Transfusion transmitted infections reported to National Blood Service/HPA infection surveillance: 2004

The surveillance of suspected transfusion transmitted infections (TTIs) began in October 1995 and is coordinated by the National Blood Service (NBS)/ Health Protection Agency (HPA) Centre for Infections (CfI). The collected data forms part of the Serious Hazards of Transfusion (SHOT) haemovigilance scheme. Data presented here are for the NBS/HPA CfI surveillance scheme only. The 2004 SHOT Annual Report is due to be published shortly and will be available through the website <http://www.shotuk.org>.

Methods

Blood centres in England, Wales, and Northern Ireland report suspected transfusion transmitted infections (TTIs) to the TTI surveillance scheme. All twelve blood centres reported possible incidents during 2004. Blood centres in Scotland report all incidents to the Microbiology Reference Unit of the Scottish National Blood Transfusion Service, for investigation. Details and findings on each incident are passed to the NBS/HPA CfI surveillance system.

Reports of suspected transfusion transmitted infections

Between January 1 2004 and December 31 2004, 34 reports of suspected TTIs were made by blood centres throughout the United Kingdom to NBS/HPA CfI surveillance (33 in England and Wales, 1 in Scotland). After complete investigations, only one report (hepatitis E) was determined to be a transfusion transmitted infection according to the definition (Box 1). Of the 33 remaining reports, 31 (14 bacteraemia, 1 hepatitis A virus (HAV), 10 hepatitis B virus (HBV), 5 hepatitis C virus (HCV), 1 HIV) did not implicate transfusion as the source of infection. One report (HCV) involved a recipient transfused with 143 units during 1993 that could neither be confirmed nor refuted as a TTI, and one with human herpesvirus 8 (HHV-8) for whom a complete investigation is pending. A report of possible prion transmission was made for an elderly British citizen who died from vCJD in 2001 (1).

Box 1: Definition

A suspected report is classified as a transfusion transmitted infection (TTI) if, following investigation:

The recipient had evidence of infection post-transfusion, and there was no evidence of infection prior to transfusion, and no evidence of an alternative source of infection.

And, either

At least one component received by the infected recipient was donated by a donor who had evidence of the same transmissible infection,

Or

At least one component received by the infected recipient was shown to contain the agent of infection

Case report: transfusion transmitted hepatitis E

A repeat donor reported onset of jaundice 23 days after donating blood in 2004. The platelets and red cells of this donation had been transfused and the recipients were traced and tested; the plasma had been discarded. The archive sample from the donation was tested and found positive for hepatitis E virus (HEV) RNA. The recipient of the platelets (F 55y) was tested 84 days after transfusion, and had not developed any markers for HEV infection. A second recipient (M 65y) had received the red cells unit for treatment of anaemia due to lymphoma and tested positive for HEV RNA and HEV IgM two months post-transfusion. The recipient remained asymptomatic for HEV, apart from a mild jaundice and elevated liver function tests, which may not have been noted if the patient had not been under surveillance. The recipient became HEV RNA-negative three months following the transfusion. No source of the donor's infection was identified. Sequence and phylogenetic analysis showed identity between donor and recipient viruses.

Bacterial incident

In 2004, and for the first time since surveillance of TTIs began in 1995, there were no reports of bacterial infection by transfused components. However, one report was made of an incident involving the transfusion of a unit of platelets contaminated with *Staphylococcus epidermidis* from a donor's arm, but transmission to the recipient could not be confirmed. A female patient aged 75 years with chronic lymphatic leukaemia developed rigors, vomiting and pyrexia following transfusion of a five day old pooled platelet unit. The transfusion was terminated and the patient recovered. An identical strain of *Staphylococcus epidermidis* was isolated from the transfused platelet pack and from the venepuncture site of one of the four contributing donors.The organism was not, however, isolated from the recipient following the reaction. This is evidence of bacterial contamination of a platelet pool from a donor's arm and suggests arm cleansing was inadequate, although transmission to the recipient was not confirmed.

Cumulative total (1995 to 2004)

There have been 52 confirmed TTIs reported to the scheme since surveillance began in 1995, with eight deaths. Table 1 shows the cumulative number of reports of TTIs by year of transfusion.

Table 1 Cumulative total of reports of TTIs made to NBS/HPA Centre for Infections surveillance between 1 October 1995 and 31 December 2004 by year of transfusion and infection

Year of transfusion	Pre 1997	1997	1998	1999	2000	2001	2002	2003	2004	Total	Deaths
Infection											
HAV	1(1)	–	–	–	1 (1)	–	–	–	–	2	–
HBV	3(3	1(1)	1(1)	2(3)	1(1)	–	1(1)	1(1)	–	10	–
HCV	1(1)	1(1)	–	–	–	–	–	–	–	2	–
HIV	1(3)	–	–	–	–	–	1(1)	–	–	2	–
HEV	–	–	–	–	–	–	–	–	1(1)	1	–
HTLV I	2(2)	–	–	–	–	–	–	–	–	2	–
Bacteria	2(2)	3(3)	4(4)	4(4)	7(7)	5(5)	1(1)	3(3)	–	29	7
Malaria	–	1(1)	–	–	–	–	–	1(1)	–	2	1
vCJD	1(1)	–	–	–	–	–	–	–	–	1	–
Possible prion transmission	–	–	–	1(1)	–	–	–	–	–	1	–
Total	11(13)	6(6)	5(5)	7(7)	9(9)	5(5)	3(3)	5(5)	1(1)	52	8

*The number of incidents is shown with the total number of identified infected recipients in brackets.

Comment

Despite reports of suspected transfusion transmitted HBV, HCV, and HIV during 2004, all investigations concluded transfusion was not the source of the recipient's infection. The risk of HIV, HCV or HBV infectious donation entering the blood supply still remains low (2). This is in the presence of donor selection criteria and routine screening of blood donations using highly sensitive techniques, including HCV RNA testing, and combined HIV antibody and antigen assays. The absence of proven bacterial transmissions has followed the implementation in 2002 of procedures to divert the first 20 to 30 mL of each blood donation. The NBS encourage donors to report any illness post-donation, and during 2004 the report of onset of jaundice in a regular donor led to the identification of the confirmed hepatitis E transmission. Donor selection criteria have since been amended to include specific exclusion for individuals who have been in contact with an individual with hepatitis E. (General hepatitis exclusions would have applied prior to amendment , <http://www.transfusionguidelines.org.uk>. Each year the number of TTIs is small and fluctuations are

to be expected. The reporting system is likely to be biased toward ascertainment of infections that cause rapid onset of acute disease. Transfusion transmitted infections continue to be rare in the United Kingdom .

References

1. Health Protection Agency.Serious hazards of transfusion (SHOT), 2003 report. *Commun Dis Rep CDR Wkly* [serial online] 22 July 2004 [cited 27 July 2005]; **14**(30): Immunisation. Available at <http://www.hpa.org.uk/cdr/archives/2004/cdr3404.pdf>.
2. Soldan K, Davison K, Dow BC. Estimates of the frequency of HBV, HCV, and HIV infectious donations entering the blood supply in the United Kingdom, 1996 to 2003. *Eurosurveillance* 2005; **10**:9-10.

医薬品 研究報告 調査報告書

識別番号・報告回数		1	報告日	第一報入手日 2005年7月20日	新医薬品等の区分	厚生労働省処理欄
一般的名称	別紙のとおり		研究報告の公表状況	Draft 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 Draft Guidance (FDA,CBER July 2005)	公表国 米国	
販売名(企業名)	別紙のとおり					

研究報告の概要

(**問題点**：米国食品薬品局(FDA), 生物製剤評価研究センター(CBER)は、HIV-1,HCVに対するNATによる検査、製品廃棄および献血者の排除とリエントリーについてガイダンス案を公表した。)

2004年10月、FDA,CBERは、「HIV-1とHCVの伝播リスクを十分にかつ適切に減少させるための全血と血液成分（原料血漿と原料白血球を含む）のドナーからのプール及び個別検体での核酸増幅検査の使用」を業界向けガイダンスとして発行し、HIV-1とHCVのリボ核酸を検出する供血者のスクリーニングテストとしてNATを承認し、これらの承認された検査法が既承認検査法（抗原抗体検査法）よりもかなり早い段階で感染を感知することができることを血液と原料血漿処理業者に通知しているが、2005年7月、FDA,CBERはHIV-1,HCVのNAT反応陽性について、製品廃棄、献血者排除基準、献血者の追跡調査、NATと血清学的検査結果を考慮した献血者への通知とリエントリー基準、遡及調査に関するガイダンス案を示した。

NATアルゴリズム：
プールNAT→個別またはサブプールNAT→陽性/陰性→リエントリー

HIV-1は8週後、HCVは6ヵ月後に再検査し、追跡検査でNAT反応陽性の場合は永久排除、NAT陰性でEIA陰性の場合はリエントリーする。

使用上の注意記載状況・その他参考事項等

記載なし

報告企業の意見	今後の対応
別紙のとおり	現時点においては、特段の対応は不要と考えるが、今後とも関連情報の収集に努め、本剤の安全性の確保を図っていきたい。

別紙

一般的名称	①人血清アルブミン②人血清アルブミン③人血清アルブミン④人免役グロブリン⑤乾燥ペプシン処理人免疫グロブリン⑥乾燥スルホ化人免疫グロブリン⑦乾燥スルホ化人免疫グロブリン⑧乾燥濃縮人活性化プロテインＣ⑨乾燥濃縮人血液凝固第Ⅷ因子⑩乾燥濃縮人血液凝固第Ⅸ因子⑪乾燥抗破傷風人免疫グロブリン⑫抗ＨＢｓ人免疫グロブリン⑬トロンビン⑭フィブリノゲン加第ＸⅢ因子⑮乾燥濃縮人アンチトロンビンⅢ⑯ヒスタミン加人免疫グロブリン製剤⑰人血清アルブミン⑱人血清アルブミン⑲乾燥ペプシン処理人免役グロブリン⑳乾燥人血液凝固第Ⅸ因子複合体㉑沈降精製百日せきジフテリア破傷風混合ワクチン㉒沈降精製百日せきジフテリア破傷風混合ワクチン㉓沈降精製百日せきワクチン㉔乾燥弱毒生風しんワクチン㉕乾燥弱毒生おたふくかぜワクチン
販売名（企業名）	①献血アルブミン20“化血研”②献血アルブミン25“化血研”③人血清アルブミン“化血研”④“化血研”ガンマーグロブリン⑤献血静注グロブリン“化血研”⑥献血ベニロンーＩ⑦ベニロン⑧注射用アナクトＣ2,500単位⑨コンファクトＦ⑩ノバクトM⑪テタノセーラ⑫ヘパトセーラ⑬トロンビン“化血研”⑭ボルヒール⑮アンスロビンＰ⑯ヒスタグロビン⑰アルブミン20%化血研⑱アルブミン5%化血研⑲静注グロブリン⑳ノバクトＦ㉑DPT“化血研”シリンジ㉒沈降精製百日せきジフテリア破傷風混合ワクチン㉓沈降精製百日せきワクチン㉔乾燥弱毒生風しんワクチン㉕乾燥弱毒生おたふくかぜワクチン「化血研」
報告企業の意見	日本においては、HBV、HCV及びHIVを対象として、「血液製剤等に係る遡及調査ガイドライン」（薬食発第0310011号／平成17年3月10日付け）によりスクリーニング検査等で陽性が確認された場合の手順について示されているところである。 弊所では上記通知に基づき対処しており、該当事例発生の際は適切に対応できているものと考えている。 なお、弊所の血漿分画製剤に対するウイルス安全性は、原料血漿におけるＮＡＴ及び血清学的検査によるスクリーニングに加え、製造工程での効果的なウイルス不活化・除去、更には小分け品でのＮＡＴ、血清学的検査による確認というステップにより確保されている。 また、これらの工程を経た製品によるHBV、HCV及びHIV感染の確認例はなく、弊所製品のこれらのウイルスに対する安全性は高いレベルで確保されていると考える。 今後とも情報収集に努め製剤の安全性の確保を図っていきたい。

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

DRAFT GUIDANCE

This guidance is being distributed for comment purposes only.

Submit comments on this draft guidance by the date provided in the *Federal Register* notice announcing the availability of the draft guidance. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. You should identify all comments by the docket number listed in the notice of availability that publishes in the *Federal Register*.

Additional copies of this draft guidance are available from the Office of Communication, Training and Manufacturers Assistance (HFM-40), Suite 200N, 1401 Rockville Pike, Rockville, MD 20852-1448, or by calling 1-800-835-4709 or 301-827-1800, or from the Internet at http://www.fda.gov/cber/guidelines.htm.

For questions on the content of this draft guidance, contact Paul A. Mied, Ph.D., at 301-827-3008.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
July 2005

Draft –Not For Implementation

Contains Nonbinding Recommendations

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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

This draft guidance, when finalized, will represent 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 alternate approach if the approach satisfies the requirements of the applicable statutes or regulations. If you want to discuss an alternate 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

During the past decade there has been a dramatic reduction in the transmission of Human Immunodeficiency Virus Type 1 (HIV-1) and Hepatitis C Virus (HCV) by human blood and blood components. Primarily, this is due to the implementation of sensitive tests for viral antibody, antigen (for HIV-1), and nucleic acids, and in the case of plasma derivatives, the use of effective virus removal and inactivation methods. The sources of remaining risk of HIV-1 and HCV transmission are marker-negative "window period" donations (made during the period that the donor is infected with a virus, but neither the virus nor antibodies to the virus are detectable by current tests), donors infected with immunovariant viral strains, persistent antibody-negative (immunosilent) carriers, and laboratory test procedure errors. According to a recent report, donations during the window period constitute most of the risk of HIV-1 and HCV transmission (Ref. 1). Therefore, measures to reduce the window period could further reduce significantly the low residual risk of HIV-1 and HCV transmission by human blood and blood components.

Studies performed using seroconversion panels indicate the value of Nucleic Acid Testing (NAT) in reducing the window period for HIV-1 and HCV. The estimated mean window-period reduction for HIV-1 ribonucleic acid (RNA) by pooled sample NAT is approximately 11 to 15 days relative to antibody and 5 to 9 days relative to HIV-1 p24 antigen testing (Refs. 2-4). NAT for detection of HCV has been estimated to reduce the window period by 50-60 days relative to that for HCV antibody. In large-scale studies performed nationwide, NAT for HIV-1 detected 4 antigen-negative/antibody-negative

window period donations and in the case of NAT for HCV, detected 42 additional antibody-negative window period donations. As a result, subsequent to implementation of NAT, the residual risk of HIV-1 and HCV in screened human blood and blood component donations is currently estimated to be approximately 1 in 2,135,000 donations for HIV-1 and 1 in 1,935,000 donations for HCV (Ref. 3).

We, the Food and Drug Administration (FDA), have previously issued recommendations on serologic testing for HIV-1 and HCV and use of NAT to establishments that collect blood and blood components including Source Plasma and Source Leukocytes in "Use of Nucleic Acid Tests on Pooled and Individual Samples from Donors of Whole Blood and Blood Components (including Source Plasma and Source Leukocytes) to Adequately and Appropriately Reduce the Risk of Transmission of HIV-1 and HCV." In this guidance document we are providing recommendations to you, blood and plasma establishments, manufacturers, and testing laboratories that are implementing a licensed method for HIV-1/HCV NAT, on testing individual samples or pooled samples from donors of human blood and blood components for HIV-1 RNA and HCV RNA. This document contains recommendations regarding product disposition (§ 610.40(h)), and donor management (§ 610.41 and § 630.6) based on the results of NAT and serologic testing for markers of HIV-1 and HCV infection on samples, collected at the time of donation, from donors of human blood and blood component donations.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the 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 guidances means that something is suggested or recommended, but not required.

This guidance, when final, is intended to supersede the recommendations in the FDA Memorandum to Blood Establishments dated April 23, 1992, August 5, 1993, and August 8, 1995, for reentry of donors deferred because of anti-HIV-1 test results, HIV-1 p24 antigen test results, and anti-HCV test results (Refs. 5-7).

II. DEFINITIONS

Master Pool: A pool of donor samples on which NAT is performed as a screening test. A Master Pool is formed by pooling of samples from subpools or by directly pooling samples from individual donors.

Subpool: A pool of donor samples that was used with other (sub)pools to form the Master Pool or that was formed during "deconstruction" of the Master Pool.

Deconstruction: Resolution of the reactivity of a Master Pool by testing subpools (original or freshly made) or samples from individual donors that formed the Master Pool. Deconstruction of a Reactive Master Pool to individual units is a required step for all approved tests.

Multiplex NAT: A NAT that simultaneously detects HIV-1 RNA and HCV RNA.

Discriminatory NAT: A NAT that uses specific primers for HIV-1 or HCV to identify the RNA in the Reactive multiplex NAT sample as HIV-1 RNA or HCV RNA. Performing a Discriminatory NAT is a required step for those establishments using a multiplex test such as the Procleix HIV-1/HCV NAT.

Additional NAT: A NAT that uses an amplification technology and/or primers that are different from those that were used for the original NAT screening test, and that has been validated for use with samples from individual donors. This test is not used to make the initial determination of donor suitability, but is used for donor counseling and to determine whether lookback should include notification of transfusion recipients.

Lookback: A series of actions taken by a blood establishment based on donor test results indicating infection with HIV-1 or HCV. These actions relate to prior donations from that donor that possibly were donated during the window period when HIV-1 or HCV RNA and antibody were not detectable by screening tests but the infectious agent might be present in the donor's blood. These actions include: quarantining of prior collections from that donor that remain in inventory, notifying consignees to quarantine prior collections, further testing of the donor, destroying or relabeling potentially infectious prior collections, and notifying transfusion recipients who received human blood or blood components from that donor, when appropriate.

In the proposed HCV lookback rule published in November 2000 (Ref. 8) we proposed changes to § 610.46 that would require lookback to be performed on the basis of a reactive NAT result, even when serological testing is non-reactive. When that rule becomes final, lookback for HIV-1 and for HCV will be required. In the meantime, we recommend that you perform lookback for HIV-1 and for HCV when donor samples test Reactive using HIV-1 NAT or HCV NAT.

Donor Reentry: A procedure that qualifies a donor who was deferred as eligible to donate again. Donor reentry procedures may be used following a false positive test result and typically require the passage of time to allow for possible seroconversion prior to the performance of additional serologic testing and NAT (See sections IV.7. and IV.8.).

III. BACKGROUND AND DISCUSSION

In September 1994 we held a workshop to discuss the potential application of nucleic acid based methods to donor screening for HIV-1. We concluded at the time that these methods clearly were sensitive, but they were not ready for implementation on a large scale.

The industry actively pursued the development of NAT for screening donors of human blood and blood components. Because of the cost and labor intensiveness of NAT, there was much interest in testing pools of plasma donor samples (minipools) by NAT, and by 1997, some manufacturers in Europe had voluntarily instituted NAT on minipools. At about that time, the European Union issued a directive that, by July 1, 1999, HCV RNA

testing would be required in Europe for all plasma for fractionation, and that the requirement for HIV-1 RNA testing would follow at a later date.

Large-scale clinical studies were needed to demonstrate the efficacy of NAT because of the low frequency of window period donations. Small-scale studies would not identify adequate numbers of window period donations. Test kit manufacturers and testing laboratories submitted Investigational New Drug (IND) applications describing their test method and in-house validation of that method. Blood organizations and establishments intending to use the assay for donor screening also filed INDs to describe their clinical trial protocol for validation of pooled-donor sample NAT and individual donor sample NAT.

In December 1999 we issued guidance for industry on the validation of NAT methods to screen plasma donors (Ref. 9). This document provided guidance on test standards, manufacturing requirements, and clinical trial requirements for licensure of the test method for use in donor screening for transfusion transmitted viruses.

In September 2001 we licensed the first NAT system, the National Genetics Institute (NGI) UltraQual™ HIV-1 and HCV Reverse Transcription Polymerase Chain Reaction (RT-PCR) assays. Under that license, NGI performs these assays on pooled samples from donors of Source Plasma.

In February 2002 we licensed the Procleix™ HIV-1/HCV Assay, a qualitative NAT for detection of HIV-1 RNA and/or HCV RNA in plasma from donors of human blood and blood components for transfusion. This assay was approved for use with individual donor samples or pooled donor samples.

In December 2002 we licensed the COBAS AmpliScreen™ HCV Test, v 2.0 and the COBAS AmpliScreen™ HIV-1 Test, v 1.5. These tests are qualitative in vitro tests for the direct detection of HCV RNA and HIV-1 RNA in plasma samples from individual human donors, including donors of Whole Blood and blood components, Source Plasma, and other living donors. They are also intended for use in screening organ donors when specimens are obtained while the donor's heart is still beating. These assays were approved for use with individual donor samples or pooled donor samples.

In October 2004 we issued a final guidance, "Use of Nucleic Acid Tests on Pooled and Individual Samples from Donors of Whole Blood and Blood Components (including Source Plasma and Source Leukocytes) to Adequately and Appropriately Reduce the Risk of Transmission of HIV-1 and HCV." That guidance combined and finalized the draft guidance "Use of Nucleic Acid Tests on Pooled Samples from Source Plasma Donors to Adequately and Appropriately Reduce the Risk of Transmission of HIV-1 and HCV" dated December 2001 (January 31, 2002, 67 FR 4719) and the draft guidance "Use of Nucleic Acid Tests on Pooled and Individual Samples from Donors of Whole Blood and Blood Components for Transfusion to Adequately and Appropriately Reduce the Risk of Transmission of HIV-1 and HCV" dated March 2002 (April 9, 2002, 67 FR 17077).

That guidance informed establishments that collect blood and blood components that we have licensed NAT as tests to screen blood donors for HIV-1 RNA and HCV RNA, that these licensed tests can detect evidence of infection at a significantly earlier stage than is possible under previously approved tests using antibody or antigen detection technology, including the HIV-1 p24 antigen test, and that we believe that these newly licensed tests are now widely available and meet the criteria in 21 CFR 610.40(b) for screening tests that are necessary to reduce adequately and appropriately the risk of transmission of communicable disease through blood products.

In that guidance we recommend the use of HIV-1 NAT and HCV NAT on units that are not reactive on a donor-screening test for the detection of antibodies to HIV or HCV, respectively. However, for donations that are reactive on a test for the detection of antibodies to HIV-1 and are to be discarded or used in the manufacture of non-injectable products, we do not believe that HIV-1 NAT and HCV NAT are necessary as part of the adequate and appropriate testing required under § 610.40(b). Nevertheless, you may decide to perform HIV-1 and HCV NAT for these donations in order to obtain useful information regarding the donor's infection status. This information may be useful as part of donor notification.

This guidance is intended to assist you with testing, product disposition, donor deferral, donor notification, donor reentry, and lookback. We have written this document in general form because additional NAT may be approved in the future. However, where appropriate, we will identify sections that apply to NAT that are already approved. You must follow manufacturers' instructions regarding testing (§ 610.40(b)). Note that screening of donors of human blood and blood components for HIV-1 p24 antigen may be replaced by a NAT that has been validated by the manufacturer as a replacement for the HIV-1 p24 antigen EIA.

A. NAT Algorithms

Under § 610.40(b), you must use approved screening tests "in accordance with the manufacturer's instructions." If you perform NAT on pooled samples and obtain a Reactive NAT result on a Master Pool, the manufacturer's instructions instruct you to perform subsequent testing to identify the individual unit(s) that contains the RNA identified in the Master Pool test. Once you have identified a positive unit, either by subsequent testing of a Master Pool, or by initial individual test, you must not use the donation for transfusion or for manufacturing into injectable products (§ 610.41(h)(1)) unless an exception applies (§ 610.40(h)(2)). You must defer the donor (§610.41(a)), and you must inform the donor of the deferral and the basis for the deferral including test results (§ 630.6). A Reactive NAT result may indicate ongoing infection of the donor, and thus prior donations from that donor, although NAT-Non-Reactive, may pose a risk to transfusion recipients. We recommend that you perform lookback when donor samples test Reactive for HIV-1 NAT or HCV NAT.