

# Questions and Answers Regarding “Recommendations for Donor Screening, Deferral, and Product Management to Reduce the Risk of Transfusion-Transmission of Zika Virus: Guidance for Industry”

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## Guidance for Industry

**This guidance is for immediate implementation.**

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(4)(i). Submit one set of either electronic or written comments on this guidance at anytime. Submit electronic comments to <http://www.regulations.gov>. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. You should identify all comments with docket number FDA-2016-D-0545.

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002, or by calling 1-800-835-4709 or 240-402-8010, or email [ocod@fda.hhs.gov](mailto:ocod@fda.hhs.gov), or from the Internet at <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

For questions on the content of this guidance, contact OCOD at the phone numbers or email address listed above.

U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Biologics Evaluation and Research  
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**Contains Nonbinding Recommendations**

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# Questions and Answers Regarding “Recommendations for Donor Screening, Deferral, and Product Management to Reduce the Risk of Transfusion-Transmission of Zika Virus: Guidance for Industry”

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## Guidance for Industry

*This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.*

### I. INTRODUCTION

This guidance provides answers to common questions from blood establishments asked in response to “Recommendations for Donor Screening, Deferral, and Product Management to Reduce the Risk of Transfusion-Transmission of Zika Virus: Guidance for Industry,” dated February 2016 (February 2016 guidance).<sup>1</sup> The guidance was issued for immediate implementation in accordance with 21 CFR 10.115(g)(2) without seeking prior comment because the agency determined that prior public participation is not feasible or appropriate. We are providing answers to these questions to assist blood establishments in implementing the recommendations in the February 2016 guidance.

FDA’s guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the FDA’s current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA’s guidances means that something is suggested or recommended, but not required.

### II. QUESTIONS AND ANSWERS

#### 1. Does FDA recommend that blood establishments ask donors specific questions regarding sexual contact with someone who traveled to an area with active transmission of Zika virus (ZIKV)?

In areas without active transmission of ZIKV, we do not recommend asking donors a specific question with respect to sexual contact, although blood establishments may elect to do so. In these areas, we recommend that the donor educational materials instruct

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<sup>1</sup><http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/UCM486360.pdf>

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donors to self-defer for 4 weeks after the last sexual contact with a man who has been diagnosed with ZIKV or who traveled to or resided in an area with active transmission of ZIKV in the 3 months prior to that instance of sexual contact.

In areas with active transmission of ZIKV, we recommend adding a question to the donor history questionnaire to assess donors for a history of sexual contact in the past 4 weeks with a man who has been diagnosed with or had symptoms suggestive of ZIKV in 3 months prior to that instance of sexual contact, in addition to providing information in the donor educational materials.

- 2. In areas without active transmission of ZIKV, the guidance recommends a 4 week deferral for donors with a history of ZIKV or symptoms suggestive of ZIKV that arose within 2 weeks of departure from an area with active transmission, and a 4 week deferral for sexual contact with a man who has been diagnosed with ZIKV or who traveled to or resided in an area with active transmission of ZIKV in the 3 months prior to that instance of sexual contact. How should blood establishments defer donors for these risk factors if the guidance does not recommend adding specific questions to the donor history questionnaire?**

The guidance does not recommend adding questions to the donor history questionnaire with respect to these risk factors in areas without active transmission of ZIKV, but does recommend adding information with respect to these risk factors to the donor educational materials. If a donor volunteers this information during the screening process or contacts the blood establishment with post-donation information with respect to these risk factors, the blood establishment should defer the donor and quarantine and destroy any undistributed in-date blood or blood components collected from that donor consistent with the recommendations in the guidance.

- 3. For blood establishments in areas without active transmission of ZIKV, the guidance recommends adding a question to assess donors for travel to or residence in areas with active transmission of ZIKV in the past 4 weeks. Is it necessary to instruct donors to self-defer for travel in the donor educational materials?**

The guidance does not recommend updating the donor educational materials to instruct donors to self-defer for travel to an area with active transmission of ZIKV, although blood establishments may include this information in their donor educational materials in addition to the question that addresses screening for travel risk.

- 4. For areas without active transmission of ZIKV, the February 2016 guidance recommends that the donor history questionnaire assess prospective donors for a history of residence in or travel to an area with active transmission of ZIKV in the past 4 weeks. Is this the only question that blood establishments should ask donors with respect to risk of ZIKV in areas without active transmission of ZIKV?**

Yes, this is the only question recommended for areas without active transmission of ZIKV. Blood establishments should update the donor educational material to instruct

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donors to self-defer for the risk factors as recommended in Section III.A.1.a. of the February 2016 guidance.

- 5. For areas with active transmission of ZIKV, the February 2016 guidance recommends that the donor history questionnaire assess prospective donors for a history of ZIKV infection or symptoms suggestive of ZIKV in the past 4 weeks, and a history of sexual contact in the past 4 weeks with a man who has been diagnosed with or had symptoms suggestive of ZIKV in 3 months prior to that instance of sexual contact. Do these recommendations apply if a blood establishment has implemented FDA-approved pathogen reduction technology or testing blood components using an FDA-licensed test, should such a test become available?**

Yes, the recommendations for donor deferral questions in areas with active transmission of ZIKV apply even when the blood establishment has implemented such additional measures.

- 6. Will FDA expedite review of revised donor history questionnaires?**

The February 2016 guidance recommends that blood establishments update their donor history questionnaires, including full length and abbreviated donor history questionnaires, and accompanying materials and standard operating procedures, as necessary, to incorporate the recommendation provided in the guidance. Consistent with 21 CFR 601.12, licensed blood establishments may implement these changes without FDA's prior approval and must report these changes in their annual report.

- 7. Will FDA provide blood establishments with specific questions or algorithms to screen donors for risk of ZIKV in areas without active transmission?**

FDA has not recommended specific questions or algorithms to screen donors for risk of ZIKV. Blood establishments in areas without active transmission of ZIKV should update their donor history questionnaires to assess donors for travel to or residence in an area with active transmission of ZIKV in the four weeks prior to donation. If blood establishments use capture questions to assess donors for travel outside of the United States, the blood establishments should ensure the questions are adequate to identify travel to or residence in areas with active transmission of ZIKV. (Refer to the Centers for Disease Control and Prevention (CDC) website (<http://www.cdc.gov/zika/geo/index.html>) to identify areas with active transmission of ZIKV). As necessary, capture questions may be revised or a new question may be added to the donor history questionnaires to identify areas with active transmission of ZIKV. Consistent with 21 CFR 601.12, licensed blood establishments may implement these changes to their revised donor history questionnaires without FDA's prior approval and must report these changes in their annual report.

The AABB Donor History Task Force has developed questions to evaluate donors for risk of ZIKV infections for use in collection areas with and without active ZIKV transmission (<http://www.aabb.org/tm/questionnaires/Pages/Additional-Questions-to->

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[Evaluate-Donors-for-Risk-of-Zika-Virus-Infection.aspx](#)). In developing your updated donor history questions, you may wish to review these questions.

- 8. Why does the guidance recommend a 4 week deferral for sexual contact with a man who has been diagnosed with ZIKV, had symptoms suggestive of ZIKV or who traveled to an area with ZIKV in the 3 months prior to that instance of sexual contact?**

Sexual transmission of ZIKV has been reported from men to their sexual partners. The maximum time ZIKV may persist in semen is currently unknown, but has been shown to be more than 60 days. This deferral will help to ensure that the virus has not been transmitted to the sexual partner of the at-risk male.

- 9. Does the recommendation for deferral for sexual contact with a man who has been diagnosed with ZIKV apply to sexual contact with a man who has been diagnosed with ZIKV ever?**

No, the 4 week deferral is recommended for a donor who has had sexual contact with a man who had been diagnosed with ZIKV in the three months prior to the sexual contact.

- 10. The February 2016 guidance defines an area with “active transmission of ZIKV” as an area included on the CDC website listing of countries and U.S. states and territories with local vector-borne (mosquito-acquired) transmission of ZIKV. How should blood establishments apply the recommendations in the guidance if local vector-borne (mosquito-acquired) transmission is reported in U.S. states?**

FDA recommends that blood establishments refer to the CDC website (<http://www.cdc.gov/zika/geo/index.html>) to identify areas with active transmission of ZIKV. If an area within the continental United States experiences active transmission of ZIKV, we recommend that blood collection establishments located in the affected area follow the recommendations in Section III.B. of the February 2016 guidance.

At this time, we do not anticipate that an entire state would be designated as an area of active transmission if a more localized region could be identified. However, such determinations are under discussion at this time. In the interim, we recommend that you contact your state and local health departments to determine areas with active transmission of ZIKV should a locally acquired case be reported in your state on the CDC website.

If ZIKV transmission becomes widespread in the continental United States we will reassess our recommendations.

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### **11. How is a location removed from the list of areas with active transmission?**

The CDC and state health departments will determine when an area no longer has active ZIKV transmission. For the purpose of the February 2016 guidance document, we recommend that you refer to the CDC website (<http://www.cdc.gov/zika/geo/index.html>) and contact the relevant state and local health departments to determine if an area has active ZIKV transmission.

### **12. How long will the recommendations in the guidance remain in place? Will the guidance be updated to reflect new areas in the United States with active transmission of ZIKV?**

The recommendations remain in place unless the February 2016 guidance is updated or withdrawn. The February 2016 guidance recommends that blood establishments refer to the CDC's website for a listing of countries and U.S. states and territories with active ZIKV transmission (<http://www.cdc.gov/zika/geo/index.html>).

### **13. With respect to assessing post-donation information, should travel history to an area with active transmission be considered when a donor reports symptoms suggestive of ZIKV after donation?**

When assessing post-donation symptoms reported by a donor, at-risk exposure through travel, residence, or sexual contact should be considered. FDA recommends that in-date blood or blood components be quarantined and destroyed when a donor with a recent history of travel to or residence in an area with active ZIKV transmission or sexual contact with an at-risk male reports symptoms suggestive of ZIKV in the 2 weeks following donation. Further, if blood components from such a donor have been transfused, we recommend that blood establishments advise the recipient's physician of record regarding the potential need for monitoring the recipient for a possible ZIKV infection. Blood donors and medical directors may refer to guidance from CDC regarding symptom histories suggestive of ZIKV infection (<http://www.cdc.gov/zika/symptoms/index.html>). If a donor reports post-donation information with symptoms, but does not have a history of travel to or residence in an areas with ZIKV transmission or sexual contact with an at-risk male, medical directors should use their medical judgment about quarantining and destroying in-date components or advising the recipient's physician of record if the components have been transfused.

### **14. Does FDA recommend that blood establishments quarantine and destroy recovered plasma intended for further manufacture upon receipt of post-donation information that the donor was at risk for ZIKV infection at the time of donation?**

Viral inactivation and removal methods are currently used to clear viruses in the manufacturing process for plasma-derived products. For this reason, recovered plasma intended for further manufacture may be labeled and released for manufacture into injectable products upon receipt of post-donation information that the donor was at risk for ZIKV infection at the time of donation. Consistent with 21 CFR 606.121(c)(10),

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recovered plasma intended for further manufacture into injectable products must be labeled with the following statement: “Caution: For Manufacturing Use Only.”

### **15. When should a blood establishment advise transfusion services to inform the transfusion recipient’s physician of record regarding the need for monitoring the recipient for a possible ZIKV infection?**

We recommend that blood establishments advise the transfusion service to inform the transfusion recipient’s physician of record regarding the potential need for monitoring the recipient for a possible ZIKV infection if:

- 1) blood components collected from a donor with a history of ZIKV in the 4 weeks prior to donation have been transfused; or
- 2) blood components from a donor who reports symptoms suggestive of ZIKV infection within 2 weeks after donation and who has recently departed from an area with active transmission of ZIKV have been transfused.

These recommendations do not apply to blood components that have been pathogen reduced using an FDA-approved device. We also note that an investigational pathogen reduction device may be permitted in situations where approved technologies are unavailable.

### **16. The guidance states that information on the signs and symptoms of ZIKV infection can be found on CDC’s website (<http://www.cdc.gov/zika/symptoms/index.html>). Is it acceptable to use a minimum of two of the signs and symptoms to instruct donors on self-deferral and when to provide post-donation information; ask donor questions; and manage products after the receipt of post-donation information?**

The guidance does not recommend a specific number of signs and symptoms. We recommend providing the donor with information from the CDC website on the signs and symptoms of ZIKV infection, including fever, rash, joint pain, or conjunctivitis (red eyes). We think it is reasonable that the donor exhibit more than one symptom of ZIKV infection before he or she self-defers or is deferred by the blood establishment. However, we defer to the judgment of the blood establishment medical director to address the potential risk associated with a specific donor.

### **17. Are autologous collections acceptable in areas with active transmission of ZIKV?**

Yes, collections intended for autologous use are acceptable in areas with active transmission of ZIKV. Blood establishments should have measures in place to ensure that the autologous donor is in good health at the time of collection. Medical discretion may be needed in cases where a patient donates blood for autologous use after a procedure associated with significant immune suppression. Autologous collections in areas with active transmission should not be issued for allogeneic use.

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- 18. The guidance recommends that blood establishments in areas with active transmission of ZIKV implement the recommendations of the February 2016 guidance immediately for collections intended for intrauterine transfusion, transfusion in pregnant women, or transfusion in other at-risk recipients when requested by the prescribing physician. How should blood establishments implement the recommendations if they do not know the intended recipients for the products they distribute?**

We recommend that blood establishments establish appropriate communication with transfusion services to help ensure at risk-recipients are provided the most appropriate product. Blood establishments may also establish a process to inform transfusion services of blood components that are from areas of the U.S. without active transmission of ZIKV, or have been pathogen-reduced.

- 19. How should blood establishments in areas with active transmission manage their inventory of blood components collected before the issuance of the February 2016 guidance?**

FDA recommends that you destroy or re-label (consistent with the recommendations in Section III.D. of the February 2016 guidance) in-date blood components that were collected after active transmission has been determined in your area. (Refer to the CDC website (<http://www.cdc.gov/zika/geo/index.html>) to identify areas with active transmission of ZIKV). FDA recommends blood establishments contact FDA to discuss any unresolved issues regarding the immediate need for blood components.

In-date blood components remaining in inventory that were collected prior to active transmission of ZIKV in your area do not need to be destroyed or relabeled.

For example, active transmission of ZIKV was first reported in the United States territory of the Commonwealth of Puerto Rico on December 31, 2015. Blood establishments located in Puerto Rico should destroy or re-label in-date blood components collected after December 31, 2015. Active transmission was first reported in the U.S. Virgin Islands and American Samoa on January 22, 2016 and February 18, 2016, respectively. Blood establishments located in the U.S. Virgin Islands and American Samoa should destroy or re-label in-date blood components collected in these locations after January 22, 2016 and February 18, 2016, respectively.

- 20. The guidance recommends that blood establishments in areas with active transmission of ZIKV implement the recommendations in the guidance immediately for collections intended for at-risk recipients and as soon as feasible, but not later than 2 weeks after the guidance issue date for all other collections. What if a blood establishment cannot implement the recommendations within this timeframe?**

FDA expects that blood establishments in areas with active transmission will work to implement the recommendations within the timeframes recommended in the guidance. Blood establishment may wish to contact the AABB Interorganizational Task Force on

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Domestic Disasters and Terrorism to find out about sources of blood components from within the continental United States for sourcing into an area experiencing active ZIKV transmission.

Further information is available at <http://www.aabb.org/programs/disasterresponse>. For blood supply emergencies contact the AABB Disaster Task Force at 1-800-458-9388.

### **21. How can blood establishments in areas with active transmissions of ZIKV learn more about participation in an investigational study for a ZIKV donor screening test or pathogen reduction technology for Whole Blood or Red Blood Cells?**

Several companies are developing candidate donor screening tests that potentially could become available under an investigational new drug application in the near future. Also, two companies that have published scientific papers on pathogen inactivation technologies for Whole Blood or Red Blood Cells publicly have expressed interest in making their devices available under an investigational device exemption application. Blood establishments may contact these manufacturers about investigational studies in which they might participate. Alternatively, blood establishments may contact the Office of Blood Research and Review and we will inform the product manufacturers of the blood establishment's interest in participating in investigational studies.

### **22. Are there any licensed ZIKV blood donor screening tests for use within the United States?**

Currently, there are no FDA-licensed blood donor screening tests for ZIKV. FDA is working with device manufacturers and U.S. government partners to facilitate the development of a blood donor screening test.

### **23. If a donor screening test for ZIKV is licensed, will FDA issue guidance on implementation of the test?**

FDA may issue a guidance document providing recommendations on the implementation of a licensed donor screening test, when such a test becomes available.

### **24. What is the FDA contact information for sponsors interested in pursuing development of nucleic acid tests (NAT) for ZIKV?**

FDA is working directly with candidate device manufacturers to facilitate the development of investigational NAT for ZIKV. We recommend that sponsors contact the FDA's Office of Blood Research and Review at 240-402-8630 with any questions.

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### **25. Who should blood establishments contact with questions regarding the implementation of the guidance?**

Blood establishments should contact their FDA Consumer Safety Officer if they have questions.

FDA's Office of Communication, Outreach and Development can also be contacted as follows:

Phone: 1-800-835-4709 (toll free) or 1-240-402-8010

Email: [industry.biologics@fda.hhs.gov](mailto:industry.biologics@fda.hhs.gov) (for industry questions) and [ocod@fda.hhs.gov](mailto:ocod@fda.hhs.gov) (for questions from other stakeholders)

### **26. Where can one find additional information on ZIKV?**

One may access the CDC website at <http://www.cdc.gov/zika/> for additional information on ZIKV.