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May 18, 2005

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

**Docket No. 2005D-0133 “Draft Guidance for Industry: Assessing Donor Suitability and Blood and Blood Product Safety in Cases of Known or Suspected West Nile Virus Infection”**

Dear Docket Manager:

The blood banking community members of the AABB Interorganizational Task Force on West Nile Virus (WNV), representing AABB, ABC, ARC and DoD, wish to comment on the Draft Guidance for Industry: Assessing Donor Suitability and Blood and Blood Products Safety in Cases of Known or Suspected West Nile Virus Infection. The comments address the process by which the guidance was issued and the content of the guidance.

Process

The issue of guidance for assessing donor suitability and blood and blood products safety in cases of known or suspected WNV infection was handled with extraordinary lack of attention to timeliness. Implementation of these recommendations requires significant operational changes, including items such as revised Standard Operating Procedures, computer changes that must be validated, and staff training. In addition, because tests are still being performed under IND, changes must be approved by multiple local IRBs. The draft guidance states that “The earliest onset of human infections in the United States was in July 2000 and 2001, May in 2002, and April in 2003 and 2004.” **The Federal Register notice announcing the draft guidance did not appear until April 20, 2005, clearly not providing sufficient time to be implemented prior to the potential 2005 West Nile Virus season.**

8101 Glenbrook Road  
Bethesda, MD 20814-2749  
301.907.6977 MAIN  
301.907.6895 FAX  
[www.aabb.org](http://www.aabb.org)

This delay in providing guidance is especially burdensome because FDA's current thinking on donor deferral for potential or documented infection with West Nile Virus was discussed extensively at the October 22, 2004 meeting of the Blood Products Advisory Committee (BPAC), and again at the March 17, 2005 meeting.

### Process Background

Data concerning viremia/experience with individual donation testing (IDT) NAT was presented to BPAC October 22, 2004. The AABB WNV Interorganizational Task Force and BPAC recommended extending the deferral period of 28 days to 56 days for blood donors with a positive WNV NAT screening test. Both the WNV Task Force and BPAC recommended obtaining a negative result by IDT NAT prior to re-entry at 56 days for blood donors who are deferred. The WNV task force also recommended that automatic re-entry (i.e., no IDT NAT required) be permitted for those donors who do not return for an extended period of time. On February 24, 2005 further communication from the WNV Task Force was sent to FDA stating that 90 days should be considered an acceptable time period for automatic re-entry. This communication also stated the need for urgency and requested a response within one week. Members of the WNV Task Force also provided data to the FDA over the next month summarizing extended follow-up studies of WNV-infected donors.

FDA updated its current considerations for guidance at the March 17, 2005 BPAC meeting, indicating that the guidance would support re-entry at 90 days without additional testing, and re-entry would be possible at 56 days based upon negative IDT NAT on a reinstatement (or donation) sample drawn 56 days or more subsequent to the index WNV-RNA-reactive donation. The Task Force asked for further consideration of when the IDT sample could be collected, noting that it is operationally impractical to divert a donation sample from minipool (MP) NAT to IDT NAT, and reiterating that a negative IDT NAT anytime prior to the 56 day re-entry should be acceptable.

### Content

**This current draft guidance is extraordinarily flawed as late changes were made deleting automatic re-entry, changing the deferral period to 120 days, and requiring a negative IDT NAT prior to re-entry at 120 days.** This new policy is based upon a single case that generated one WNV-RNA reactive result out of six replicates on samples collected at 83 and 104 days from the index donation. Such samples would probably not have been detected by any routine approach to testing since multiple replicates are not tested; indeed, both samples had tested negative by initial IDT NAT performed as part of routine follow-up testing. This unusual case needs to be offset against the several hundred cases with well-analyzed serial follow-up data points that support a very different conclusion, as discussed at the October BPAC meeting. Setting the deferral policy based on a single outlier case is scientifically inappropriate. Importantly, both

low-level RNA reactive samples in this case had high-level WNV antibody demonstrated by IgM, IgG and plaque reduction neutralization activity (PRNT). Extensive epidemiological data available indicates that significant numbers of low viremic seropositive units with similar RNA and serological profiles have been transfused at the tail end of massive WNV epidemics over the past two years, with no transfusion transmission of WNV by such units. Indeed, since the mean length of the low-level RNA positive window period detected by 6-replicate TMA testing but missed by singlet TMA (6.1 days, 95% CI 4.2-8.0 days) is approximately equivalent to the length of the MP-detectable window period (6.9 days [3.0-10.7 days]). It is likely that over 1000 such units were donated and missed by routine WNV NAT screening without resulting in clinically overt cases in the past two years. Moreover, large scale retrospective IDT NAT studies, conducted at the request of FDA, have traced recipients of IDT NAT-only seroreactive units, with no cases of WNV transmission documented.

**The concept that there can be no automatic re-entry is again based on the outlier case rather than the predominance of data. There is no evidence in human or animal WNV infections for a persistent carrier state, and hence indefinite deferral beyond a reasonable period to account for clearance of the acute viremia is not warranted.**

If the 120 day deferral period in the proposed Guidance is maintained for donors with a negative ID NAT, then the AABB Interorganizational Task Force suggests that an automatic reentry period be set at 180 days.

### Section III Recommendations for Donor Deferral are inconsistent

Section III A, Diagnosed or Suspected Acute West Nile Virus Illness or Infection, recommends that you defer a potential donor with a medical diagnosis or suspicion of WNV infection (based on symptoms and/or laboratory results) for 120 days following diagnosis or onset of illness whichever is later. There is no mention of additional testing necessary before re-entry at 120 days. Section III C recommends this same action for donors who report an otherwise unexplained post-donation febrile illness with headache or other symptoms of WNV infection.

Yet Section III B, Presumptive Viremic Donors, recommends that if a donor has tested reactive for WNV using the investigational WNV NAT donor screening test, you may choose to re-enter such donors after 120 days from their reactive donation provided that they are retested and found negative by IDT NAT on a follow-up sample. Section III D recommends this same action (re-entry at 120 days following the date of donation based upon a negative IDT NAT) for blood donors whose blood or blood components were potentially associated with a transfusion-related WNV transmission.

The task force fails to see the difference in whether the potential donor tested positive on a donor screening test, or was diagnosed by some other method. If the concern is to detect low level viremia, then additional IDT NAT should be required in both scenarios. However, as noted above, the task force strongly believes that automatic re-entry is

appropriate, but for those that wish to perform IDT NAT, a negative IDT NAT should permit re-entry at an earlier time, such as 56 days.

Section IV Recommendations for Retrieval and Quarantine of Blood and Blood Components Including Recovered Plasma, Source Plasma, and Source Leukocytes

**We request that the final guidance clearly delineate the necessary action for product retrieval and quarantine for donors who test reactive by an investigational WNV donor screening assay.** This section does not exist in the draft guidance. Since such donors must be deferred for 120 days, then in order to be consistent, product retrieval and quarantine should be required for 120 days prior to the reactive donation. There is no way to know when the test would have become positive during the preceding 120 days. However, given the arguments above, we believe that a 56-day retrieval and quarantine period is scientifically based and appropriate.

Mechanism for obtaining additional data

The guidance states “We are continuing to consult with experts on WNV at the CDC and elsewhere to ensure the greatest possible safety of the blood supply. Epidemiological and laboratory investigations are rapidly evolving: therefore we promptly will evaluate any new data or experiences related to the issue and provide further updates as appropriate.” The task force wishes to continue to be involved with FDA in evaluating new data or experiences. The task force believes the appropriate way to obtain such information is through requirements delineated in the IND, or research studies designed and conducted in concert with industry and optimally supported by PHS, as documented by the success of the joint efforts involving regulators, NHLBI, industry and blood collectors occurring since the FDA sponsored the West Nile Workshop in 2002.

Implementation

Finally, FDA did not allow sufficient time for blood collection facilities to act. It is unreasonable to expect that the final guidance can be implemented within 30 days after it is issued. Because of the need for IRB approvals, SOP changes, software changes and personnel training we recommend an implementation period no shorter than 120 days.

Thank you very much for the opportunity to comment. If you have any questions, please contact Kay Gregory, MT ASCP) SBB, at [kayg@aabb.org](mailto:kayg@aabb.org) or 910-842-2790.

Sincerely,

Roger Dodd, PhD  
Chair, AABB Interorganizational WNV Task Force