



Advancing Transfusion and
Cellular Therapies Worldwide

ASSOCIATION BULLETIN #08-03

Date: April 18, 2008
To: AABB Members
From: J. Daniel Connor, MM, President
Karen Shoos Lipton, JD, Chief Executive Officer
Re: West Nile Virus – Revised Recommendations for Triggering Individual Donation Nucleic Acid Testing and Use of Communication Plans

Summary

This Association Bulletin contains revised recommendations for facilities to implement for the 2008 West Nile virus (WNV) mosquito season. The goals of the recommendations are to: 1) help ensure that all facilities are prepared to implement appropriate individual donation nucleic acid testing (ID-NAT) triggering criteria for the 2008 WNV mosquito season and 2) encourage and facilitate the continued sharing of WNV donor screening data among multiple facilities serving overlapping and adjacent geographic areas. Association Bulletins #04-03,¹ #04-04² and #07-02³ are updated by this Bulletin.

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. This bulletin contains a recommendation developed and submitted to the AABB Board by the Transfusion Transmitted Diseases (TTD) committee, which is comprised of 14 voting members, as well as representatives from 9 organizations/agencies. During the course of developing the recommendation, members and representatives of the committee also consulted a number of additional organizations and facilities, including blood centers and testing facilities. To assist AABB members in understanding the basis for this recommendation, AABB will offer a free audioconference in which the data underpinning the recommendation will be reviewed and discussed. Information about the audioconference will be posted on the member section of the AABB Web site.

Background

WNV has been present in the United States since 1999; however, it was first recognized as a transfusion-transmitted agent in 2002 with 23 recipients confirmed to be infected from 16 WNV-infected (RNA-positive) donors. ID-NAT can identify viremic donations that are not detectable by minipool NAT (MP-NAT). In 2003-2004, seven cases of WNV transmission not detected by MP-NAT were reported to the Centers for Disease Control and Prevention (CDC).⁴ On the basis of this information, most blood collection and testing facilities developed local criteria for triggering conversion from MP-NAT to ID-NAT (and resumption of MP-NAT) during limited periods of the epidemic seasons of 2004-2006. Despite such efforts, two additional cases of WNV transmission from one donor later found to be infected were reported in 2006.⁵ At that

time, data were lacking to support a recommendation for a single trigger that would have optimal sensitivity and also meet blood center needs to conserve limited resources.

In preparation for the 2007 WNV season, the AABB WNV Task Force (which includes representatives from the national blood organizations and obtains input from liaison representatives from the Food and Drug Administration and CDC) in collaboration with the TTD committee developed an Association Bulletin (#07-02) to provide a standardized approach to WNV testing that included suggested triggering criteria. Reports in peer-reviewed journals suggested that statistically meaningful triggering criteria should include both the frequency of reactive MPs that contain individually reactive donations and the absolute number of WNV-reactive donations identified from MP-NAT within a predetermined geographic area (eg, the facility's collection area or a portion of this area when the blood center subdivides its territory). In 2007, suggested triggers were defined as two initially reactive donations and a rate per given geographic area of 1:1000, and that if sites in overlapping and/or adjacent areas had reactive donations, their numbers could be combined to establish "multi-site" triggers. In practice, most facilities used presumed viremic donations (PVDs) in place of initially reactive donations for triggering decisions (PVDs are defined later in this Association Bulletin). The "multi-site" trigger strategy worked well; blood facilities in the United States and Canada communicated directly via email and telephone, and were supported by the AABB Web site for entry/review of WNV-reactive donations by state/province and zip/postal code of donor residence. Effective communication plans permitted efficient application of triggering criteria based on complete information about WNV infection rates among donors in a geographic area. No transfusion-transmitted WNV infection was reported in 2007.

During the 2007 WNV season, the American Red Cross performed a study to assess the sensitivity of the recommended trigger criteria (two PVDs and 1:1000 rate) within the American Red Cross system, using a trigger of one PVD detected by MP-NAT in WNV-endemic locations (ie, regions known to have recurring WNV outbreaks or in areas where outbreaks would be predicted for 2007). The yield (by using a trigger of one PVD) could then be evaluated against the 2007 recommended trigger to determine if the ID-NAT-reactive donors would have been detected by MP-NAT in the period between detection of the first PVD and the 2007 recommended trigger being met. Previously, triggers had not been assessed in retrospective or prospective studies. Six American Red Cross regions were selected for prospective study on the basis of their location in geographic areas that have experienced repeated WNV epidemics. Entire collection regions were used to define the geographic area; these collection regions ranged in size from several hundred collections per day to large regions that collect 1000 or more collections per day. Each of the six regions converted to ID-NAT in response to a trigger of one PVD, and during the period of ID-NAT implementation identified 30 WNV confirmed-positive blood donors whose donation samples required ID-NAT for detection (ie, MP-NAT nonreactive).

A summary of the data are contained in the following table.

**30 ID NAT Detectable WNV Confirmed Positive Donations from Validation Regions
Detected by One PVD**

	No. Detected by Different Triggers		
Trigger	<u>1 PVD</u>	<u>2 PVDs</u>	<u>2 PVDs + rate 1:1000</u>
Yield	30	20	5
Incremental Yield		10	15
		25	
IgM neg detected	7 (1)	6 (4)	2
IgM pos detected (Incremental Yield)	23 (9)	14 (11)	3

Within the American Red Cross system, based on testing of 136,388 donations, the use of a frequency of 1:1000 in the triggering criteria, in addition to detection of two PVDs, missed a number of these 30 viremic donors. The data show that, despite the absence of transfusion-transmitted WNV cases in 2007, 25 WNV-infected donors (MP-NAT nonreactive) who would have been detected using one PVD as the triggering criteria, were undetected with a trigger of two PVDs and a 1:1000 rate. Use of two PVDs without a rate requirement would have detected 15 of the 25 donors, four of whom were IgM-antibody negative and most likely to be infectious to recipients. A fifth IgM antibody-negative donor was detected only with the use of one PVD as a trigger. The remaining 20 samples that were not detected by the use of two PVDs and a rate of 1:1000 were IgM antibody positive (11 of which were detected by 2 PVDs and 9 additional that were detected by 1 PVD). The data demonstrate that within the American Red Cross system, the trigger developed for the prior WNV season (2 PVDs, 1:1000) misses viremic donors and that a trigger based only on detection of PVDs without a rate function is more sensitive.

The WNV Task Force, which has continued to meet periodically to review issues relating to human WNV infection in the United States and Canada, has reviewed these data and referred the data to the TTD committee. Based on the findings above, it is the consensus of the TTD committee that the criteria for triggering and de-triggering ID-NAT contained in Association Bulletin #07-02 should be updated as follows:

Recommendations

Triggering and De-triggering Criteria

The new triggering (conversion from MP-NAT to ID-NAT) and de-triggering (resumption of MP-NAT) criteria recommended in this Association Bulletin represent an approach that, if

adopted, is believed to reduce the 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 PVDs (before obtaining confirmatory results unless confirmatory results are immediately available).

A PVD is defined as an initially reactive donation that repeats as reactive on the original sample from the donation or one that has a signal-to-cutoff ratio ≥ 17 (the latter may be applied to the Chiron Procleix™ WNV Assay; samples having a signal-to-cutoff ratio < 17 , or initially reactive using the Roche cobas TaqScreen WNV Test, must be repeated to determine if they are PVDs). In this recommendation, an initially reactive sample that is not a PVD is not counted toward triggering and de-triggering decisions; however, all initially reactive donations should still be submitted for confirmatory testing. A confirmed-positive donor is defined as having repeat NAT or IgM antibody reactivity on a second independent sample from the donation or from a follow-up sample.

Centralized testing facilities and their external customers should agree upon the triggering and de-triggering criteria in advance of the WNV season so that the testing laboratories may take appropriate actions prior to 48 hours from the collection time of the PVD (see below).

- I. On the basis of these 2007 data, AABB recommends consideration of the following criteria for initiating the conversion from MP-NAT to ID-NAT:

Two PVDs within a 7-day rolling period without a rate requirement

- a. De-trigger based on a minimum of 7 days without a PVD.
- b. Continue ID-NAT for > 7 days in areas with ongoing WNV activity in blood donors from facilities that collect in overlapping areas, or with local conditions (including clinical, avian or mosquito WNV activity, where that information is available in a timely fashion), or with prior trigger history, or at the discretion of the medical director. In these circumstances, continuing ID-NAT for 14 days should be considered.

Note: the use of the revised trigger criteria will consume more reagents; within the American Red Cross system, with the application of the revised criteria above, usage during times of ID-NAT would double.

- II. The donor's residential zip/postal code should be used as the location of the 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. A facility with a PVD, either testing laboratory or collection facility but not both, is requested to enter the donor data elements into the AABB Biovigilance Network (see below).
- III. Monitoring of reactive donations should occur in real time. When a defined geographic area has reached its trigger, conversion to ID-NAT should occur ideally within 48 hours of the collection time of the most recent reactive donation 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 when the triggering criteria were met.

Communication Plan

All blood collection and testing facilities serving overlapping and adjacent geographic areas should work together to create a communication plan for linking data to develop a “multi-site” trigger. Responsibility for tracking both the number of reactive donations and the total number of tested donations, as well as the monitoring of overlapping and adjacent collection areas, should be clearly defined among collection and testing facilities to ensure that each PVD is reported only once.

The communication plan should address the following:

- I. The AABB Web site has an established WNV Biovigilance Network for monitoring WNV activity in blood donors. Facilities should enter data for all reactive donations, not only PVDs (use 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 Web site; however, this is not a substitute for direct communication with other organizations serving overlapping and adjacent geographic areas.
- II. Facilities should review the entries of overlapping and adjacent collection and testing facilities on a regular basis—frequently enough to ascertain complete information about WNV infection rates among donors in their geographic area. It is essential for facilities within a geographic area using a two-PVD outcome to communicate when combined data indicate that a multi-site trigger may have been reached. Combined data include PVDs from other blood collection facilities as well as review of clinical or epidemiological evidence of ongoing WNV activity that may be useful for discussion by blood facilities in overlapping and adjacent geographical areas.
- III. AABB has provided a listing of facilities that have given contact information for reporting their WNV data on the AABB Web site. 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 facilities—regardless of the number of blood collectors in a given area—will permit efficient application of a facility’s triggering criteria that is based on complete information about WNV infection rates among donors in a geographic area.

References

1. Sazama K, Lipton KS. Update on WNV-related activities and considerations, 2004; a summary of the WNV Task Force meeting. Association Bulletin #04-03. Bethesda, MD: AABB, 2004:1-3.
2. Sazama K, Lipton KS. Joint statement of AABB, America's Blood Centers and American Red Cross on implementation of individual donation nucleic acid amplification testing for West Nile virus. Association Bulletin #04-04. Bethesda, MD: AABB, 2004:1-3.
3. Strong D, Lipton KS. West Nile virus – recommendations for triggering individual donation nucleic acid testing and developing a communication plan. Association Bulletin #07-02. Bethesda, MD: AABB, 2007:1-3.
4. Montgomery SP, Brown JA, Kuehnert M, et al. Transfusion-associated transmission of West Nile virus, United States 2003-2005. Transfusion 2006;46:2038-46.
5. Centers for Disease Control and Prevention. West Nile virus transmission—South Dakota, 2006. MMWR Morb Mortal Wkly Rep 2007;56:76-9.