



American Red Cross

National Headquarters

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

9284 00 SEP -6 P122

**RE: Guidance for Industry: Recommendations for Donor Questioning
Regarding Possible Exposure to Malaria [Docket No. 00D-1267, 65 Fed. Reg.
36452 (June 8, 2000)]**

Dear Docket Officer:

The American Red Cross (ARC/Red Cross) wishes to thank the Food and Drug Administration (FDA) for the opportunity to comment on the draft guidance regarding: *Recommendations for Donor Questioning Regarding Possible Exposure to Malaria*

Since our ability to solicit and collect blood from our volunteer donors is an integral part of the effort to supply almost 50 percent of the nation's blood needs, ARC is pleased to participate in the public comment process on a guidance that will directly impact our interactions with potential blood donors.

The attached set of comments describe more fully ARC's concerns and recommendations. Our main points include the following:

- The addition of new donor questions, particularly questions that have not been validated, may have an effect opposite to that intended since they may result in unnecessary deferral of donors who do not pose a health risk, and perhaps by accepting donors who may pose a health risk.
- ARC believes that deferring donors who have entered non-risk areas of countries containing malaria-risk areas will unnecessarily expand the number of deferrals. ARC recommends that FDA base the deferral policy only on consideration of whether the donor actually entered the specific part of the country designated as a "risk" area.
- ARC recommends that FDA further clarify its deferral policies. We make this request to avoid potential misunderstandings that are likely to arise when different blood banks interpret the current draft differently from FDA investigators and from each other. Further clarification will also aid blood facilities who are likely to encounter potential donors who have made numerous trips and/or spent extensive time throughout the world.

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- ARC also recommends that FDA provide more precise definitions of such terms as "travel" and "residence" as well as the terms "endemic country," "area" and "risk area." We believe that such precision will aid compliance with the deferral clarification requested above.
- Clarification of the deferral policy will eliminate the need for including specific questions in the final Guidance. Blood facilities can then determine the best course of action to meet the guidance's requirements.
- Finally, we urge FDA to recognize the serious nature of this deferral policy. Even with greater clarification, more unnecessary donor deferrals may occur, which would have an impact on the availability of the blood supply. Thus, it is imperative that FDA revise the draft policy and reissue it for further review prior to final release. Moreover, if FDA is not persuaded that additional donor questions are unnecessary, we urge that the Agency first validate new questions before incorporating them into the guidance itself.

Thank you for the opportunity to review and comment on this draft guidance. It is our hope that with clear and complete instructions, the intent of the FDA in terms of donor acceptance following potential malaria exposure can be accurately and consistently applied across all donor programs. If you have any questions regarding this letter, please feel free to contact Dr. Linda Chambers, Senior Medical Officer at 703-312-5610, or Anita Ducca, Director, Regulatory Relations at 703-312-5601.

Sincerely,

Anita T. Ducca
for
Glenn Mattei, Esq.
Interim Vice President
Quality Assurance
and Regulatory Affairs

Attachment

**Comments by The American Red Cross on the FDA Draft Guidance:
Recommendations for Donor Questioning
Regarding Possible Exposure to Malaria
[Docket No. 00D-1267, 65 Fed. Reg. 36452 (June 8, 2000)]**

THE AMERICAN RED CROSS

Each year, the American Red Cross (ARC or Red Cross) collects, processes, and distributes approximately 6 million units of whole blood, representing almost half the nation's blood supply. Blood collection for transfusion is conducted throughout the nation by 36 regional Red Cross blood centers, utilizing several hundred registered auxiliary collection sites, and daily mobile collection sites throughout the community. The Red Cross processes units of whole blood into specific components such as red blood cells, platelets and other products that are distributed to over 3,000 hospitals in the United States.

All collections are from volunteer donors who make personal sacrifices to help provide these life-saving products to patients who need them.

OVERARCHING CONCERNS

Given the dependence on our donors for ensuring the availability of blood and blood products, the first concern we wish to discuss is FDA's recommendation to include additional questions on the blood donor questionnaire. Currently, there are 39 questions on the ARC blood donor questionnaire that an individual must answer before they may be considered as a donor. As we have indicated previously,¹ there is an increasing concern that with each question added to the donor questionnaire, ARC and other blood collection facilities may find that more questions:

- Weaken the value of the questionnaire as a screening tool due to the donor's reduced ability to assimilate and, therefore, accurately answer the numerous questions, and
- Diminish our ability to solicit donors who must take time from their busy schedules to voluntarily provide blood for this critical national need.

Moreover, the draft guidance's questions, as worded, will not provide the information to collection facilities that is needed to reach an acceptance or deferral decision.

The question "Were you born in the United States?" raises particularly serious concerns. A donor who is fearful of any form of authority discovering his or her immigration status may deliberately provide an untruthful answer to evade a potential investigation. Thus, instead of identifying donors potentially at risk of exposure, this question may inadvertently *encourage* them to hide their background, where an alternative approach would not. Other donors may be

¹ See, for example, testimony by Dr. Rebecca Haley, Senior Medical Officer, American Red Cross Biomedical Services, before the Xenotransplantation Subcommittee of the Biological Response Modifiers Committee on FDA's Draft "Guidance for Industry: Precautionary Measures to Reduce the Possible Risk of Transmission of Zoonoses by Blood and Blood Products from Xenotransplantation Product Recipients and Their Contacts" January 13, 2000.

offended by a question that they perceive as inappropriate for a volunteer donor, particularly if the donor is a member of a minority group. Similarly, donor offense may result in their unwillingness to donate at a future time.

Even if the above sensitivities were not a concern, it will be possible for a donor to be born in the United States, but move to a risk area shortly thereafter. Such donors could be at greater risk than, say, a donor born outside of the U.S. but not in a malaria-risk area, but who moved to the U.S. for the remainder of their life. Families of U.S. Military personnel are an example of donors who may experience these exposure situations.

A second overarching concern is the potential for a substantial number of donors to be unnecessarily deferred based on recommendation III.3. of the draft guidance. Many donors may reside in "endemic countries" but never visit a "risk area." Consider for example, donors from Mexico who visit blood centers in the Southwestern part of the United States. Such donors may have recently resided in North Mexico but never visited malaria areas (for example, the Yucatan Peninsula) and deferral would be unnecessary.

An additional concern is that the draft guidance does not clearly define the terms used, including the difference between "travel" and "residence". For example, it is not clear whether the 5-year period that establishes residency needs to be a continuous interval and how travel during that 5 year period does or does not affect the designation as a resident. Similarly, the critical terms "endemic country," "area" and "risk area" stated in FDA's malaria deferral policy are not defined and appear to be used interchangeably. As a result, the guidance's questions are unlikely to solicit the kind of information needed to make an appropriate acceptance/deferral decision.

Thus, ARC recommends that FDA reconsider the current draft and prepare revisions based on the discussion below.

FUNDAMENTAL DEFERRAL POLICY

ARC's first recommendation is that FDA reconsider the deferral policy, particularly with respect to donor's travel/residence location. Specifically, we recommend that the deferral policy pertain only to those who travel or reside in the *specific geographic location* where an exposure risk may occur. This is a particularly important concept since a country may have malaria areas, but that does not mean that everyone who visits anywhere within that country has been in a risk area.

The example above of donors from Mexico describes the case where donors could easily enter or live in a country containing a risk area, but never enter the risk area itself. We would not wish to exclude these individuals as potential donors based on the country (rather than the area) from which they came.

We also recommend that FDA clarify the concept of "exposure" for purposes of constructing a deferral policy. From our reading of the draft guidance, we understand that FDA

intends blood centers to evaluate certain features of a donor's type of visit and the location as a surrogate for an exact assessment of their exposure. The surrogate information for malaria exposure used to determine the proper deferral period, includes:

- (1) the potential for exposure based on the donor's presence in a particular geographic area (as defined by CDC's maps/criteria),
- (2) the duration of the potential exposure, and
- (3) the interval between the potential exposure and the proposed donation.

ARC agrees that using these factors as the basis for a deferral policy will result in appropriate and effective donor eligibility determinations.

TERMS AND DEFINITIONS

In order to accurately and consistently use the surrogate exposure indicators, it will be important that the regulatory terminology and definitions be clear. In the draft guidance, terms such as "area" and "country" are used interchangeably, and the descriptions "endemic area", "endemic country", "malarious area" and "malaria-risk region" are used. We suggest the use of the single term, "risk area", which we define as follows:

- **Risk Area:** the individual subsection/locality/city defined as malaria-risk by the most recent edition of the CDC's Health Information for International Travel (Yellow Book).

ARC urges using this single term to be consistent with our earlier recommendation, i.e., to avoid deferring a donor just because they happened to have entered a country containing a locality where risk of exposure is possible, but did not enter the actual risk area. Other benefits of using only one term include streamlining development of Standard Operating Procedures (SOPs) and training for collection staff. Thus, the use of a single term will greatly simplify our ability to comply with the guidance. Further, it will go a long way to standardize deferral practices throughout the blood collection community and as a result, help avoid the potential for a donor to go from blood bank to blood bank seeking one that will allow them to donate.

Should FDA believe that they must expand the terms used in the guidance, we recommend one additional term "Country with a Malaria-Risk Area," defined as follows:

- **Country with a Malaria-Risk Area:** a country with **any** areas that have malaria risk according to the most recent edition of the CDC's Health Information for International Travel (Yellow Book).

By these definitions, many countries have both risk and non-risk areas. In some cases, the entire country may be a risk area, but the risk areas are not necessarily the entire country.

Equally important is the guidance's reference to "travel" and "residence". Additional clarification is needed. For example, there is no indication as to whether the five-year period that establishes a person as a "resident" is to be a continuous five-year period without a break or

whether travel outside of the malaria-risk area during that time frame can "restart the clock." We suggest the following definitions:

- **"Resident," "Residence" or "Lived In":** presence in a country a majority of each year (e.g. 10 months or longer) for 5 years (60 months) or more consecutively.
- **Travel:** presence in a country for less than 5 years (60 months) consecutively or for the lesser part of a year (e.g., less than 10 months).

CRITERIA

Donor eligibility criteria could then be defined for each possible combination of visit type (travel or resident) and location type (risk area) and using the definitions above. Based on our reading of the draft guidance, some of these possible combinations are addressed, but for others, the intent of FDA in terms of donor eligibility is not clear. This is our recommended reading of the instructions in the current guidance draft, combined with our previous recommendations for deferral policy and definitions:

DEFERRAL POLICY

<i>Visit type</i>	<i>Location type</i>	<i>Acceptance/deferral decision</i>
<i>Travel</i>	Risk area, donor was <u>not</u> previously a resident of a malaria-risk area	Defer 1 year from end of travel
<i>Travel</i>	Risk area, donor <u>was</u> previously a resident of a malaria risk area	Defer 3 years from end of travel or residence (whichever results in the longer deferral)
<i>Resident</i>	Risk area	Defer 3 years from end of residence

QUESTIONNAIRE

We recommend that the final guidance focus on a set of deferral criteria, such as those above, but without a set of mandated questions. As long as the appropriate deferral takes place, it should not be of concern how or where the questions are added. If FDA believes it must include questions, we urge the Agency to revise the questions. The specific questions suggested in the draft guidance do not properly categorize a donor who is born in a non-risk area, moves and resides in a risk area, then returns to a non-risk area to donate within 3 years of travel back to the risk area. Basically, the hierarchy of the questions in the draft assumes that a person born in the USA has never been a resident of a malaria-endemic country, and this assumption may not be valid.

ARC believes that FDA should also validate any questions required or suggested in the guidance. We believe this is a fair expectation for two reasons.

- First, if a blood bank finds that donors misunderstand a question required by FDA, they may not eliminate or modify the question without a variance or until FDA changes the guidance. Each of these actions can be a lengthy process. In the meantime, donors who should not be donating may be inadvertently included, or donors who are acceptable may be deferred. Neither outcome is desirable and both compromise the safety and availability of the blood supply.
- Second, ARC believes that as FDA enacts guidances and policies that reduce the available pool of donors and potentially reduce the availability of the blood supply, the Agency has a greater burden of proof for demonstrating that the new requirements effectively improve blood safety. We believe that it is the Agency's obligation to help ensure that while in the process of decreasing one form of safety risk (potential malarial-infectious transfusion), it does not amplify another (blood shortage).

IMPLEMENTATION

Given that not every situation can be defined in a guidance document, we urge the FDA to consider adopting the following policy for implementation of these donor eligibility criteria:

- Provide blood centers with flexibility to implement the guidance. We recommend that the final guidance focus on a set of deferral criteria, such as those above, but without a set of mandated questions. Allow the donor centers to determine the most appropriate and least disruptive means for compliance with the deferral criteria.
- After evaluating the public comments and revising the draft guidance, re-propose the draft guidance for public comment. ARC urges this revision due to the very tenuous availability of the blood supply. A policy that may result in reducing the availability of the blood supply, and that may change substantially prior to finalization, should be subject to additional, comprehensive public review to ensure full comprehension, and minimal disruption of donor solicitation prior to finalization.

Again, the American Red Cross appreciates the opportunity to express its views. If you have any questions regarding this attachment, please contact Dr. Linda Chambers, Senior Medical Officer at 703-312-5610, or Anita Ducca, Director, Regulatory Relations at 703-312-5601.