



**American
Red Cross**

Together, we can save a life

April 12, 2002

Dockets Management Branch (HFA-305)
Docket No. 02D-0096
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Draft Guidance for Industry: Use of Nucleic Acid Tests on Pooled and Individual Samples from Donors of Whole Blood and Blood Components for Transfusion to Adequately and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 (67 FR 17077; April 9, 2002) [Docket No. 02D-0096]

Dear Docket Officer:

This letter is to provide public comments on behalf of the American Red Cross (ARC or Red Cross) concerning the Food and Drug Administration's (FDA or Agency) *Draft Guidance for Industry: Use of Nucleic Acid Tests on Pooled and Individual Samples from Donors of Whole Blood and Blood Components for Transfusion to Adequately and Appropriately Reduce the Risk of Transmission of HIV-1 and HCV* (draft guidance).

The Red Cross, through its 36 Blood Services regions and 9 testing laboratories, supplies approximately half of the nation's blood for transfusion needs. Blood donated by Red Cross volunteers is also processed or fractionated into plasma derivatives, and the Red Cross is a large supplier of human allograft tissue.

The Red Cross is committed to the safety of our donors, our patients, and the public we serve. Thus, we fully support the guidance's intent, which is to require the use of Nucleic Acid Tests (NAT) and to give consignees appropriate notification. The Red Cross provides these comments in the hope that they will be constructive in aiding the development of a final guidance.

Our comments focus on four points:

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1. The final disposition of the Investigational New Drug Application (IND),
2. Labeling requirements noted in the guidance,
3. Infrequent volunteer source plasma donations (which are excluded from the licensed test manufacturer's package insert), and
4. Application of NAT requirements to autologous donations.

The final disposition of the Investigational New Drug Application (IND)
(Draft Guidance, Section IV. A)

The draft guidance states in Section IV.A that:

some establishments that use the now-licensed test under IND may need up to six months to fully implement the licensed test with all approved components, including the licensed test and supporting software cleared as a device. During this transition period, when establishments are using some, but not all, of the licensed or cleared components, establishments should continue their existing INDs and report the use of the licensed assay or the related cleared components as an amendment to their existing INDs. When an establishment implements all licensed or cleared components of the test system, we recommend that you withdraw the IND.

ARC, however, requests that FDA allow INDs to remain open for a period of time beyond implementation of the licensed test to aid in completing certain product and donor issues that will remain. This period of time is defined as the time needed to address and implement the following items through an FDA Guidance:

- Management of NAT-reactive donors who had donated under the IND, including guidance on donor reentry,
- Management of products collected from prior donations from NAT-reactive donors and notification of recipients of those products (i.e., lookback),
- Use of supplemental NAT for donor counseling and for lookback,
- NAT of infrequent voluntary source plasmapheresis (IVSP) collections,
- NAT of autologous donations.

We encourage FDA to use this time frame to address the above issues in a separate guidance so that implementation will be uniform and complete for all blood establishments, their donors, and the patients who depend on these products.

Labeling requirements noted in the guidance (Draft Guidance, Section IV. B.)

Sections IV.B.1 and IV.B.2 of the draft guidance contain several labeling provisions, including:

- Two separate statements, one each for pooled and individual samples, to be included in the Circular of Information (CI), and
- Two separate label statements for blood components for further manufacture into injectable or non-injectable products; i.e., one with label language for pooled samples and different label language for individual samples.

ARC recommends that FDA revise these provisions and include one label statement for the CI as follows: *“Licensed Nucleic Acid Testing (NAT) for HCV RNA and HIV-1 RNA has been performed on pooled, or infrequently, on individual samples and found to be non-reactive.”*

We understand that the following alternative language has been recommended: *“Licensed Nucleic Acid Testing (NAT) for HCV RNA and HIV-1 RNA has been performed and found to be non-reactive.”* This language is also acceptable to ARC.

We also understand through discussions with the industry that FDA intends to modify the draft guidance so that the labels for recovered plasma to be manufactured into injectables could read: *“Negative by tests for antibodies to HIV-1/2, HTLV-I/II, HCV and nonreactive for HBsAg, STS, HCV RNA and HIV-1 RNA.”* Labels for noninjectable products would contain the above labeling language with an additional indication that testing was performed and found negative by anti-HBc. This language is also acceptable.

ARC urges FDA to make this labeling revision a high priority consideration, particularly for the blood components for further manufacture as specified in section B.2. Our reasons include:

- ARC’s currently approved computer systems do not allow for differentiating between pooled and individual sample testing. Substantial modifications to a number of computer systems would be required, at a considerable cost in both time and resources.
- If the distinction between pooled and individual samples remains in the labeling language, sweeping operational revisions, including a fundamental change in the process and accompanying Standard Operating Procedures, will be required. For example, a new system for product codes, which are currently prepared in the same manner regardless of the testing process, would be needed, and may also require a manual system.

- The time frame for development of the revised computer systems and new procedures to meet the differing label requirements would be extensive. Although determining the length of time to make revisions would depend on the final guidance's requirements, we have no doubt it would far exceed the 6-month implementation date anticipated in the draft guidance.
- Differing label requirements increase the risk of labeling error.
- Differing label requirements may serve to needlessly create confusion for consignees. They may not understand why they see dissimilar labels for what should be the exact same product shipped from the same supplier on the same day.
- Currently, there is very little room remaining on the labels for additional printed information. It is essential to keep any new labeling requirements as simple as possible to minimize the additional wording placement and reorganization needed to fit in the new language.
- ARC believes that the value of the minimal additional information conveyed by different labels does not outweigh the other risks and concerns noted above.

Infrequent volunteer source plasma (IVSP) donations

As stated earlier in this letter, the package insert for the licensed Procleix HIV-1/HCV Assay states that it is intended to test for "HIV-1 and/or HCV in human plasma from donations of whole blood and blood components for transfusion." IVSP is not specifically addressed in either the package insert or in either of the draft guidances issued for use of NAT.¹

Exact data are being collated currently, but greater than 50,000 IVSP donations have been collected and tested under the current ARC IND; this represents close to 0.3% of the total donations tested by NAT from March 1999 to the end of February 2002. These samples are collected as whole blood that is not diluted in anticoagulant and is obtained directly from the donor into a Plasma Preparation Tube (PPT). This is the identical process as is used for the collection of whole blood samples from routine blood donors (see Attachment 1). Since the process for collection of samples is identical for both IVSP and whole blood donors, we recommend that FDA allow testing of IVSP

¹ In addition to the *Draft Guidance: Use of NAT on Pooled and Individual Samples from Donors of Whole Blood and Blood Components for Transfusion*, the subject of this letter, FDA has also issued the *Draft Guidance: Use of Nucleic Acid Tests on Pooled Samples from Source Plasma Donors* [67 FR 4719, Jan. 31, 2002]. The ARC public comment letter in response to the source plasma draft guidance is attached.

donations using a NAT assay licensed for whole blood and blood components, and without using a different NAT assay licensed for source plasma donations.

Analyzed data from IVSP donation samples will be provided to CBER and to the test kit manufacturer (Gen-Probe) to demonstrate equivalence with samples from whole blood donors. We believe that FDA will concur with our interpretation i.e., that the data derived from these two donation sets are equivalent. If FDA concurs with our interpretation, ARC requests that FDA indicate its agreement in the final version of both the guidance for individual samples from donors of whole blood and blood components and in the guidance for samples from source plasma donors.

Autologous donations

It should be noted that autologous donations are not mentioned in either the package insert or in the draft guidance document. In contrast to IVSP donations, there are no data to support the use of NAT with autologous donations. However, ARC assumes that FDA intended to include a requirement for NAT of autologous donations and plans to move forward with establishing procedures to do so. ARC requests that FDA clarify whether it was the agency's intention to require such testing of autologous donations.

Again, we appreciate the opportunity to comment on the draft guidance. If you have any questions, please contact Anita Ducca, Director, Regulatory Affairs, at 703-312-5601 or Susan Stramer, Ph.D., Executive Scientific Officer, at 301-212 2801.

Sincerely,



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cc: Karan Blum
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Attachments

American Red Cross Apheresis, Collections, and Sampling Information

This table provides a description of the methods of plasma collection by apheresis employed by the American Red Cross. As noted below, the equipment is used for the collection of plasma by either plasmapheresis, plateletpheresis, or red cell apheresis procedures. Regardless of the instrument or the type of procedure performed, the plasma can be collected as either FFP or Source Plasma. All samples are obtained prior to the actual start of the collection procedure. There is no anticoagulant or saline diluting the samples. Therefore the tubes collected from IVSP donors are equivalent to those collected from whole blood donors.

Apheresis Instrument	Procedure Types	Sampling Method
COBE Spectra	<ul style="list-style-type: none"> • Plateletpheresis • Concurrent plasma as either FFP or Source Plasma 	<ul style="list-style-type: none"> • Dual needle - vacutainer on return line needle • Single needle - sampling pouch/vacutainer
Autopheresis-C	Plasmapheresis as either FFP or Source Plasma	Vacutainer
Fenwal CS-3000	<ul style="list-style-type: none"> • Plateletpheresis • Concurrent plasma as either FFP or Source Plasma 	Sampling pouch/vacutainer
Fenwal Amicus	<ul style="list-style-type: none"> • Plateletpheresis • Concurrent plasma as either FFP or Source Plasma 	Sampling pouch/vacutainer
Haemonetics MCS+LN8150	<ul style="list-style-type: none"> • Red cell apheresis • Concurrent plasma as either FFP or Source Plasma 	Sampling pouch/vacutainer
Haemonetics MCS+LN9000	<ul style="list-style-type: none"> • Plateletpheresis • Concurrent plasma as either FFP or Source Plasma 	Sampling pouch/vacutainer
COBE Trima	<ul style="list-style-type: none"> • Plateletpheresis • Red cell apheresis • Concurrent plasma as either FFP or Source Plasma 	Sampling pouch/vacutainer

As of April 2, 2002