	

Table 5 (Continued) Historical Review

You should take the following steps when donor test results for antibody to Hepatitis C Virus (anti-HCV) by **Licensed HCV EIA 1.0** are **repeatedly reactive.** You should identify and quarantine prior collections, notify the consignees and request them to quarantine prior collections. Then …

If the historical initial test is a licensed …		**And the additional testing[1] is a licensed or investigational …**		**Then …**			
				Notify Consignee of test result	Destroy/ Relabel prior collection	Transfusion services notify recipients or recipient's physician of record	Release prior collection
EIA 1.0	RR	RIBA 1.0 or 2.0; or Neut-Peptide EIA	Indeterminate	X	X	X	
		(NFT)					
EIA 1.0	RR	NAT	Nonreactive	X	X	X	
		(NFT)					
EIA 1.0	RR	RIBA 1.0 or 2.0; or Neut-Peptide EIA	Indeterminate	X			X
		NAT	Nonreactive				
		(MTA) EIA 3.0 or alternative; or RIBA 3.0		See Table 3			
EIA 1.0	RR	RIBA 1.0 or 2.0; or Neut-Peptide EIA	Indeterminate	X			X
		NAT	Nonreactive or NP				
		(MTA) EIA 3.0 or alternative; or	Nonreactive				
		RIBA 3.0	Negative				
EIA 1.0	RR	RIBA 3.0	Indeterminate	X	X		
EIA 1.0	RR	RIBA 2.0 or 3.0	Negative	X			X
		NAT	Nonreactive or NP				
EIA 1.0	RR	RIBA 2.0 or 3.0	Negative	X			X[3]
		NAT	Reactive				
EIA 1.0	RR	RIBA 1.0 or Neut-Peptide EIA	Negative	X	X		
		(NFT)					
EIA 1.0	RR	RIBA 1.0 or Neut-Peptide EIA	Negative	See outcomes above			
		(MTA) EIA 2.0 or 3.0 or alternative; or RIBA 3.0; or NAT					

[1]Appropriate additional testing includes all the antigens contained in the screening test that was performed
[2]Collections during the 12 months prior to the date of the donation testing NAT reactive
[3]Release collections more than 12 months prior to the date of the donation testing NAT reactive
NR means non-reactive
RR means repeatedly reactive
MTA means may test again
NFT means not further tested