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## **Association Bulletin #13-02**

**Date:** June 28, 2013

**To:** AABB Members

**From:** Susan L. Stramer, PhD – President  
Miriam A. Markowitz – Chief Executive Officer

**Re:** West Nile Virus Nucleic Acid Testing - Revised Recommendations

### **Summary**

The AABB Board of Directors has approved recommendations of the AABB Transfusion-Transmitted Diseases Committee regarding West Nile virus (WNV) nucleic acid testing (NAT). These recommendations update previous criteria used to convert to individual-donation-NAT (ID-NAT) from mini-pool-NAT (MP-NAT), referred to as "triggering," and reversion to MP-NAT following the cessation of WNV activity ("de-triggering"). The goals are 1) ensuring that all facilities are prepared to implement appropriate ID-NAT triggering and de-triggering criteria, and 2) encouraging and facilitating the sharing of WNV donor screening data among facilities serving the United States (U.S.) and Canada so that timely triggering may occur in WNV-affected areas.

Association Bulletins, which are approved for distribution by the AABB Board of Directors, may include announcements of standards or requirements for accreditation, recommendations on emerging trends or best practice, and/or pertinent information. These recommendations update and supersede those published in Association Bulletin #08-03 "West Nile Virus – Revised Recommendations for Triggering Individual Donation Nucleic Acid Testing and Use of Communication Plans."

### **Background**

WNV has been present in the U.S. since 1999 and was first recognized as a transfusion-transmitted agent in 2002 with 23 recipients confirmed infected from 16 WNV-infected (RNA-positive) donors. Blood centers implemented WNV NAT in 2003, mostly in the MP-format with 6 to 16 donations per MP. Since 2003, a targeted ID-NAT strategy has been used to identify viremic donations that are not detectable by MP-NAT. Recent unpublished data collected by the



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American Red Cross for the 2010-2012 WNV transmission seasons indicate that 50% or more of all WNV-RNA confirmed-positive donations required ID-NAT for detection; similar data were reported in Canada (O'Brien et al). Since the implementation of WNV NAT in 2003, 11 breakthrough WNV transfusion transmissions have occurred from MP-NAT screened blood (2003-2008), with one additional clinical case reported (2010) from granulocytes untested at the time of transfusion in a region that had triggered ID-NAT due to WNV activity. During the 2012 season, one unpublished case of WNV transfusion transmission has been described. Based on preliminary information, this case would not have been prevented by ID-NAT screening.

The 2012 WNV transmission season was the most severe since 2003. A total of 5,674 human cases of WNV, including 286 deaths, were reported to the Centers for Disease Control and Prevention (CDC) of which 2,873 (51%) were neuroinvasive disease cases including meningitis, encephalitis or acute flaccid paralysis. The number of deaths was the highest since WNV was first detected in the U.S. in 1999. Clinical cases were reported from March through December 2012. (<http://www.cdc.gov/media/releases/2013/a0513-west-nile.html>).

According to AABB's WNV Biovigilance Network, 752 WNV-reactive donations were identified in 2012 ([www.aabb.org/research/hemovigilance/Pages/wnv.aspx](http://www.aabb.org/research/hemovigilance/Pages/wnv.aspx)). To date, ID-NAT triggering and de-triggering criteria have been widely implemented as the result of prior AABB recommendations and FDA guidance. However, due to the unpredictable nature of annual outbreaks and the potential for cases of breakthrough transfusion transmissions, refinements of those criteria and updated communication plans are needed. Thus, the purpose of this bulletin is to provide the most current recommended criteria and communication plans to facilitate timely use of ID-NAT in areas reporting WNV activity.

## **Recommendations**

The triggering and de-triggering criteria recommended in this Association Bulletin represent an approach that, if adopted, will reduce the residual risk of WNV transmission through blood transfusions. Facilities are free to establish their own criteria; however, it is recommended that facilities consider these data and the benefits of establishing uniform criteria.

The recommended criteria for conversion from MP-NAT to ID-NAT are based on presumptive viremic donations (PVDs). A PVD is defined as 1) a WNV-initially reactive donation with a



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signal-to-cutoff (S/CO) ratio of greater than or equal to 17 using the WNV Transcription-mediated Amplification Assay (Hologic/Gen-Probe and Novartis) or 2) a WNV-initially reactive donation with an S/CO ratio of less than 17 if upon repeat testing the sample is repeatedly reactive. Similarly, WNV-initially reactive donations identified using the Cobas TaqScreen WNV Test (Roche) should be retested to determine if they are PVDs based on repeat reactivity. PVDs have a 95% or greater chance of being confirmed positive by additional testing (repeat testing from an independent sample including the same or alternate WNV NAT and/or IgM reactivity at index or follow-up testing; Zou et al).

Initially reactive results, whether they are determined to be PVDs or not, are the test of record. Associated donors and donations are subject to actions required by FDA guidance. Initially reactive and PVD samples may be submitted for confirmatory testing as an aid in donor counseling to better understand the meaning of the test results and, when combined nationally, as a measure of the magnitude of the WNV season.

Centralized testing facilities and their external customers should agree upon the triggering and de-triggering criteria in advance of each WNV season so that the testing laboratories may take appropriate actions when a WNV-reactive donation/PVD occurs (see below).

**I.** On the basis of data generated from the 2003-2012 WNV seasons, AABB recommends the use of one of the following criteria for initiating the conversion from MP-NAT to ID-NAT:

- a. One PVD with evidence of other WNV activity in a collection region.
- b. Two PVDs in a 7-day rolling period if there is no other WNV activity reported in a collection region.
- c. One PVD if the collection facility decides not to include considerations of other WNV activity in the region in its triggering decision.

Given the time needed for repeat WNV testing, facilities may trigger ID-NAT based on WNV NAT-initially reactive donations (rather than PVDs). The disadvantage of this approach is that not all WNV-reactive donations are PVDs.



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For the purposes of this Association Bulletin, the following definitions apply:

*A collection region is defined as a given geographic area where one or multiple blood centers collect blood; this may include one or multiple counties but would be defined as larger than a single zip code.*

Other WNV activity is defined as one or more of the following:

- PVDs at another blood center in the collection region.
- Human WNV cases reported to county/state health departments or CDC.
- Reports of WNV activity in mosquitoes or animals (e.g., equine or avian).

The CDC website (<http://www.cdc.gov/westnile/index.html>) provides links to human, mosquito and animal activity in the U.S.; state information on tracking in humans, mosquitoes and animals to the county level is available through links to the U.S. Geological Services ([http://diseasemaps.usgs.gov/wnv\\_us\\_human.html](http://diseasemaps.usgs.gov/wnv_us_human.html)). Close communication with local public health authorities may be required for access to the most timely surveillance information.

The AABB WNV Biovigilance Network reports cases of WNV-reactive blood donations including confirmatory data reported by blood centers using the criteria in this Association Bulletin.

The donor's residential zip/postal code should be used as the location of the WNV-reactive donation or PVD. Although exposure may occur at any location, it is most likely that exposure occurred while the donor was at his or her residence (dawn or dusk, when mosquito activity is highest). The use of residential zip/postal codes provides a standardized method for data collection.

The collection facility with a WNV-reactive donation/PVD is requested to enter the donor data elements into the AABB WNV Biovigilance Network, as opposed to data entry by a centralized testing facility.

**II.** On the basis of data generated from 2003-2012 WNV seasons and modeling data (Biggerstaff and Petersen), AABB recommends the following criteria for resuming MP-NAT from ID-NAT:



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- a. De-trigger based on a minimum of 14 days without a WNV initially reactive and in the absence of other indicators of WNV activity.
- b. If these conditions are not met, continue ID-NAT in defined collection regions with ongoing WNV activity in humans, mosquitoes or animals.
- c. Assessments as to when to de-trigger could be made at 7-day intervals (e.g., 21 days, 28 days after triggering), corresponding with updates to public health surveillance sites, to determine when MP-NAT should be resumed.

**III.** Monitoring of WNV-reactive donations/PVDs should occur in real time. When a defined collection region has reached its trigger, conversion to ID-NAT should occur promptly (i.e., ideally within 24 hours of receipt of the test results, and in no case longer than 48 hours from the time of the collection of the most recent WNV-reactive donation/PVD responsible for the trigger being reached). If the conversion to ID-NAT cannot take place within this period, facilities should consider retrospective testing of retained samples from donations dating back to the collection date of the WNV-reactive donation/PVD.

**IV.** All facilities should work together to create a plan for communicating WNV-reactive donations/PVDs. This has been most effectively accomplished for past WNV seasons by having a representative from each collection or testing facility as part of a multi-site email link (see d. below). WNV reactivity, PVDs, confirmed positivity and triggering/de-triggering activities are communicated to all participating facilities by such links. This is the timeliest method of communicating WNV-reactive/PVD donors in a collection region. Responsibility for reporting the number of WNV-reactive donations/PVDs in a collection region should be clearly defined among all collection and testing facilities to ensure that each WNV-reactive donation/PVD is reported promptly and only once to the AABB reporting site.

The communication plan should address the following:

- a. The AABB website has an established WNV Biovigilance Network for monitoring WNV activity in blood donors ([www.aabb.org/research/hemovigilance/Pages/wnv.aspx](http://www.aabb.org/research/hemovigilance/Pages/wnv.aspx)). Facilities should enter data for all initially reactive donations, not only PVDs (use



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original sample identification number) within 24 hours following the facility's verification of the test results. Facilities are requested to enter and track data on the AABB website; however, this is not a substitute for direct communication with other facilities within a collection region.

- b. Facilities should review the entries of other facilities in their collection region on a regular basis to be able to ascertain complete information about WNV activity in their collection region. Facilities should also review ongoing WNV activity on the CDC or state public health website that may be useful in triggering/de-triggering decisions.
- c. Close communication with local public health authorities may be required for access to the most timely surveillance information.
- d. As an attachment to this Association Bulletin, AABB has provided a listing of facilities that have given contact information for reporting their WNV data on the AABB Biovigilance Network. This information includes facility name and address, as well as the contact person's name, telephone and email address. This listing is intended to assist facilities in making necessary arrangements for real-time communications during the WNV season.

Effective communication among all facilities in a collection region (regardless of the number of such collectors) will permit efficient and timely application of triggering and de-triggering in each geographic area.

Contact [biovigilance@aabb.org](mailto:biovigilance@aabb.org) for assistance with reporting information on the AABB WNV Biovigilance Network or to update information on the West Nile Virus Web Reporting Lab Contacts List.

## **References**

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