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October 24, 2005

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

Dear Sirs:

Michigan Community Blood Centers wishes to comment on the proposed 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, July 2005.

As a facility that performs Individual Donor Multiplex NAT testing, donor deferral and reentry based on an FDA approved package insert, we appreciate the opportunity to comment on the Guidance.

As an individual donor NAT testing facility, we have some concerns with this Guidance being biased toward the pooled testing facility and issues revolving around the definition of a "reactive" result. The draft guidance assesses "reactive" as follows:

NAT Algorithms (p 5)

"Under 21 CFR 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 [21 CFR 610.41(h)(1)] unless an exception applies [21 CFR 610.40(h)(2)]. You must defer the donor [21 CFR 610.41(a)], and you must inform the donor of the deferral and the basis for the deferral including test results (21 CFR 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."

It is noted, on page 6 of the Guidance, that you may obtain discrepant reactions for various reasons using the Multiplex NAT. "At the meeting of the Blood Products Advisory Committee (BPAC) in March 2001..... Data generated using NAT under IND that was presented in the BPAC meeting showed that in each discrepant case it was the Master Pool that was falsely reactive, due to contamination either during specimen handling or during the assay run."

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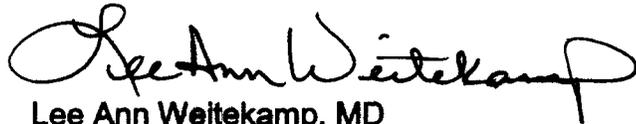
Acknowledging technical difficulties with the test, we would propose the definition of "Reactive" be modified similar to EIA testing to 2 out of 3 reactive results. See attached proposed algorithm, Figure 1. We propose acting on product, donor deferral and lookback based on this definition.

We have compiled test data on our individual donor Multiplex NAT testing from 2003 to present (see Attachment A) which shows that initial reactives which do not discriminate have lower initial signal/cutoff ratios, would presumably have low duplicate repeat signal/cutoff values and do not progress to Reactive on subsequent donation(s). The proposed guidance makes the assumption that individual donor multiplex testing does not suffer from the same false reactives as pooled testing. This assumption is incorrect and is supported by our data.

In any case, either the current guidance proposal or our proposal will require a change to the Chiron package insert.

Thank you for the opportunity to comment and your review is appreciated.

Sincerely,

A handwritten signature in black ink, appearing to read "Lee Ann Weitkamp". The signature is fluid and cursive, with the first name "Lee" and last name "Weitkamp" clearly legible.

Lee Ann Weitkamp, MD
Medical Director

During the period of September 17, 2003 to September 30, 2005, Michigan Community Blood Centers tested 195,233 donations. Two hundred and four (204) samples were initially reactive on individual donor HIV/HCV multiplex testing. Fifty-four (54) of the 204 initial reactive samples discriminated as HCV or HIV. Fifty (50) samples tested HCV NAT reactive and four (4) samples tested HIV NAT reactive upon discriminatory testing. No sample was reactive for both HIV and HCV.

Initial Reactives that discriminated (n=54)

	Range	Median	Mean
Initial Multiplex S/CO	8.24 - 25.08	10.47	11.54
Discriminatory S/CO			
HCV reactive	19.91 - 28.38	24.87	24.90
HIV reactive	21.59 - 24.80	23.55	23.37
HCV Negative	0.03 - 0.14	0.04	0.06
HIV Negative	0.04 - 0.33	0.09	0.12

Initial Reactives that did NOT discriminate (n=150)

	Range	Median	Mean
Initial Multiplex S/CO	1.0 - 10.98	1.45	2.49
Discriminatory S/CO			
HCV Negative	0.0 - 0.82	0.07	0.06
HIV Negative	0.02 - 0.39	0.15	0.12
<hr/>			
Subsequent donation multiplex S/CO	0.08 - 0.68	0.13	0.16

Seventy-four (74) of the 150 donors returned before September 1, 2005 donating a total of 175 units which all tested negative.

MCBC proposed changes to FIGURE #1
TESTING, PRODUCT DISTRIBUTION, AND DONOR MANAGEMENT FOR AN INDIVIDUAL DONOR SAMPLE THAT IS REACTIVE
ON A MULTIPLEX NAT AFTER A NEGATIVE ANTIBODY SCREENING TEST

