



Advancing Transfusion and
Cellular Therapies Worldwide



26 May 2016

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

Submitted via <http://www.regulations.gov>

Re: Docket No. FDA-2016-D-0545, “Recommendations for Donor Screening, Deferral, and Product Management To Reduce the Risk of Transfusion-Transmission of Zika Virus,” 16 February 2016.

Dear Dockets Manager:

We appreciate the opportunity to provide comments to the Food and Drug Administration (FDA) on the guidance titled “Recommendations for Donor Screening, Deferral, and Product Management To Reduce the Risk of Transfusion-Transmission of Zika Virus.” The day after the guidance was released, AABB held an audioconference titled “Reducing the Risk of Transfusion-Transmitted Zika Virus in the US/Canada,” and afterwards gathered questions from audience participants during a Question and Answer session. These questions were then presented to the FDA, via personal communication, asking for clarification of some topics covered in this February guidance as well as asking for responses to topics for which no recommendations were presented in the February guidance. (The [questions](#) are attached to this communication so that they are officially submitted to the identified docket). The FDA responded to many but not all of these questions in the March Q&A Guidance titled “Questions and Answers Regarding Recommendations for Donor Screening, Deferral, and Product Management to Reduce the Risk of Transfusion-Transmission of Zika Virus,” released 14 March 2016.

Definition of an area with active transmission of Zika virus infection

Blood establishments are having difficulty making preparations to comply with one recommendation of the February guidance. Page 3, Section III, Recommendations states:

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For the purpose of this guidance, an area with “active transmission of ZIKV” is an area included on the CDC website listing of countries and U.S. states and territories with local vector-borne (i.e., mosquito-acquired) transmission of ZIKV: <http://www.cdc.gov/zika/geo/index.html>.³

Footnote³ In general, an area is considered to have active transmission of ZIKV when locally transmitted, mosquito-borne ZIKV has been reported.

AABB’s Transfusion Transmitted Diseases Committee and its Arboviruses subgroup has continued to engage in discussions with liaisons from the FDA, the Centers for Disease Control and Prevention (CDC), and the Council of State and Territorial Epidemiologists (CSTE) to better understand how state and local jurisdictions in the United States (the 50 states plus the District of Columbia) will determine local vector-borne areas of active transmission of Zika virus for the purpose of triggering the aspects of the above referenced FDA guidance specific to local transmission. Currently, it is not evident that state and local jurisdictions will use a standardized definition of areas of active vector-borne transmission that would activate blood safety interventions. AABB appreciates the efforts of CSTE to coordinate an effort to establish a minimum definition with the various jurisdictions and to impress the need for real-time reporting to the CDC web site as recommended in the February FDA guidance. (A copy of the [CSTE consensus recommendation](#) is attached to this document). In a separate communication, AABB, the American Red Cross and America’s Blood Centers requested that the FDA should be the agency that defines areas of active vector-borne transmission that would be used to activate the blood safety intervention recommended in the FDA guidance. Workable definitions (for both public health jurisdictions and blood centers) will also be critical for areas with local transmission that must receive blood from “non-affected” areas if they are to be confident they are receiving safe components.

We recommend that the agency update the February guidance to acknowledge this important issue and provide notice of the acceptable minimum definitions blood establishments may use if active Zika transmission is recognized in the United States.

Cessation of risk-exposure deferrals when other measures are implemented

The February guidance document contains recommendations for blood centers operating in Zika non-affected areas (without active transmission of Zika virus) and Zika-affected areas (with active transmission of Zika virus). We believe the FDA has taken an incomplete approach to the use of donor screening tests by not addressing the potential use of the test in Zika non-affected areas.

The recommendations for blood establishments operating in Zika-affected areas do not require that the “Donor History Questionnaire” (DHQ) contains a question to evaluate prospective donors for travel to Zika risk areas if a Zika screening test (licensed or investigational) or pathogen reduction technology is used. However, blood establishments operating in Zika non-affected areas must apply for an FDA variance if they want to use a screening test (or pathogen reduction technology) in lieu of a travel/residence question. FDA should update the guidance with procedures that are already listed as a recommendation for blood centers operating in Zika-affected areas.

We recommend that the FDA update the February guidance document with this same option to cease use of the travel/residence question on the DHQ upon implementation of a screening test (licensed or investigational), or use of pathogen reduction technology, as an alternative for blood establishments operating in Zika non-affected areas.

The recommendations for blood establishments operating in Zika-affected areas require that the DHQ contains questions to evaluate donors for a history (in the past 4 weeks) of Zika virus infection, symptoms suggestive of Zika virus, and a history of sexual contact with a man who has been diagnosed with or had symptoms suggestive of Zika virus in 3 months prior to that instance of sexual contact, even when a Zika screening test (licensed or investigational) or pathogen reduction technology is used. We do not see the value of requiring these questions when products are pathogen reduced (apheresis platelets or plasma) or when the units are tested for Zika virus RNA using sensitive nucleic acid tests. These technologies have been shown to detect or inactivate low levels of virus and presumably it is these data that have allowed those technologies to be used in place of a cessation of collections in Zika-affected areas in Puerto Rico. Given that no additional questions are being asked about Zika virus transmission via mosquito bites-- which represents the greatest transmission risk--the rationale is unclear for additional questions related to symptoms, diagnosis, or sexual contact. It is worth noting that there is no current requirement to ask such symptom questions about West Nile virus (WNV) infection and that the previously required symptom-related question was dropped with the widespread implementation of NAT (including during the initial testing period with investigational assays performed in mini-pools prior to the development of validated ID-NAT triggers). Further, donor follow-up studies with WNV, an arbovirus with a similar rate of asymptomatic infection, demonstrated that the symptom question (fever with headache) had no value with testing in place.

In the case of Zika virus, blood establishments have implemented the pre-donation reading materials and postdonation information sheets which are provided to all donors, each lists the CDC-posted Zika virus symptoms. Based on the widespread use of these materials, we believe that asking the specific questions as part of the donor interview will add no additional value. Additionally, all published reports of sexual transmission have been associated with symptoms in both partners. The pre-donation reading materials and postdonation information sheets would be expected to guard against the small risk of a donor infected by sexual exposure presenting to donate and testing NAT nonreactive using sensitive investigational tests or having a viral load exceeding the capacity of the licensed pathogen reduction platform.

We recommend that the FDA update the February guidance document to remove the recommendation to use questions on the DHQ to assess donors for the following risk exposures for blood establishments that have implemented an investigational Zika screening test, or use of pathogen reduction technology.

- travel to or residence in Zika risk areas,
- a history of a Zika virus infection,
- symptoms suggestive of a Zika virus infection,
- a history of sexual contact with a man who has been diagnosed with or had symptoms suggestive of Zika virus in 3 months prior to that instance of sexual contact

Selective testing

We further recommend that FDA update the February guidance document to allow selective investigational testing and distribution of test-negative donations from donors with Zika-risk factors including those identified by the history questionnaire in Zika-affected and non-affected areas.

Some blood establishment computer systems cannot manage more than 1 version of the DHQ within a single blood establishment. Such systems cannot have one set of questions for Zika-affected versus non-affected areas. Nor, can they turn questions on and off for travel/residence for non-affected areas and areas implementing investigational testing. Thus, blood centers must search for other options for the required travel/residence question in Zika affected areas allowing them to retain the question in non-affected areas, such as to have donors with a “yes” response for travel/residence if in an active area to be cleared for suitability by an investigational test-negative result (i.e. selective donor testing). Similarly, a donor with a “yes” response for any risk factor, should be allowed to be cleared to donate by an investigational test-negative result.

De-triggering thresholds and timeframes to implement interventions

A de-triggering threshold for Zika-active areas is also needed for the blood safety interventions recommended in the guidance when those areas are no longer Zika-affected.

We recommend that the agency update the February guidance document with the criteria that will be used to “de-trigger” areas of active transmission such that blood safety interventions will be relaxed or will cease. We suggest 4 weeks without additional vector-borne cases as reported through public health and in the absence of NAT-reactive donors if investigational NAT is in place.

Additionally, maximum timeframes for implementation of actions required by blood establishments operating in Zika-affected areas are needed as these areas go from non-affected to affected.

AABB is an international, not-for-profit association representing individuals and institutions involved in the fields of transfusion medicine and cellular therapies. The association is committed to improving health through the development and delivery of standards, accreditation and educational programs that focus on optimizing patient and donor care and safety. AABB membership includes physicians, nurses, scientists, researchers, administrators, medical technologists and other health care providers. AABB members are located in more than 80 countries and AABB accredits institutions in over 50 countries.

Founded in 1962, America's Blood Centers is North America's largest network of community-based, independent blood programs. The network operates more than 600 blood donor centers providing over half of the U.S., and a quarter of the Canadian blood supply. These blood centers serve more than 150 million people and provide blood products and services to more than 3,500 hospitals and healthcare facilities across North America. America's Blood Centers' U.S. members are licensed and regulated by the U.S. Food and Drug Administration. Canadian members are regulated by Health Canada.

The American Red Cross shelters, feeds and provides emotional support to victims of disasters; supplies about 40 percent of the nation's blood; teaches skills that save lives; provides international humanitarian aid; and supports military members and their families. The Red Cross is a not-for-profit organization that depends on volunteers and the generosity of the American public to perform its mission. About 5.6 million units of whole blood are collected from roughly 3.3 million Red Cross volunteer donors, separated into 8 million transfusable blood products and supplied to approximately 2,700 hospitals and transfusion centers across the country for patients in need.

Thank you for the opportunity to offer these comments. We look forward to continuing to work with the FDA on patient and donor safety initiatives. Questions concerning these comments may be directed to acarrgreer@aabb.org.

Sincerely,

M. Allene Carr-Greer
Director, Regulatory Affairs
AABB