

Guidance for Industry

Recommendations for Donor Questioning, Deferral, Reentry and Product Management to Reduce the Risk of Transfusion-Transmitted Malaria

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 [Docket No. FDA-2000-D-0187 (formerly Docket No. 2000-D-1267)].

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 240-402-7800, or email 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
August 2013
Updated August 2014**

Guidance for Industry

Recommendations for Donor Questioning, Deferral, Reentry and Product Management to Reduce the Risk of Transfusion-Transmitted Malaria

Note: Changes have been made to update the “Guidance for Industry: Recommendations for Donor Questioning, Deferral, Reentry and Product Management to Reduce the Risk of Transfusion-Transmitted Malaria” dated August 2013, including:

- Updates to recognize revisions to certain flow charts contained in the accompanying materials for the Full-Length Donor History Questionnaire (v.1.3 dated May 2008) and Abbreviated Donor History Questionnaire (v.1.3 dated December 2012) prepared by the AABB Donor History Task Force, as acceptable for use in screening donors of blood and blood components for risk of malaria (see new section VI).
- Revised recommendations in section VII on how licensed establishments must report the implementation of the recommendations contained herein to FDA.

**U.S. Department of Health and Human Services
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Contains Nonbinding Recommendations

Table of Contents

I. INTRODUCTION..... 1

II. BACKGROUND 2

III. DEFINITIONS 4

IV. RECOMMENDATIONS..... 5

A. Donor History Questionnaire..... 5

B. Donor Deferral and Reentry 5

**C. Product Retrieval and Quarantine, and Notification of Consignees of Blood
and Blood Components..... 6**

D. Product Disposition and Labeling 7

E. Reporting a Biological Product Deviation (BPD) 8

V. ADDITIONAL CONSIDERATIONS 8

**VI. RECOGNITION OF THE REVISED DONOR HISTORY QUESTIONNAIRE
(DHQ) DOCUMENTS..... 8**

A. Recognition of the Revised DHQ Documents..... 8

B. Implementation of the Acceptable DHQ Documents 9

VII. IMPLEMENTATION OF RECOMMENDATIONS..... 10

VIII. REFERENCES..... 12

Guidance for Industry

Recommendations for Donor Questioning, Deferral, Reentry and Product Management to Reduce the Risk of Transfusion-Transmitted Malaria

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the appropriate FDA staff. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This guidance document provides you, blood establishments that collect blood and blood components, with our, FDA's, recommendations for questioning and deferring donors of blood and blood components, allowing their reentry, and product management to reduce the risk of transfusion-transmitted malaria. The recommendations contained in this guidance apply to the collection of Whole Blood and all blood components with the exception of Source Plasma. Donors of Source Plasma are excluded from deferral due to malaria risk under Title 21 of the Code of Federal Regulations 640.63(c)(9) (21 CFR 640.63(c)(9)).

This guidance supersedes the guidance of the same title dated August 2013 (78 FR 50421, August 19, 2013), which in turn finalized the draft guidance entitled "Recommendations for Donor Questioning, Deferral, Reentry and Product Management to Reduce the Risk of Transfusion-Transmitted Malaria" dated June 2012, and superseded the FDA memorandum to all registered blood establishments entitled "Recommendations for Deferral of Donors for Malaria Risk" dated July 26, 1994 (July 26, 1994 memorandum) (Ref. 1).

In this guidance, we recognize revisions to certain flow charts contained in the accompanying materials for the Full-Length Donor History Questionnaire (v.1.3 dated May 2008) and Abbreviated Donor History Questionnaire (v.1.3 dated December 2012) prepared by the AABB Donor History Task Force, as acceptable for use in screening donors of blood and blood components for risk of malaria. The revised flow charts are dated April 2014.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency'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 Agency guidance means that something is suggested or recommended, but not required.

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II. BACKGROUND

Transfusion-transmitted malaria occurs rarely, but is a serious concern in transfusion medicine (Refs. 2, 3). It has been shown to be caused by any of the following four *Plasmodium* species: *P. falciparum*; *P. malariae*; *P. ovale*; or *P. vivax*. In the absence of a licensed test for donor screening, the measure used to reduce transfusion-transmitted malaria in the United States (U.S.) has been the deferral of donors who have had a malaria infection or had a possible exposure risk to malaria. Accurate identification of donors with the potential to transmit malaria depends on the donor exposure history obtained during the donor interview, which may be facilitated through use of a donor questionnaire (Refs. 4-6).

The July 26, 1994 memorandum had the following recommendations:

- Permanent residents of non-endemic countries who travel to an area considered endemic for malaria should not be accepted as donors of Whole Blood and blood components prior to one year after departure from the endemic area. After one year after departure, such otherwise suitable prospective donors may be accepted provided that they have been free of unexplained symptoms suggestive of malaria.
- Prospective donors who have had malaria should be deferred for three years after becoming asymptomatic.
- Citizens, residents, immigrants or refugees of endemic countries should not be accepted as donors of Whole Blood and blood components prior to three years after departure from the area. After the 3-year period, otherwise suitable prospective donors may be accepted if they have remained free of unexplained symptoms suggestive of malaria.

Public comments on the July 26, 1994 memorandum and the June 2000 draft guidance on screening of donors for malaria risk raised several concerns about the need to standardize definitions used in the recommendations, and the scientific basis for the recommended deferral periods. These concerns prompted public discussions, including a meeting of the FDA Blood Products Advisory Committee (BPAC or Committee) on September 16, 1999. At that meeting, BPAC reviewed the current status of transfusion-transmitted malaria and its impact on blood safety in the United States. BPAC also reviewed the usefulness of the available laboratory test methods to detect current malaria infection or to provide evidence of past exposure to malaria parasites.

On July 12, 2006, FDA convened a scientific workshop entitled “Testing for Malarial Infections in Blood Donors” to seek public discussion of scientific developments that might support donor testing for malaria infections as part of pre-donation testing, or as follow-up testing to permit a reduced deferral period for donors deferred for malaria risk (Ref. 7). There are no FDA-licensed tests to screen blood donors for malaria. Nucleic acid-based tests were deemed unsuitable for donor screening due to the limitation of the small sample size used in nucleic acid extraction; however, several speakers and panel members emphasized the value of antibody testing to reenter deferred malaria-risk donors who tested negative for malarial antibodies (Refs. 7, 8). The outcome of the workshop was summarized at the BPAC meeting held on July 13, 2006 (Ref. 9).

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At the BPAC meeting on September 11, 2008, the Committee discussed donor testing for malarial antibodies as an indicator of possible exposure to malaria parasites (Ref. 10). At the meeting, FDA presented risk assessment data for three possible scenarios in which antibody testing could be of value: (1) testing all donors (universal testing); (2) reentry testing of all at-risk donors with a history of potential exposure to malaria anywhere in the world; and (3) reentry testing of only those donors who had traveled to malaria-endemic areas in Mexico. The risk assessment model assumed that donors would be deferred for four months after returning from endemic areas of Mexico or other parts of the world before antibody testing would be performed on the donor. At the meeting, two blood organizations (the American Red Cross and America's Blood Centers) also presented data from surveys showing that approximately 41% of all blood donors deferred for risk of malaria exposure had been deferred because they had traveled to malaria-endemic areas in Mexico (Refs. 10, 11). The Committee considered all three risk assessment scenarios and the possible role that antibody testing could play in identifying or reentering malaria-risk donors, especially those donors who had traveled to endemic areas in Mexico. In the end, the Committee felt that additional risk analysis would be needed, and that the analysis should account for malaria risk globally and in Mexico, with and without antibody testing.

On November 16, 2009, FDA again sought advice from BPAC on an alternative strategy to minimize donor loss associated with deferrals for malaria risk. Specifically, FDA asked the Committee to consider a new risk assessment model which was focused on travel to malaria-endemic states in Mexico, and asked whether it was acceptable to allow blood collections without any deferral from individuals who have traveled to certain Mexican states that have a low malaria transmission rate. At that meeting, FDA presented data which showed that while travel to Mexico was a major contributor to donor deferrals due to malaria risk (about 41%), from 2006-2009, malaria transmission in Mexico was shown to be very low (average 2400 malaria cases annually) and limited only to certain Mexican states (Ref. 12). The malaria transmission rate was shown to be particularly low in Quintana Roo, a Mexican state that includes Cancun and Cozumel and is known to receive a high volume of U.S. travelers. Estimates also suggested that there was a great disparity in the contribution of different Mexican states to the number of donor deferrals among U.S. travelers. Data collected by the American Red Cross and Blood Systems Research Institute suggested that in 2006, among the 10 malaria-endemic states, Quintana Roo alone contributed approximately 70% of all malaria-risk-associated donor deferrals for travel to Mexico (Refs. 12, 13). While donors deferred because of travel to Quintana Roo were a significant percentage of deferrals, FDA's risk assessment found that the calculated overall risk to the blood supply would be expected to increase by 1.1% (an absolute increase of 0.0166 infected blood unit per year, or one in 60 years) if prospective blood donors who visited Quintana Roo and another state, Jalisco, which includes the cities of Puerto Vallarta and Guadalajara, were allowed to donate blood without any deferral for malaria risk. However, the donor pool would increase by approximately 45,000 donors (79,000 blood units) each year (Ref. 13). FDA also found that the actual donor gain might be significantly higher if the Agency took into account the total donor loss due to self-deferrals and the non-return of donors deferred under the current policy (Ref. 7). After these presentations and discussion, the Committee voted 17-1 in favor of allowing blood collection, without any deferral for malaria

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risk, from U.S. residents who have visited Quintana Roo. The Committee also discussed extending the proposed policy to other malaria-endemic states of Mexico that have a low malaria transmission rate.

III. DEFINITIONS

Malaria - An infectious disease caused by a parasitic protozoan of the genus *Plasmodium*. Malaria diagnosis in a prospective donor is based on a positive laboratory test indicating *Plasmodium* infection, or a determination of a history of malaria made by the blood establishment's Medical Director. For additional information regarding malaria and its associated symptoms, visit the Centers for Disease Control and Prevention (CDC) website at <http://www.cdc.gov/malaria/>.

Malaria-endemic area - Any areas with malaria where CDC recommends anti-malarial chemoprophylaxis in travelers in the most current version of the *CDC Health Information for International Travel* (commonly known as *The Yellow Book*) at the time the donor is screened. We recommend you access the "Malaria Information, by Country" table in the Malaria chapter of *The Yellow Book* for the most current recommendations on anti-malarial chemoprophylaxis. *The Yellow Book* is available on the CDC website at <http://wwwnc.cdc.gov/travel/page/yellowbook-2012-home.htm>.

Malaria-endemic country - Any country having an area or areas with malaria where CDC recommends anti-malarial chemoprophylaxis in travelers in *The Yellow Book* at the time the donor is screened. A country that has any malaria-endemic areas should be considered to be malaria-endemic in its entirety.

Residence in a malaria-endemic country - For purposes of this guidance, residence is defined as a continuous stay of longer than 5 years in a country or countries having any malaria-endemic area (see definition above). In determining residence, consideration is by malaria-endemic country and not by malaria-endemic area since the geographic distribution of malaria-endemic areas may change during the period of residence, or the resident may have traveled from a non-endemic area to an endemic area in the country during his or her stay.

Travel to a malaria-endemic area - Any travel to or through a malaria-endemic area or areas, as identified by CDC (see definition above). The duration of travel to a malaria-endemic area is defined as more than 24 hours to less than 5 years. Note that a passage greater than 24 hours through a malaria-endemic area while on route to a malaria-free area is considered a sufficient possible exposure to trigger donor deferral. Common examples of such possible exposure include passage through a malaria-endemic area to visit a tourist resort in a malaria-free area, or passage through a malaria-endemic area to board a cruise ship, or on-shore excursions into a malaria-endemic area when traveling on a ship. Travel to or through a malaria-free area within a malaria-endemic country does not constitute travel to a malaria-endemic area.

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IV. RECOMMENDATIONS

FDA's scientific rationale and further explanation for our recommendations are provided in the Appendix.

A. Donor History Questionnaire

1. We recommend that you update your donor history questionnaire, including full length and abbreviated donor history questionnaires, to incorporate the recommendations provided in this guidance.
2. We recommend that the updated donor history questionnaire include the following elements to assess prospective donors for malaria risk (note definitions in section III of this guidance):
 - a. A history of malaria in the past three years;
 - b. A history of prior residence in a malaria-endemic country;
 - c. A history of travel to a malaria-endemic area in the past one year; and
 - d. A history of travel to a malaria-endemic area in the past three years, if previously a resident of a malaria-endemic country.

B. Donor Deferral and Reentry¹

1. History of Malaria
 - a. We recommend that you defer for 3 years a donor who has a history of malaria.
 - b. If that donor has remained free of malaria symptoms for a 3-year period while residing in a non-endemic country, the Medical Director may decide to accept the donor, provided the donor meets all other donor eligibility criteria.
2. Residence in a Malaria-endemic Country

We recommend that you defer a donor for 3 years who had been a prior resident (as defined in section III of this guidance) in a malaria-endemic country. After the 3-year deferral period, the donor may be eligible to donate provided the donor has been free from malaria during this period and meets all other donor eligibility criteria.

¹ See Appendix for detailed scientific rationale for the recommendations contained in this guidance.

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3. Travel to a Malaria-endemic Area
 - a. We recommend that you defer for 1 year after the last departure from a malaria-endemic area (as defined in section III of this guidance) a donor who is a resident of a non-endemic country and who has traveled to or through any malaria-endemic area, whether or not the donor has received malaria chemoprophylaxis. After the 1-year deferral period, the donor may be eligible to donate, provided the donor has been free from malaria during this period and meets all other donor eligibility criteria.
 - b. We recommend that you defer for 3 years after a visit to a malaria-endemic area a donor who is a prior resident of a malaria-endemic country (as defined in section III of this guidance) and who has been a resident of non-endemic countries for less than 3 consecutive years. After the 3-year deferral period, the donor may be eligible to donate, provided the donor has been free from malaria during this period and meets all other donor eligibility criteria.
 - c. We recommend that if a prior resident of a malaria-endemic country returns to a malaria-endemic area after residence for 3 years consecutively in non-endemic countries, that you defer that donor for 1 year from the time that they return to the non-endemic country. After the 1-year deferral period, the donor may be eligible to donate, provided the donor has been free from malaria during this period and meets all other donor eligibility criteria.

C. Product Retrieval and Quarantine, and Notification of Consignees of Blood and Blood Components

We recommend that you take the following actions if you determine that blood or blood components have been collected from a donor who should have been deferred according to the recommendations in section IV.B of this guidance.

1. If you collected cellular blood components intended for transfusion or for further manufacturing from a donor who should have been deferred according to the recommendations in section IV.B. of this guidance, we recommend that you quarantine any undistributed in-date cellular blood components collected from that donor.
2. If you distributed cellular blood components intended for transfusion or for further manufacturing collected from a donor with a clinical history of malaria who should have been deferred according to the recommendation in section IV.B.1. of this guidance, we recommend that you notify consignees to retrieve and quarantine the in-date cellular blood components collected from that donor.

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Additionally, in this situation, if cellular blood components have been transfused, you should encourage consignees to notify the transfusion recipient's physician of record regarding the need for monitoring of the recipient for a possible malaria infection for a period of 3 months post-transfusion.

3. If you distributed cellular blood components intended for transfusion collected from a donor who should have been deferred for malaria-risk associated with travel or prior residence according to recommendations in sections IV.B.2 or 3 of this guidance, we recommend that you notify consignees to retrieve and quarantine the in-date cellular blood components collected from that donor.
4. If you collected acellular blood components (i.e., frozen plasma products) intended for transfusion or for further manufacturing from a donor who should have been deferred according to the recommendations in section IV.B. of this guidance, we recommend that you quarantine any undistributed in-date acellular blood components collected from that donor. (Note that based on the very low risk for transmission of malaria, we are not recommending notification of consignees if you distributed such acellular products.)

D. Product Disposition and Labeling

1. We recommend that you destroy or relabel cellular blood components that were collected from a donor who should have been deferred according to the recommendations in section IV.B of this guidance. If you relabel the cellular blood components, they may be released for research, or for manufacture into noninjectable products or in vitro diagnostic reagents as described in section IV.D.3. of this guidance.
2. Although not suitable for transfusion, acellular blood components inadvertently collected from a donor who should have been deferred according to the recommendations in section IV.B. of this guidance may be released for research, or for further manufacture into injectable (i.e., plasma derivative) or non-injectable products, or in vitro diagnostic reagents, if labeled appropriately as described below.
3. You should use the following statements to prominently relabel the blood components:
 - a. "NOT FOR TRANSFUSION: Collected From A Donor Determined To Be At Risk For Infection With Malaria Parasites"
 - and
 - b. "Caution: For Laboratory Research Only"
 - or

Contains Nonbinding Recommendations

“Caution: For Further Manufacturing into *In Vitro* Diagnostic Reagents For Which There Are No Alternative Sources”

or

“Caution: For Use in Manufacturing Noninjectable Products Only”

or

“Caution: “For Manufacturing Use Only” (used for acellular products intended for further manufacture into injectable products).

You should not label these products with a U.S. license number unless FDA specifically approves you to do so. If appropriate, unlicensed products may be shipped solely to a manufacturer of a product subject to licensure, under a short supply agreement (21 CFR 601.22).

E. Reporting a Biological Product Deviation (BPD)

If you have distributed any cellular blood components for transfusion or for further manufacturing, collected from a donor at risk for malaria according to section IV.B. of this guidance, you should report a BPD as soon as possible, but you must report within 45 calendar days from the date you acquire the information reasonably suggesting that a reportable event has occurred (21 CFR 606.171).

You are not required to report a BPD if you have distributed an acellular blood component intended for transfusion or further manufacturing from a donor at risk for malaria.

V. ADDITIONAL CONSIDERATIONS

Whole Blood and blood components intended for transfusion should not be collected from a possible malaria risk donor with the intent of converting or relabeling those products for further manufacturing use (e.g., relabeling of Fresh Frozen Plasma as recovered plasma).

VI. RECOGNITION OF THE REVISED DONOR HISTORY QUESTIONNAIRE (DHQ) DOCUMENTS

A. Recognition of the Revised DHQ Documents

The AABB Donor History Task Force has revised the flow charts for the following questions:

Contains Nonbinding Recommendations

- The Full-Length Donor History Questionnaire, v.1.3 dated May 2008
 - In the past 3 years have been outside the United States or Canada?
 - Have you ever had malaria?

- The Abbreviated Donor History Questionnaire, v.1.3 dated December 2012
 - Since your last donation have you been outside the United States or Canada?

FDA finds the revised AABB DHQ flow charts for the questions above (v.1.3 dated April 2014) to be acceptable for use in screening blood donors consistent with the recommendations contained in this guidance.²

While we recognize the DHQ documents prepared by the AABB Task Force as acceptable, you are not required to implement them. You may continue to use any donor history questionnaire and accompanying materials developed by your establishment that have been revised to reflect the recommendations contained in this guidance and, for licensed blood establishments, have been approved by FDA. Your materials may include procedures and wording that are different from those in the AABB DHQ documents.

B. Implementation of the Acceptable DHQ Documents

To ensure the correct implementation of the revised DHQ flow charts described in section VI. A of this guidance), we recommend you use the process described below:

- Implementing the new flow charts for the full-length DHQ, v.1.3 dated April 2014:
 - Replace the flow charts v.1.3 dated May 2008 with the revised flow charts v.1.3 dated April 2014

- Implementing the new flow chart for the abbreviated DHQ, v.1.3 dated April 2014:
 - Add the following question from the full-length DHQ to the abbreviated DHQ in the space reserved for extra questions:
 - In the past 3 years have you been outside the United States or Canada?
 - Include the v.1.3 dated April 2014 flow chart for this question from the full-length DHQ in your procedures.

² You may view v.1.3 of the DHQ documents prepared by AABB, including the revised flow charts, on the FDA website at <http://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedP roductsBLAs/BloodDonorScreening/ucm164185.htm>. On this website, you may also view the FDA guidance documents that recognized v.1.3 of the full-length and abbreviated DHQs and accompanying materials.

Contains Nonbinding Recommendations

- Retain this question and corresponding flow chart on the abbreviated DHQ for 1 year from the time that you implement these procedures. After 1 year, you may remove this question and the corresponding flow chart from the abbreviated DHQ.
- Concurrently, retain this current question on the abbreviated DHQ:
 - Since your last donation have you been outside the United States or Canada?
- Replace the flow chart dated v.1.3 December 2012 for this question with the v.1.3 dated April 2014 flow chart from the abbreviated DHQ for same question.
- For the one year that you are including the question and flow chart from the full-length DHQ, you may use one of the following methods to implement the revised flowchart for the abbreviated DHQ:
 - Use the v.1.3 dated April 2014 flow chart for the abbreviated DHQ in its entirety, or
 - Skip the part of the flow chart for the abbreviated DHQ that evaluates the donor for travel to malaria-endemic countries and areas and proceed to the sections on the flow chart for evaluating travel to HIV-1 Group O and vCJD endemic countries.
- At the end of the 1 year period, if you are not already doing so, use the revised v.1.3 dated April 2014 flow chart for the abbreviated DHQ in its entirety.

VII. IMPLEMENTATION OF RECOMMENDATIONS

You may implement the recommendations contained in this guidance once you have revised your donor history questionnaire (DHQ), including full-length and abbreviated DHQs, and accompanying materials as necessary to reflect the new donor deferral recommendations.

Licensed blood establishments must report the changes to FDA in the following manner:

1. Revision of your own DHQ and accompanying materials: report as a major change if revising your own DHQ and accompanying materials to implement the new recommendations. Report such a change to FDA as a prior approval supplement (PAS) under 21 CFR 601.12(b).
2. Revision of a previously FDA accepted DHQ and accompanying materials: report as a major change if you are revising the FDA accepted DHQ and accompanying materials to implement these new recommendations. Report such a change to FDA as a prior approval supplement (PAS) under 21 CFR 601.12(b).

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3. Use of full-length DHQ (v.1.3 dated May 2008) and abbreviated DHQ (v.1.3 dated December 2012) with revised flow charts v.1.3 dated April 2014:
 - a. If the revised flow charts are implemented without modifications and in their entirety using the process in section VI. B of this guidance, the change is considered to be minor. You must report such changes to FDA in your annual report consistent with 21 CFR 601.12(d), noting the date the process was implemented.
 - b. If you make changes to the format of the revised flow charts but the content remains consistent, or you adopt stricter donor deferral criteria, the changes are considered minor. You must report such changes to FDA in your annual report under 21 CFR 601.12(d), noting the date the process was implemented and describing how you modified the acceptable flow charts.
 - c. If the revised flow charts are implemented with modifications other than formatting, the change is considered to be major. You must report such changes as a prior approval supplement (PAS) consistent with 21 CFR 601.12(b).
 - d. If the revised flow charts are implemented using a process that differs from that in section VI.B, the change is considered to be major. You must report such changes as a prior approval supplement (PAS) consistent with 21 CFR 601.12(b).

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Contains Nonbinding Recommendations

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APPENDIX

SCIENTIFIC RATIONALE AND FURTHER EXPLANATION FOR THE RECOMMENDATIONS

The scientific basis and further explanation for the recommendations in section IV of this guidance are as follows:

- The recommendation for a 3-year deferral of a donor following residence in a malaria-endemic country (recommendations B.2. and B.3.b.) is based on the possible presence of low-grade parasitemia in individuals with clinical immunity to malaria, or with a chronic malaria infection who have not received definitive treatment after departure from the malaria-endemic area. Although it is not known how long parasitemia can last in such persons, it is believed that most (though not all) will either develop clinical malaria or else resolve their infection over time. This is because anti-malarial immunity is thought to wane in the absence of repeated infections. Data reported by CDC showed that out of 4,229 reported cases of malaria in foreign-born residents, only 7 cases (0.2%) had an episode of clinical malaria more than three years after the patient had left a malaria-endemic country (Ref. 3). These data suggest that a deferral period of 3 years would be adequate for resolution of parasitemia in most cases. This recommendation will be reconsidered periodically based on new scientific data.
- Recommendation B.3.a of a 1-year deferral period for a donor who is a resident of a non-endemic country and who has traveled to or through a malaria-endemic area (whether or not the donor received malaria prophylaxis), is based on the malaria surveillance reports by CDC showing that out of 2,167 imported malaria cases reported between 2008-2010 for which the date of arrival and the onset of illness was known, only 2 (0.09%) experienced clinical malaria more than 1 year after their return to the U.S. (Refs. 14-16). The 1-year deferral for residents of non-endemic countries applies to the last departure from the endemic area.
- Blood centers should use the new definition of malaria-endemic area (see section III of this guidance) in deciding whether a donor had traveled to a malaria-endemic area.

Based on the current epidemiological data and the definition of malaria-endemic area in this guidance, FDA does not currently recommend deferral of donors who have traveled to the Mexican states of Quintana Roo and Jalisco; thus, these donors, if otherwise eligible, may donate. Please note that the designation of malaria-endemic areas in Mexico or in any malaria-endemic country and accordingly, a recommendation for donor deferral, are subject to change based on the most updated malaria transmission information with respect to that area, as listed in *The Yellow Book*. For example, if malaria transmission in these states changes and anti-malarial chemoprophylaxis is recommended by CDC, then the donor deferral recommendations would encompass donors who travel to these areas.

- The recommendation for a one year deferral from the time of return to a non-endemic country of a donor who was a prior resident of a malaria-endemic country and who

Contains Nonbinding Recommendations

had not traveled to a malaria-endemic area for 3 consecutive years preceding the most recent travel to a malaria-endemic area (recommendation B.3.c.) is based on information indicating that continued exposure to malaria parasites is necessary to maintain clinical immunity (Refs. 17, 18). Consequently, we believe it is a reasonable safeguard to assume that after 3 or more continuous years of residence in a non-endemic country, the majority of prior residents of malaria-endemic areas will not maintain their clinical immunity. Thus, after 3 years of continued residence in a non-endemic country, a prior resident of a malaria-endemic country may be treated as a resident of a non-endemic country. Such individuals should be deferred for only 1 year after each return from travel to a malaria-endemic area consistent with the deferral for travelers from non-endemic countries.

- In many parts of the world, transmission of malaria and dengue can occur in the same area. FDA is aware that under the new definition of a malaria-endemic area, potentially eligible donors may have traveled to areas where dengue virus is transmitted. FDA is currently evaluating the risk of dengue virus infections in blood donors that are acquired either locally or elsewhere in the world, and may address this issue in future guidance.
- The recommendation that consignee notification include instructions for notification of the transfusion recipient or the transfusion recipient's physician of record regarding the need for monitoring of the recipient for a possible malaria infection for a period of 3 months post-transfusion (recommendation C.2.) is based on the analysis of incubation periods in 57 cases of transfusion-transmitted malaria in the U.S., in which the maximum period observed between transfusion and onset of clinical symptoms was 90 days (range 8 to 90 days) (Ref. 3). This recommendation is limited to the highest risk circumstance of unintentional release of a unit from a donor at risk of malaria, namely a unit from a donor who had a clinical history of malaria who may not have been treated or who failed to be deferred for at least 3 years.
- The recommendation to allow the use of acellular blood components inadvertently collected from a donor who was later determined to be at risk for malaria to make injectable products is based on the knowledge that licensed plasma derivatives do not transmit malaria. In addition, notification of consignees is not recommended and reporting of biological product deviation is not required for acellular components inadvertently collected and distributed from a donor at risk for malaria because of the lack of a documented case of transfusion-transmitted malaria from acellular blood components. According to a CDC surveillance study (Ref. 3), 93 cases of transfusion transmitted malaria were reported in the U.S. from 1963-1999. Among the 70 cases for which information was available, the following blood components were implicated: whole blood (63%); red cells (31%); and platelets (6%). Plasma components were not shown as a source of transfusion-transmitted malaria.