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25 OCTOBER 2005

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket Number 2005D-0261: Draft Guidance for Industry Nucleic Acid Testing (NAT) for Human Immunodeficiency Virus Type 1 (HIV-1) and Hepatitis C Virus (HCV): Testing, Product Disposition, and Donor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

Dear Docket Officer:

On July 27, 2005 the Food and Drug Administration published in the Federal Register a proposed rule entitled "Draft Guidance for Industry Nucleic Acid Testing (NAT) for Human Immunodeficiency Virus Type 1 (HIV-1) and Hepatitis C Virus (HCV): Testing, Product Disposition, and Donor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." America's Blood Centers (ABC) would like to take this opportunity to provide our comments.

For your information, ABC member centers supply about half of the United States of America's blood and blood components for transfusion.

ABC commends the FDA for their efforts to updated guidance for the use of NAT testing. Updating the guidance to include scientific and industry advances is vital to assure the safety, purity and potency of the volunteer blood supply.

Overall, ABC concurs with this long awaited Draft Guidance. However, we provide the following specific comments for your consideration:

1. **Lookback.** (Page 3, Para II): The time frames for lookback are not detailed in this document. Title 21 CFR Part 610.46 details the requirements for lookback following a repeatably reactive HIV-1/2 result as a period of 5 years from the positive test result for a transfusable product (6 months for a product for further manufacture), or 12 months from the most recent negative test result. Given the remarkable sensitivity of NAT tests and the recommendations in this draft guidance that donors wait a period of 8 weeks for HIV and 6 months for HCV prior to being considered for reentry, we believe that the lookback period can be shortened.

It is also well known that lookback, a procedure with intrinsically low yields, becomes even less productive with longer periods because hospitals cannot locate records, patients cannot be located, and many patients died because of the primary disease that led to the transfusion.

Please consider recommending a period of one year from a positive test result, and 6 months from a prior negative test result, for both HIV and HCV, in order to simplify the lookback process and focus efforts on patients that most likely will benefit from the notification process.

2. **Donor Reentry for HIV-1 Tests.** (Page 6, Para III B/Page 20, Para IV.7/Page 32, Figure 7)
 - a. **Please allow repeat testing after HIV-1 Western Blots with unreadable test results. Unreadable Western blots result from random technical issues that are unrelated to test sensitivity. The unreadable result should be discarded as a test that did not meet specifications. Only readable test results should be considered tests of record. A subsequent negative test result for a donor who had an unreadable Western blot should be acceptable as the test of record.**
 - b. **The guidance should provide specific instructions for reentry of donors when the test run (NAT or EIA) on the original donation is not available/no longer in use (investigational NAT). It also identifies tests that are not yet available, such as HIV-2 supplemental test, and HIV Group O. Please clarify that this provision is being offered in the event such tests become available.**
 - c. **The requirement to defer permanently a donor who tests repeatedly reactive for anti-HIV-1/2 EIA prior to the end of an 8-week period after an initial reactive anti-HIV may defer unnecessarily dedicated donors who give a whole blood donation at a blood drive a few days after an anti-HIV reactive platelet donation yet prior to notification of deferral or donors who are tested for counseling purposes. Persistent unconfirmed EIA reactivity detected for purposes of donor counseling should not disqualify a donor from the opportunity for reentry since the same lot numbers may still be in use when subsequent testing was performed.**
3. **Individual Donor Sample Reactive on Multiplex NAT.** (Page 11, Para IV, 1, a, ii (a)/Page 26, Figure 1). We have two comments on this section.
 - a. **We recommend that the guidance provide the option of performing discriminatory testing on a new sample from the donor for the purposes of determining the extent of lookback. Often, insufficient sample remains for follow-up testing or an alternative sample does not meet the requirements for NAT testing. (We recognize that such testing on a newly collected sample could not be used to determine product handling or donor reentry.)**
 - b. **When there is an insufficient sample for discriminatory testing and a new sample cannot be collected, we recommend a lookback period of one year prior to the index donation. We also suggest that the patient notification in these circumstances indicate that the infectious agent could not be identified and that the patient should be tested for both HIV and HCV.**
4. **Investigation of Unresolved Pools** (Page 13, Para IV, 3a(i)). ABC agrees that unresolved pools should be investigated. However, the investigation of NAT reactive unresolved pools

is analogous to the investigation of an initially reactive anti-HIV or anti-HCV EIA test that is not repeat reactive. Investigations of initially reactive specimens in serology are only carried out by blood centers when the incidence of the marker in the sample population in a certain period exceeds that expected from the data provided by the manufacturer in the package insert, suggesting a system failure. Investigation of isolated events is not productive and does not lead to changes in practice that eliminate non-repeatable initially reactive test results. Thus, investigation of occasional NAT pools that do not resolve is not productive.

Obviously, an increase in the incidence of unresolved pools above a certain threshold should be investigated. In addition, pools that are resolved and the individual sample, or samples identified as positive are recognized as false positive in confirmatory testing, should be investigated because this is often the result of contamination by a seropositive, RNA positive specimen. These contamination events should be investigated and controlled because they result in loss of the donation and the donor. Thus, laborious investigations should focus on events that lead to serious consequences and can be addressed by changes in practice. The unfocused investigation of occasional unresolved pools will not contribute to the quality of the testing process.

ABC recommends that investigation of unresolved pools be required only when the frequency of unresolved pools exceeds a certain pre-determined threshold for each blood center based upon their historical data, or when there are indications of possible contamination of negative samples with positive specimens.

5. **HIV-1 p24 Reentry.** (Page 20, para IV, 7). The draft guidance allows the reentry of donors who were NAT non-reactive, HIV; antibody negative, and positive or indeterminate HIV-1 p24 EIA result if after 8 weeks they test negative for NAT and anti-HIV 1 / 2 EIA.

We request that this allowance be extended to donors who were positive or indeterminate in HIV-1 p24 EIA on more than one occasion. Most of the individuals positive in the antigen test were false positive. In addition most were retested as part of donor follow up and counseling and many continued to be positive because of non-specificity inherent in the test. In these cases, waiting time after index donation and NAT testing will make it highly unlikely that a true positive would be missed. Please modify the draft to indicate that a donor with an Indeterminate HIV-1 p24 antigen on more than one occasion is eligible for reentry.

Thank you for the opportunity to comment.

Yours truly,



Celso Bianco, MD
Executive Vice President