



## Blood Systems, Inc.

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October 26, 2005

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

RE: Docket No. 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" 27 July 2005

Dear Docket Officer:

Blood Systems (BSI) is the parent company for United Blood Services, which operates 18 blood centers situated in 12 states west of the Mississippi, collecting 1.1 million units of red blood cells and about 120,000 apheresis platelet concentrates. We operate two centralized donor testing labs and 1 transfusion medicine research institute in San Francisco, California.

BSI, under separate cover, submitted comments to request allowing donors with unreadable anti-HIV-1 Western Blot to be eligible for re-entry. In this submission, BSI feels that the prolonged deferral of non-discriminated reactive donors is inappropriate and wishes to provide FDA with data in support of alternative approaches for re-entry of donors who were seronegative for anti-HIV-1/2 and for anti-HCV, but were reactive in Multiplex NAT (in minipool or individual donation testing) with nonreactive discriminatory tests for HIV and HCV (so-called 'non-discriminated reactive - NDR)

When a reactive minipool is observed there is a low but significant rate at which one of the individual donation samples in the pool tests reactive by multiplex NAT but then negative on both discriminatory assays (NDR). The rate of NDR results with minipool NAT has declined over time, but remains in the range of 1 in 25,000 donations.

These cases are often attributable to cross contamination from true positive samples tested in the same pool resolution run, although NDR results are also observed at a very low rate (~1:100,000 donations) due to concordant non-specificity in minipool and resolution test runs. Extensive studies by Blood Systems that included donor follow-up have shown that none of the NDR donors identified from minipool NAT have proved to be infected with HIV or HCV (McAuley JD, Caglioti S, Williams RC, Robertson GF, Morgan L, Tobler LH, Busch MP. *Clinical Significance of Nondiscriminated Reactive Results with the Chiron Procleix HIV-1 and HCV Assay*. Transfusion, 2004; 44:91-96). (NDR results are even more frequently observed when individual donation NAT screening is performed, although in this setting there is greater concern that the finding could represent very low level viremia since discriminatory assays are performed on samples that were first identified by neat (rather than diluted minipool) testing.)

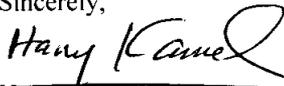
Although we agree that all NDR units should be discarded (whether derived from minipool or individual donation screening), we believe that these donors should be reassured that they are not infected and preferably automatically reinstated after 56 days without a requirement for reentry testing.

The draft guidance not only requires notification and deferral of these donors, but also requires retesting for reentry that is more complex than for donors with discriminated reactive (confirmed) results (i.e., for NDR donors both HIV and HCV serology and virus specific NAT assays must be performed, presumably with a minimum 6 month deferral based on the HCV algorithm). It seems inappropriate that these reactive donors with the lowest probability of infection have the longest deferral and the most complex series of reinstatement assays.

We request that FDA consider allowing reinstatement of NDR donors after 8 weeks without a requirement for non-donation sample testing, or alternatively that a non-reactive result on the multiplex NAT assay, rather than both dTMAs and serology tests, on a follow up sample collected at least 8 weeks after NDR index donations be considered acceptable for donor reentry.

Questions concerning these comments may be directed to Nancy Lynch, Senior Regulatory Associate at [nlynch@bloodsystems.org](mailto:nlynch@bloodsystems.org) or (480) 675-5606.

Sincerely,

A handwritten signature in black ink that reads "Hany Kamel". The signature is fluid and cursive, with a long, sweeping underline that extends to the right.

Hany Kamel, M.D.  
Corporate Medical Director  
Blood Systems Inc.