July 14, 2015

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

Submitted via http://www.regulations.gov

Re: Docket No. FDA-2015-D-1211 "Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products," draft guidance.

Dear Dockets Manager:

We appreciate the opportunity to provide comments to the Food and Drug Administration on the draft guidance titled "Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products" The top priorities of the blood banking community are the safety of recipients of blood transfusions and the provision of useful, understandable information to donors to that end. We have long held that a recommendation to change the current indefinite deferral for men who have had sex with men (MSM) to a 12-month deferral would align the donor deferral period for MSM with criteria for other activities that may pose a similar risk of transfusion-transmissible infections, would maintain current levels of safety and would make sense to blood donors. We commend the FDA for taking this step forward and for providing a pathway for previously deferred donors to give blood.

The Federal Register Notice that accompanied the draft guidance requested comments on signs and symptoms associated with HIV that would be most appropriate for inclusion in the donor education materials, as the draft guidance does not provide such a list. We continue to object to a recommendation that donors be provided with education materials that list, "the signs and symptoms associated with HIV infection…," as stated in **Section III. Recommendations. A. Donor Education Material and Donor History Questionnaire. 1.**, and strongly recommend that this not be included in the final guidance.

8101 Glenbrook Road
Bethesda, MD 20814-2749
301.907.6977 MAIN
301.907.6895 FAX
www.aabb.org

The signs and symptoms of HIV in the current FDA accepted AABB DHQ donor education materials are:

- Unexplained weight loss or night sweats;
- Blue or purple spots in your mouth or skin
- Swollen lymph nodes for more than one month;
- White spots or unusual sores in your mouth;
- Cough that won't go away or shortness of breath;
- Diarrhea that won't go away;
- Fever of more than 100.5 F for more than 10 days.

These are nonspecific and insensitive for the intended purpose— identification of HIV infected donors— and largely redundant when donors are asked and required to be well on the day of donation.

Prior to the 1985 advent of HIV testing and the evolution of ever more sensitive and specific serological tests and nucleic acid amplification assays, this recommendation was eminently reasonable—there were few alternatives except this information and risk factor deferrals available to mitigate HIV risk. However, they are no longer relevant under the current testing regime.

Donors with advanced immunodeficiency from HIV (i.e. AIDS) will be reactive in one or both screening approaches – serological test and NAT. Under current GMP procedures, erroneous release of reactive donations is no longer an issue. Donors with acute retroviral syndrome, in the process of seroconverting, have positive NAT tests. They have only non-specific signs and symptoms (not likely to be included in the list above) that have a low positive predictive value for the presence of HIV infection. Further, in order for donors to be deemed eligible to donate they must respond affirmatively to the explicit question "are you feeling well and healthy today?" and must have a normal temperature.

In the current draft guidance, the agency does not cite any literature to document the effectiveness of eliciting signs and symptoms of HIV/AIDS in promoting blood safety in the current environment. The final rule published May 22, 2015, "Requirements for Blood and Blood Components Intended for Transfusion or for Further Manufacturing Use," provides citations regarding this information (references 6,7,8,31,32 and 33) [I]. After review of these citations, they provide no primary data to support any assumed increment of transfusion safety from HIV transmission by providing donors signs and symptoms of HIV infection.

Most donors have limited motivation to read pre-donation materials, and this issue is frequently compounded by low literacy levels. This results in skim reading and poor attention[II, III,IV] . These signs and symptoms are not specific for HIV infection but, more importantly, their sheer volume is distracting from more critical education needed by donors. The latter includes new information being developed to apprise donors of risks from iron depletion, a growing list of unacceptable medications, a more structured effort to educate donors about risks and responses to donor vasovagal reactions, and efforts to improve donor's provision of accurate responses to risk behavior questions.

Finally, the amendments to the Code of Federal Regulations included in the final rule require that the educational materials [630.10 (b)] provide "an explanation of the readily identifiable risk factors closely associated with exposure to the relevant transfusion-transmitted infection."

Elsewhere in the same section is a clarification that HIV is the relevant transfusion-transmitted infection to which this requirement applies. The requirement in the Final Rule is for "risk factors" not "signs and symptoms" in the educational materials. The FDA-accepted AABB Donor Educational Materials do contain risk factors for HIV. Further, new 630.10(e) describes how to conduct the medical history interview with a requirement in (1)(iii) to capture any information the donor provides that would be "Signs and/or symptoms of a relevant transfusion-transmitted infection." As mentioned above, the AABB Donor History Questionnaire (DHQ) requires the donor to affirm feeling well and healthy. Additionally, a temperature must be recorded.

To summarize, we believe a continued recommendation to provide donors with signs and symptoms of HIV infection is obsolete, nonspecific, and no longer relevant under the current testing regime. Further, it is distracting in the face of a growing volume of more important information that donors should integrate before donation.

Comments to specific recommendations in the guidance document are arranged in the following format:

Section – language from draft guidance reprinted.
Recommendation or Request for Clarification – recommendation or clarification request.
Rationale/Supporting Information – rationale in support of the recommendation /clarification request.

Section – II. Background.

F. Status of Other Deferral Categories.

In the case of the deferral for persons with hemophilia or related clotting disorders who have received clotting factor concentrates, the rationale for deferral has changed from prevention of HIV transmission to that of ensuring that donors are not harmed by the use of large bore needles used during the donation process. While 21 CFR 640.3(c)(3) currently requires deferral for receipt of any derivative of human blood which the FDA has advised is a possible source of viral hepatitis, given the enhanced safety measures now used in the manufacture of clotting factor concentrates (Ref. 16), FDA does not consider the receipt of FDA-licensed clotting factor concentrates to be a risk factor for hepatitis. Further, FDA has not recommended a deferral for the receipt of other FDA-licensed plasma-derivatives because of HIV or hepatitis risk, and we intend to consider revisions to the current regulations.

Recommendation – We recommend that the guidance be finalized with this update as written.

Rationale – The update to the guidance is congruent with the Final Rule mentioned above. Also, the AABB Donor History Task Force (DHTF) is updating the FDA-accepted DHQ in accordance with the draft recommendation.

Section – III. Recommendations.

A. Donor Education Material and Donor History Questionnaire

Given the passage of time, and in order to simplify practical application of these criteria for donors and blood collection establishments, reference to "since 1977" present currently for some criteria has been dropped as the period of time during which individuals are assessed to be at risk of transmitting HIV.

Recommendation – We recommend that the guidance be finalized with this sentence as written.

Rationale – The AABB DHTF is updating the FDA-accepted DHQ in accordance with the draft recommendation.

Section – III. Recommendations.

A. Donor Education Material and Donor History Questionnaire.

1. …We recommend that donors be provided donor education material before each donation explaining the risk of HIV transmission by blood and blood products, certain behaviors associated with the risk of HIV infection, and the signs and symptoms associated with HIV infection, so that donors can self defer.

Recommendations –The recommendation regarding the signs and symptoms of HIV infection should be deleted.

Rationale – See above

Section – III. Recommendations.

A. Donor Education Material and Donor History Questionnaire

3. We recommend that the updated DHQ include the following elements to assess donors for risk:

i. A history ever of a positive (footnote 4) test for HIV.

Footnote 4: In this context, "positive" includes positive test results on an HIV diagnostic assay and repeatedly reactive or reactive results on antibody or NAT blood donor screening assays, respectively.

Recommendation – The footnote should include that a donor who has successfully completed a reentry program can reply "No" to this question.

Rationale – This is an ongoing problem. The FDA has previously provided personal communication on the subject and should now formalize the information in a guidance document.

Section – III. Recommendations.

A. Donor Education Material and Donor History Questionnaire

3. We recommend that the updated DHQ include the following elements to assess donors for risk:

iv. A history in the past 12 months of sex with a person with a positive test for HIV, a history of exchanging sex for money or drugs, or a history of non-prescription injection drug use

Recommendation – Footnote 4 added to the guidance to support element i. (In this context, "positive" includes positive test results on an HIV diagnostic assay and repeatedly reactive or reactive results on antibody or NAT blood donor screening assays, respectively) should be expanded to allow this donor to be eligible unless the sexual contact had a confirmed positive test for HIV or has not had a negative confirmatory test result.

Rationale – There are few cases these days when HIV positive or reactive test results are not reflexed to confirmatory testing. Updating the footnote as recommended will allow donors to continue to donate if their partners have not received confirmed positive test results.

Section – III. Recommendations.

A. Donor Education Material and Donor History Questionnaire

3. We recommend that the updated DHQ include the following elements to assess donors for risk:

ix. For male donors: a history in the past 12 months of sex with another man

Recommendation – We support this update to the 1992 memorandum and recommend that the guidance be finalized with this element as stated.

Rationale – The update aligns the donor deferral period for MSM with criteria for other activities that may pose a similar risk of transfusion-transmissible infections. In addition, the AABB Donor History Task Force (DHTF) is updating the FDA-accepted DHQ in accordance with the draft recommendation.

Section – III. Recommendations.

A. Donor Education Material and Donor History Questionnaire

3. We recommend that the updated DHQ include the following elements to assess donors for risk:

x. For female donors: a history in the past 12 months of sex with a man who has had sex with another man

Recommendation – This element to assess donors for risk should be written as **"**For female donors: a history in the past 12 months of sex with a man who has had sex with another man in the past 12 months."

Rationale – The final recommendation should clarify that the period of evaluation for the sexual contact between the two males is the 12 months prior to the sexual contact the female had with the male. It appears to be inferred in the requalification criteria but should be clear in the assessment elements.

Section – III. Recommendations.

A. Donor Education Material and Donor History Questionnaire

Note: In the context of the donor history questionnaire, male or female gender is taken to be self-identified and self-reported. In instances where a donor has asserted a change in gender identification, medical directors may exercise discretion with regard to donor eligibility.

Recommendation – We recommend that the guidance be finalized with this Note as written.

Rationale – We appreciate that the agency has previously addressed gender identification at AABB FDA Liaison Committee meetings and find it an especially relevant addition to the guidance.

Section – III. Recommendations

C. Donor Requalification

6. Male donors previously deferred because of a history of sex with another man, even one time, since 1977, may be eligible to donate provided that they have not had sex with another man during the past 12 months and they meet all other donor eligibility criteria.

Recommendation – We recommend that the guidance be finalized with this requalification criteria as written.

Rationale – The requalification criteria is clear and we appreciate having the information immediately available in the guidance.

Section – III. Recommendations

C. Donor Requalification

7. Male donors deferred because of a history of sex with another man in the past 12 months may be eligible to donate provided they have not had sex with another man during the past 12 months and they meet all other donor eligibility criteria.

Recommendation – We recommend that the guidance be finalized with this requalification criteria as written.

Rationale – The requalification criteria is clear and we appreciate having the information immediately available in the guidance.

AABB is an international, not-for-profit association representing individuals and institutions involved in the field of transfusion medicine and cellular therapies. The association is committed to improving health by developing and delivering standards, accreditation and educational programs that focus on optimizing patient and donor care and safety. AABB membership consists of nearly 2,000 institutions and 8,000 individuals, including physicians, nurses,

scientists, researchers, administrators, medical technologists and other health care providers. AABB members are located in more than 80 countries.

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

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

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

Sincerely,

M. Allene Carr-Greer
Director, Regulatory Affairs

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I. References cited in Final Rule "Requirements for Blood and Blood Components Intended for Transfusion or for Further Manufacturing Use," May 22, 2015

6. FDA, "Guidance for Industry: Implementation of Acceptable Full-Length Donor History Questionnaire and Accompanying Materials for Use in Screening Donors of Blood and Blood Components," October 2006, *http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/ucm073445.htm.*

7. FDA, "Guidance for Industry: Implementation of an Acceptable Full- Length and Abbreviated Donor History Questionnaires and Accompanying Materials for Use in Screening Donors of Source Plasma," February 2013, *http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBlood Products/ApprovedProducts/Licensed ProductsBLAs/BloodDonorScreening/ UCM341088.pdf.*

8. FDA, "Guidance for Industry: Implementation of an Acceptable Abbreviated Donor History Questionnaire and Accompanying Materials for Use in Screening Frequent Donors of Blood and Blood Components," May 2013, *http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatory Information/Guidances/Blood/ ucm351107.htm*.

31. AABB Association Bulletin #03-14, "Deferral for Risk of Leishmaniasis Exposure," October 10, 2003.

32. Bai, N. Donor Fatigue. The Red Cross Has Banned Chronic Fatigue Syndrome Sufferers from Giving Blood. But Does a Virus Really Cause the Disease? Scientific American July 2011;305(1):26.

33. Young, S., A Fink, S. Geiger, et al. Community Blood Donors' Knowledge of Anemia and Design of a Literacy- Appropriate Educational Intervention.Transfusion 2010;50:75-9.

II. O'Brien SF, Osmond L, Choquet K, Yi QL, Goldman M. Donor attention to reading materials. Vox Sang 2015, DOI:10.1111/vox.12298.

III. Rugege-Hakiza SE, Glynn SA, Hutching ST, et al. Do blood donors read and understand screening educational materials? Transfusion 2003;43:1075-83.

IV. National Center for Education Statistics: *http://nces.ed.gov/fastfacts/display.asp?id=69* (Accessed June 12, 2015).