Revised Recommendations to Reduce the Risk of Transfusion-Transmitted Malaria

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Guidance for Industry

This guidance is for immediate implementation.

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 https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances or https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders.

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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Preface

Public Comment

Given the public health emergency related to COVID-19 declared by the Department of Health and Human Services (HHS), this guidance is being implemented without prior public comment because FDA has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C)(i) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

Comments may be submitted at any time for Agency consideration. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to https://www.regulations.gov. All comments should be identified with the docket number FDA-2000-D-0187 (formerly Docket No. 2000D-1267) and complete title of the guidance in the request.

Additional Copies

Additional copies are available from the FDA webpage titled "Coronavirus Disease 2019 (COVID-19)," *available at* https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders, and the FDA webpage titled "Search for FDA Guidance Documents" available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

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Questions

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

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Contains Nonbinding Recommendations

Revised Recommendations to Reduce the Risk of Transfusion-Transmitted Malaria

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 revised guidance document provides you, blood establishments that collect blood and blood components, with FDA's recommendations to reduce the risk of transfusion-transmitted malaria (TTM). The recommendations contained in this guidance apply to the collection of Whole Blood and blood components, except Source Plasma. Blood establishments are not required to assess Source Plasma donors for malaria risk (see 21 CFR 630.15(b)(8)).

This guidance supersedes the guidance dated August 2013 and updated August 2014, entitled, "Recommendations for Donor Questioning, Deferral, Reentry and Product Management to Reduce the Risk of Transfusion-Transmitted Malaria" (Notice of Availability, 78 FR 50421 (August 19, 2013)).

The recommendations in this revised guidance reflect the Agency's current thinking on recommendations for reducing the risk of TTM. Based on the Agency's careful evaluation of the available scientific and epidemiological data on malaria risk, and data on FDA-approved pathogen reduction devices, FDA expects implementation of these revised recommendations will not be associated with any adverse effect on the safety of the blood supply. Furthermore, early implementation of the recommendations in this guidance may help to address significant blood shortages that are occurring as a result of a current and ongoing public health emergency. In particular, there is currently an outbreak of respiratory disease caused by a novel coronavirus. The virus has been named "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19). On January 31, 2020, HHS issued a declaration of a public health emergency related to COVID-19 and

mobilized the Operating Divisions of HHS.[1] In addition, on March 13, 2020, the President declared a national emergency in response to COVID-19.[2]

As a result of this public health emergency, there is a significant shortage in the supply of blood in the United States, which early implementation of the recommendations in this guidance may help to address (even though the recommendations in this guidance are broadly applicable beyond the COVID-19 public health emergency). For this reason, this revised guidance is being implemented without prior public comment because FDA has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C)(i) of the FD&C Act and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

Because this revised guidance is being issued without prior public comment in light of the COVID-19 public health emergency, it is intended to remain in effect for the duration of this public health emergency, including any renewals made by the HHS Secretary in accordance with section 319(a)(2) of the Public Health Service Act (42 U.S.C. 247d(a)(2)). However, as noted, FDA expects that the recommendations set forth in this revised guidance will continue to apply outside the context of the current public health emergency. Therefore, within 60 days following the termination of the public health emergency, FDA intends to revise and replace this guidance with an updated guidance that incorporates any appropriate changes based on comments received on this guidance and the Agency's experience with implementation.

In general, 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.

II. BACKGROUND

Malaria is a mosquito-borne parasitic infection caused by *Plasmodia* species (*P. falciparum; P. malariae; P. ovale;* or *P. vivax*), which can also be transmitted by transfusion of blood and blood components collected from an infected but asymptomatic donor (Refs.1-6). Malaria was eradicated in the United States (U.S.) in the 1950s, although the *Anopheles* mosquito vector exists in many states. Locally-acquired mosquito-borne transmission has caused 63 small outbreaks (ranging from 1-32 malaria cases) since 1957 in the U.S., predominantly caused by *P. vivax*. The last cases were reported in 2003 (Ref. 6). In contrast, malaria affects millions of people worldwide. *Plasmodia* infections can be asymptomatic or can range in severity from a

[1] Secretary of Health and Human Services Alex M Azar, Determination that a Public Health Emergency Exists. Jan. 31, 2020. (Accessible at https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx).
[2] President Donald J. Trump, Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19). Mar. 13, 2020. (Accessible at https://www.whitehouse.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/).

mild febrile illness to life-threatening complications or death. *Plasmodium falciparum* causes the most severe disease and accounts for 90% of the malarial deaths in sub-Saharan Africa (Refs. 4-6).

TTM rarely occurs in the U.S. but remains a serious concern in transfusion medicine (Refs. 1-3). The transfusion risk stems from asymptomatic blood donors with newly-acquired or chronic malaria infection, which can be indolent and persist for years. The risk of TTM is currently estimated at less than 0.1 per million red blood cell (RBC) transfusion, or about 1 case every 2 years (Ref. 7). Whole blood or RBC components are implicated in most (94%) TTM cases, with the remainder caused by platelet components (Ref. 2). Plasma components have not been a source of TTM (Ref. 2).

Since 1994, FDA has recommended deferral of blood donors who have had malaria or have had possible exposure to malaria during travel to or residence in malaria-endemic countries. There is no FDA licensed test to screen blood donors in the U.S. The donor deferral policy as previously implemented, likely prevented cases of TTM but also resulted in a significant loss of otherwise eligible donors (Refs. 7-9). The risk of malaria among returning travelers is low in the U.S. About 28 million U.S. residents travel to a malaria-endemic country each year. U.S. residents account for most (70%) of the approximately 2,000 imported malaria cases each year, while non-U.S. residents account for the rest (30%) of the cases (Refs. 6, 7). Former residents of malaria-endemic countries are more likely to have asymptomatic infections when they return from travel to malaria-endemic areas because of likely prior exposure and persistence of clinical immunity to malaria (Refs. 10, 11). Between 2000 and 2017, the reported TTM cases (n=11) in the U.S. have implicated asymptomatic infected donors who were former residents of malaria-endemic countries or who had a prior diagnosis of malaria; none have been linked to a traveler who was a resident of a non-endemic country (Refs. 1, 3). Consequently, the deferral of thousands of prospective donors each year for travel to malaria-endemic countries is disproportionate to any associated risk of TTM (Refs. 9, 12). To minimize donor loss, several non-endemic countries (e.g., England, Australia, and France) use antibody testing to qualify donors who have malaria risk factors (Refs. 3, 8).

FDA held a scientific workshop in 2006 and Blood Product Advisory Committee (BPAC) meetings in 2008 and 2009 to discuss strategies to minimize donor loss associated with deferrals for malaria risk (Refs. 13, 14). In 2008, the BPAC considered different scenarios and the possible role that antibody testing could play in identifying or reentering donors at risk for malaria, especially those donors who had traveled to endemic areas in Mexico (Ref. 15). The BPAC concluded that additional risk analyses would be needed, and that the analyses should account for malaria risk globally and in Mexico, with and without antibody testing.

In 2009, the BPAC supported allowing blood collection, without any deferral for malaria risk, from U.S. residents who have visited the Mexican states of Quintana Roo, which includes Cancun and Cozumel (Ref. 16). At the time, these states contributed to the preponderance of malaria-risk-associated donor deferral for travel to Mexico but posed an extremely low risk to the blood supply. The risk was estimated as an absolute increase of 0.0166 infected blood unit per year, or one TTM case in 60 years, if prospective blood donors who visited Quintana Roo and Jalisco were allowed to donate blood without any deferral. Conversely, the change in

deferral criteria was projected to increase the donor pool by approximately 45,000 donors (79,000 blood units) each year (Refs. 9, 16). In addition to supporting blood collection without any deferral for malaria risk from U.S. residents who have visited Quintana Roo, the BPAC also supported extending the proposed policy to other malaria-endemic states of Mexico that have a low malaria transmission rate (Ref. 16). FDA incorporated the recommendations of the BPAC into guidance, first released in June 2012.

In 2014, FDA approved pathogen reduction devices that demonstrate effective reduction of *Plasmodium falciparum* for plasma or platelet components.

This guidance provides revised recommendations to reduce the risk of TTM, as summarized in the appendix and described in section IV below. The appendix also includes a summary of the scientific rationale for these revisions.

III. DEFINITIONS

The following definitions, which are offered for the purpose of this guidance only, provide explanations of terms used in the recommendations (section IV of this guidance), below:

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 responsible physician.

Malaria-endemic area - Any areas with malaria where the Centers for Disease Control and Prevention (CDC) recommends anti-malarial chemoprophylaxis in travelers in 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 https://wwwnc.cdc.gov/travel/page/yellowbook-home-2014.

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.

IV. RECOMMENDATIONS

The recommendations in this guidance for screening blood donors for malaria risk and for implementing pathogen reduction of indicated blood components are based on the current epidemiological data on malaria and the risk of TTM, and on the availability of FDA-approved pathogen reduction devices.

A. Donor History Questionnaire

1. We recommend that you update your donor history questionnaire, including the full-length and abbreviated donor history questionnaires, and accompanying materials as necessary to incorporate the recommendations provided in this document. You must update your standard operating procedures to reflect any such changes (21 CFR 606.100(b)).

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 three months; 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

1. Travel to a malaria-endemic area by residents of non-endemic countries

We recommend that you defer for 3 months 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, irrespective of whether the donor received malaria chemoprophylaxis. We recommend that after the 3-month 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.

Alternatively, the Director of the Center for Biologics Evaluation and Research (CBER) is providing an alternative procedure under 21 CFR 640.120(b) to the provisions in 21 CFR 630.10(a) and (h). Specifically, under this alternative procedure, you may collect platelet and/or plasma components from a donor who is a resident of a non-endemic country and who has traveled to or through a malaria endemic-area without a deferral period, provided the blood components are pathogen-reduced using an FDA-approved pathogen reduction device effective against *Plasmodium falciparum*, according to the manufacturer's instructions for use, and the donor meets all other donor eligibility criteria.

2. Prior residence in a malaria-endemic country

We recommend that you defer for 3 years a donor who had been a prior resident (as defined in section III of this guidance) in a malaria-endemic country. We recommend that 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. Note that the Director of CBER has not authorized pathogen reduction as an alternative procedure to the 3-year deferral for such donors.

3. Travel to a malaria-endemic area by prior residents of a malaria-endemic country

   a. 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*. We recommend that 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. Note that the Director of CBER has not authorized pathogen reduction as an alternative procedure to the 3-year deferral for such donors.

   b. We recommend that if a prior resident of a malaria-endemic country returns to a malaria-endemic area after residence for *3 or more years consecutively* in non-endemic countries, that you defer that donor for 3 months from the time that they return to the non-endemic country. We recommend that after the 3-month 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.

Alternatively, the Director of CBER is providing an alternative procedure under 21 CFR 640.120(b) to the provisions in 21 CFR 630.10(a) and (h). Specifically, under this alternative procedure, you may collect platelet and/or plasma components from a donor who is a prior resident of a malaria-endemic country who returns to a malaria-endemic area after residence for 3 or more years consecutively in non-endemic countries without a deferral period, provided the blood components are pathogen-reduced using an FDA-approved pathogen reduction device effective against *Plasmodium falciparum*, according to manufacturer's instructions for use, and the donor meets all other donor eligibility criteria.

4. History of malaria

We recommend that you defer for 3 years a donor who has a history of malaria. We recommend that after the 3-year deferral period, the donor may be eligible to donate, provided the donor has been free from malaria during this period while residing in a non-endemic country and meets all other donor eligibility criteria. Note that the Director of CBER has not authorized pathogen reduction as an alternative procedure to the 3-year deferral for such donors.

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 (e.g., RBCs, platelets) 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.4. of this guidance, we recommend that you notify consignees to retrieve and quarantine the in-date cellular blood components collected from that donor.

   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.1-3. 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 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 blood components they may be released for research.

2. 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"

V. IMPLEMENTATION OF RECOMMENDATIONS

You may adopt 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 changes to their approved license to FDA in accordance with 21 CFR 601.12.

1. Licensed blood establishments that revise their DHQs and accompanying material must report the change to FDA in a Changes Being Effected (CBE) Supplement

under 21 CFR 601.12(c)(5) (see 21 CFR 601.12(a)(3)). The blood and blood components collected using the change may be distributed immediately upon receipt of the supplement by FDA.

Include the following information in your CBE Supplement:

a. Form FDA 356h "Application to Market a New or Abbreviated New Drug, or Biologic for Human Use"

b. Cover letter describing the request and contents of the supplement

c. The DHQ and accompanying document(s). Please highlight the modifications.

2. Licensed blood establishments that implement a revised version of the DHQ and accompanying materials prepared by the AABB Donor History Task Force or the Plasma Proteins Therapeutic Association (PPTA) found acceptable by FDA must report the changes to FDA in an annual report under 21 CFR 601.12(d), noting the date the process was implemented.

3. Unlicensed establishments are not required to report this change to FDA.

VI. REFERENCES

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APPENDIX

Table: Comparison of Recommendations in 2013 (Updated 2014) and 2020 Guidance

Donor History	Recommendations for Donor Deferral or Pathogen Reduction (PR) August 2013 Guidance (Updated August 2014)	Recommendations for Donor Deferral or Pathogen Reduction (PR) 2020 Guidance
Travel to a malaria-endemic area (resident of a non-endemic country)	1 year	3 months or PR
Resident of a malaria-endemic country	3 years	3 years
Travel to a malaria-endemic area (resident of a malaria-endemic country) – less than 3 consecutive years in non-endemic country	3 years	3 years
Travel to a malaria-endemic area (resident of a malaria-endemic country) – 3 or more consecutive years in non-endemic country	1 year	3 months or PR
Diagnosis of malaria	3 years	3 years

SCIENTIFIC BASIS FOR RECOMMENDATIONS

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

A. Travel to malaria endemic area by residents of a non-endemic country

- A new recommendation in this guidance (March 2020) changes the 12-month deferral period to a 3-month 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). The recommendation is based on the malaria surveillance reports by CDC showing that out of 3,696 imported malaria cases reported between 2014-2016 for which the date of arrival and the onset of illness was known, 86% (3,187) developed clinical symptoms

within 1 month of return to the U.S. and 94% (3,476) developed clinical symptoms within 3 months (Refs. 4-6). The-3-month deferral for residents of non-endemic countries applies to the date of the last departure from the endemic area.

- Based on the definition in section III of this guidance of "travel to a malaria endemic area" and epidemiological data on malaria risk, FDA does not currently recommend deferral of donors who have traveled to the Mexican states of Quintana Roo and Jalisco. Please note that the designation of malaria-endemic areas in Mexico or in any malaria-endemic country is 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.

- FDA has approved pathogen reduction devices that demonstrate effective reduction of *Plasmodium falciparum* for plasma or platelet components, when used according to their instructions for use. Under the alternative procedure issued by the Director of CBER, such devices can be used as an alternative to donor deferral and allow collection of components from otherwise-eligible donors who are residents of malaria non-endemic countries and have traveled to a malaria-endemic area.

B. Prior residence in a malaria-endemic country

- The recommendation for a 3-year deferral of a donor following residence in a malaria-endemic country, which has not changed from the version of this guidance issued in 2013, is based on the possible presence of low-grade parasitemia in individuals with clinical immunity to malaria, or in individuals 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 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 residents born in a malaria-endemic country, 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. 2). These data suggest that a deferral period of 3 years is adequate for resolution of parasitemia in most cases.

- The Director of CBER has not authorized pathogen reduction as an alternative procedure to the 3-year deferral for such donors because of the higher potential risk of malaria.

C. Travel to a malaria-endemic area by prior residents of a malaria-endemic country

- The recommendation for a 3-year deferral after a visit to a malaria-endemic area for 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, which has not changed from the version of this guidance issued in 2013, is based on the possible presence of low-grade parasitemia in individuals with clinical immunity to malaria, or in individuals with a chronic malaria infection who have not received definitive treatment after departure from the malaria-endemic area.

Note that the Director of CBER has not authorized pathogen reduction as an alternative procedure to the 3-year deferral for such donors because of the higher potential risk of malaria.

- A new recommendation in this guidance (March 2020) changes the 12-month recommended deferral to a 3-month recommended 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 had not traveled to a malaria-endemic area for *3 or more consecutive years* preceding the most recent travel to a malaria-endemic area. This is based on information indicating that continued exposure to malaria parasites is necessary to maintain clinical immunity (Refs. 10-11). Consequently, we believe it is a reasonable safeguard to conclude 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, we recommend that after 3 years of continued residence in a non-endemic country, a prior resident of a malaria-endemic country may be considered to be a resident of a non-endemic country for purposes of screening blood donors. We recommend that such individuals should be deferred for 3 months after each return from travel to a malaria-endemic area consistent with the deferral for travelers from non-endemic countries.

  Under the alternative procedure issued by the Director of CBER, pathogen reduction devices can be used as an alternative to donor deferral for this group of donors.

D. Product retrieval and consignee notification

The recommendation that consignee notification include instructions for notification of 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 (section IV.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. 2). This recommendation is limited to the highest risk circumstance, namely transfusion of a unit from an ineligible donor who had a clinical history of malaria who should have been deferred for at least 3 years.