



BILLING CODE: 4150-41P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

**Request for Information (RFI) on Design of a Pilot Operational Study to Assess
Alternative Blood Donor Deferral Criteria for Men Who Have Had Sex with Other Men
(MSM)**

AGENCY: Department of Health and Human Services, Office of the Secretary, Office of the Assistant Secretary for Health.

ACTION: Notice.

SUMMARY: The Department of Health and Human Services (HHS) is seeking to identify interest and obtain information relevant to the design of a pilot operational study (or studies) on alternative donor deferral criteria that would permit blood and plasma donations (subsequently termed “blood donations”) by men who have had sex with other men (MSM).

Based upon documented higher levels of certain transfusion-transmissible infections (e.g. Human Immunodeficiency Virus (HIV) and Hepatitis B Virus (HBV)) in some groups of men who have had sex with men, all men with a history of this behavior since 1977 are currently deferred from donating blood. However, the increased effectiveness of donor testing for HIV, HBV, syphilis and other infectious agents has greatly enhanced blood safety. As a result, questions have been raised about the need to continue an indefinite deferral of all MSM and whether there could be blood donation by MSM who may not be at increased risk.

In June 2010, HHS sought advice from its Advisory Committee for Blood Safety and Availability (ACBSA) on the issue of the current MSM deferral policy. The Advisory Committee noted that the existing policy is suboptimal, but recommended that the policy should be retained pending the completion of targeted research studies that might support a safe alternative policy.

HHS and the agencies responsible for blood safety are committed to efforts to maintain and enhance the safety of the nation's blood supply, taking into account all new and emerging scientific information. Consistent with the June 2010 recommendations of the ACBSA, HHS seeks to determine through appropriate studies whether blood safety can be maintained or enhanced under revised blood donor screening criteria that would permit donation by some MSM. This request for information (RFI) is being issued in recognition of the challenges of designing such studies.

This RFI seeks information from interested parties regarding the design, logistics and feasibility of a pilot operational study (or studies) to assess alternative blood donor eligibility criteria for MSM. Responses to this RFI will inform HHS on the design, logistics and feasibility of such a study, which, if feasible, could result in identifying potential pathways toward future alternate policies that will maintain or enhance the current very high levels of blood safety. The concept is to conduct a pilot operational study, in which MSM who meet specified criteria would be permitted to donate blood, with additional safeguards in place to protect blood recipients during the course of the study. Data would be gathered to assess the effectiveness of the specified criteria to select low risk donors among MSM. Upon

completing all data collection activities, there will be a transparent and evidence-based evaluation of current and possible future MSM blood donation policies.

This RFI is for information and planning purposes only and should not be construed as a solicitation or as an obligation on the part of HHS. HHS does not intend to award a grant or contract to pay for the preparation of any information submitted or for the use of such information by HHS. Whereas all responses to this notice will be carefully considered, acknowledgment of receipt of responses will not be made, nor will respondents be notified of the evaluation by HHS of the information received. No basis for claims against HHS shall arise as a result of a response to this request for information or to the use of such information by HHS as either part of our evaluation process or in developing specifications for any subsequent announcement.

DATES: All responses must be received no later than 4 p.m. EDT on **[INSERT DATE 90 DAYS AFTER THE DATE OF PUBLICATION IN THE FEDERAL REGISTER]** at the address listed below.

ADDRESSES: You may submit comments identified by docket ID number HHS-OPHS-2012-0003, by one of the following methods:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Enter the above docket ID number in the “Enter Keyword or ID field and click on “Search.” On the next page, click the “Submit a Comment” action and follow the instructions.
- Mail/Hand delivery/Courier [For paper, disk, or CD-ROM submissions]: Richard Henry, M.L., M.P.H., Office of the Assistant Secretary for Health, U.S. Department of Health

and Human Services, 1101 Wootton Parkway, Tower Building, Suite 250, Rockville, MD 20852.

Comments received, including any personal information, will be posted without change to <http://www.regulations.gov>.

FOR FURTHER INFORMATION CONTACT: James Berger, Acting Director for Blood Safety and Availability, Office of the Assistant Secretary for Health, Office of the Secretary, U.S. Department of Health and Human Services, 1101 Wootton Parkway, Tower Building, Suite 250, Rockville, MD 20852.

SUPPLEMENTARY INFORMATION:

General Blood Safety Strategy

Current high levels of safety of the US blood supply are provided by five overlapping layers of protection. These include:

- First, potential donors are provided educational materials and also asked specific questions about their health, and about risk factors for certain transfusion-transmissible diseases (i.e., medical, behavioral and travel-related risks), as a basis for acceptance or deferral.
- Second, the donated blood is tested for evidence of transfusion transmissible infections by highly sensitive laboratory assays. These include tests for infections which can be acquired through high risk sexual behaviors including HIV, HBV, and/or syphilis.

- Third, blood establishments must keep a current list of individuals who have been deferred as donors in order to prevent future collection or use of their blood.
- Fourth, blood products are quarantined until the testing is completed and the donation records have been verified for suitability of the collections.
- Fifth, blood establishments must investigate any breaches of these safeguards, correct system deficiencies, and maintain records for FDA review.

Rationale for Current Deferral Policy for MSM

Deferral of potential donors prior to donation combined with highly sophisticated and sensitive laboratory testing of donated blood are among the multiple overlapping safeguards currently in place to protect the blood supply. Of particular concern for blood safety are infections known to be transmissible by blood transfusion, including HIV and HBV. Deferral of MSM from donation of blood is based on well-documented observations of a markedly higher prevalence¹ (current infection) and incidence² (newly acquired infection) of these transmissible agents among some MSM than in the non-MSM general population. Additionally, there is a theoretical concern that persons at increased risk for known sexually transmitted diseases might also be at increased risk to acquire sexually and blood transmitted infections that may emerge in the future and for which no donor screening tests exist.

The risk of infection from a blood transfusion is now extremely low (less than one in one million units transfused for HIV and less than one in 280,000 units transfused for HBV). These risks

¹ <http://www.cdc.gov/hiv/surveillance/resources/reports/2009report/index.htm>

² Prejean J, Song R, Hernandez A, Ziebell R, Green T, Walker F, Lin LS, An Q, Mermin J, Lansky A, Hall HI; HIV Incidence Surveillance Group. Estimated HIV Incidence in the United States, 2006-2009. PLoS One. 2011;6(8):e17502. Epub 2011 Aug 3

have diminished dramatically in the past three decades as a result of the overlapping safeguards. From recently published modeling studies, transfusion-transmitted infections, while rare, are now generally attributed to the interplay of three factors: 1) failure of donor selection measures to accurately defer an at-risk donor, either by deficiencies in the donor screening process or failure of a donor to provide accurate answers; 2) donation by an infected individual during the “window period” when early infection cannot yet be detected by current testing; and 3) inadvertent release of a donated unit of blood a) before all testing is known to be negative; b) before other criteria affecting blood safety and quality are determined to have been met; or c) despite a positive screening test or other finding of unsuitability (Quarantine Release Errors or QRE).

Reconsideration of MSM Deferral Policy

There have been advisory committee meetings³ and a public workshop⁴ over the past decade, which have reexamined the deferral policy, taking into account existing scientific evidence related to deferral of MSM from blood donation. In addition, there has been increased interest in changing this policy from some members of the U.S. Congress, the public and interested advocacy groups.

³ Blood Products Advisory Committee held September 14, 2000
<http://www.fda.gov/ohrms/dockets/ac/cber00.htm#Blood%20Prducts>

Advisory Committee on Blood Safety and Availability held June 10-11, 2010
http://www.hhs.gov/ash/bloodsafety/advisorycommittee/recommendations/msm-deferral_ga_20110722-final.pdf

⁴ FDA Workshop on Behavior-Based Donor Deferrals in the NAT Era held March 8, 2006
<http://www.fda.gov/downloads/BiologicsBloodVaccines/NewsEvents/WorkshopsMeetingsConferences/TranscriptsMinutes/UCM054430.pdf>

Most recently, in June 2010, the HHS ACBSA⁵ heard presentations of currently available scientific data and recommended to the HHS Secretary that the current MSM deferral policy, while suboptimal, should be retained pending the completion of targeted research studies that might support a safe alternative policy. Based on these recommendations, the Assistant Secretary for Health charged relevant agencies to develop and carry out such studies, including a pilot operational study of revised deferral criteria for MSM.

A public workshop was conducted and three funded studies are in progress to help re-evaluate the MSM deferral policy:

1) Workshop on Quarantine Release Errors (QREs):

FDA convened a workshop in September 2011 to better understand and find ways to prevent errors in quarantine management that could lead to inappropriate release of blood (QREs). While only a very low proportion of QREs present serious health threats, QREs continue to occur, both in community based and hospital based blood collection establishments. It was determined that human error during non-computerized operations frequently contributes to the QREs that occur. As a result of the workshop, AABB is establishing an industry-led task force to study the QRE issue, to identify best practices, and to propose additional interventions. In particular, application of human factor engineering will be brought to bear in a review of blood banking practices to better optimize the interface between human and automated steps as a way to improve process controls. The output of the task force will be

⁵Advisory Committee on Blood Safety and Availability held June 10-11, 2010
http://www.hhs.gov/ash/bloodsafety/advisorycommittee/recommendations/msm-deferral_ga_20110722-final.pdf

used by government agencies to establish guidance on best practices in quarantine control of blood components.

2) Study on the Epidemiology of Transfusion-Transmissible Infections in U.S. Blood

Donors:

An analysis of data on the prevalence and incidence of certain major transfusion-transmissible infections (e.g. HIV, HBV, and Hepatitis C Virus (HCV)) obtained from routine donation testing of blood donors was initiated in 2011. This study will provide baseline estimates of the current risks of transfusion-transmitted viral infections in the U.S. blood supply. Additionally, the current risk factors (including heterosexual) reported by infected donors and their relative prevalence compared to other donors as controls will be determined, thus providing information as to which risk factor(s) should be targeted by optimized donor screening strategies. This study is supported by the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH) and is being conducted as part of the second Retrovirus Epidemiology Donor Study (REDS-II). This study includes the American Red Cross, Blood Systems, Inc., and the New York Blood Center which together are responsible for collecting approximately 60 percent of the U.S. blood supply.

3) Study on Evaluation of the current Blood Donation History Questionnaire (DHQ):

Several factors, including culture, social conditions, and language fluency, contribute to different interpretations of the questions that comprise the current blood donation screening questionnaire. A study to assess donor understanding and interpretation of the DHQ screening questions (cognitive evaluation) was conducted approximately ten years ago by the

National Center for Health Statistics of the Centers for Disease Control and Prevention (NCHS, CDC). Because techniques for questionnaire evaluation have advanced considerably over the past decade, the HHS Office of the Assistant Secretary for Health funded NCHS, CDC to re-evaluate the DHQ, with particular emphasis on donor understanding of the behavioral risk questions intended to prevent transmissible infections. This study will help determine whether the existing MSM deferral questions are understood and properly interpreted by donors. It may also determine more effective ways to communicate with at-risk populations through donor questions.

4) Study on the Attitudes and Behaviors of MSM Toward the Blood Donation Screening Process:

Blood donors must accurately assess their individual risk(s), and then self-defer from donation or disclose their risk(s) for the current screening process to effectively maintain blood safety. Failure to self-defer or disclose risk after a potential exposure to a transfusion-transmissible infection may result in the collection and release of an infectious blood donation, which may be associated with a false negative laboratory test during early infection (the “window period”). For this reason, it is important to evaluate whether MSM with increased risk would reliably self-defer or disclose risks if permitted to donate under revised selection criteria. A study funded by the Food and Drug Administration (FDA) and being carried out by the NHLBI REDS-III program will assess attitudes and behaviors of MSM toward current and possible future blood donation policies. This study is specifically

designed to examine whether MSM comply with the current deferral criteria and whether MSM would be likely to comply with potential different deferral criteria.

Information Requested

HHS is interested in obtaining information about the design, logistics and feasibility of a pilot operational study to assess alternative blood donor acceptance criteria for MSM.

Specifically, HHS requests information from private and public sector stakeholders regarding potential pilot operational study designs, including innovative and cost effective approaches to evaluate alternative blood donor acceptance criteria for MSM.

Input is requested for the following:

- 1) Candidate acceptance criteria for a pilot operational study that would permit blood donation by MSM. For example, MSM with one year or five years of abstinence from sex with other men, or other criteria, subject to study designs with additional safeguards.
- 2) Possible study designs that would generate useful information regarding the safety of candidate acceptance criteria while maintaining current levels of blood safety during the pilot study. Possibilities might include **but are not limited to the following:**

a) Pre-donation Donor Testing

In a pre-donation testing strategy, MSM who are presently deferred, but who would be eligible to donate during the pilot operational study under modified acceptance criteria would be screened for donation with the candidate modified criteria and have a blood

sample drawn for standard donor screening⁶, and potentially, additional tests at their first session in a blood collection center. They would not be permitted to donate a unit of blood at that time. MSM donors who meet all other donor eligibility criteria, and have negative pre-donation test results, would be invited to return within a defined period, at which time standard donor screening and testing would be performed and blood for use in transfusion would then be collected.

A pre-donation testing strategy would focus on the prevalence of HIV and other transfusion-transmissible infections in the MSM population. Infected donors would be identified and deferred based on prescreening results. Quarantine release errors (QREs) would be avoided, because infectious units would not be drawn and entered into inventory.

Unanswered questions regarding a pre-donation testing option include: 1) the added costs of donor testing if provided by the collection center; 2) the added cost and complexity of tracking the results of pre-donation testing; 3) the period within which a potential MSM donor would need to return to complete an actual blood donation; 4) concern that pre-donation testing of only MSM could be seen as discriminatory; and 5) the residual impact on safety due to window period donations that would not be reduced by pre-testing.

b) Post-Donation Testing

⁶ Current tests include Antibody to HIV-1 and -2 (Anti-HIV-1, -2), HIV-1 RNA (HIV-1 NAT), Antibody to HCV (anti-HCV), HCV RNA (HCV NAT), Antibody to HTLV-I and -II (Anti-HTLV-I/II), Hepatitis B Surface Antigen (HBsAg), Antibody to Hepatitis B Core Antigen (Anti-HBc), West Nile Virus RNA (WNV NAT), Antibody to *Trypanosoma cruzi* (Chagas' disease), and a serologic test for syphilis

In a post-donation testing strategy, MSM who are presently deferred, but who would be eligible to donate during the pilot under modified deferral criteria would have a unit of blood drawn. This unit would be segregated from other units and placed in a separate quarantine. The donor would be asked to return for “post-donation testing” within a specified period following the donation that would exceed the "window period" for transfusion-transmissible infections but be within the expiration dating period of the unit of blood (i.e., within 14 to 42 days post-donation for red blood cells or from 14 days to within one year for plasma for transfusion). For donors who continue to meet acceptance criteria and have negative "post-donation test" results, the unit would be released for transfusion. Such collections would be most applicable to repeat plasma donations given the longer shelf life of frozen plasma, providing greater flexibility for the time of “post-donation testing” of the donor. Also, plasma for transfusion could be collected at the time of “post-donation testing” initiating a new quarantine for a new collection.

Placing units drawn from MSM donors in quarantine until qualifying "post-donation testing" results are obtained would address the issue of recent (i.e. “incident”) infections. Infectious units would be entered into a quarantine portion of the blood bank inventory prior to the availability of screening test results. However, if more infectious units are drawn and placed in inventory, these units would be subject to quarantine release errors

There could be the same or similar unanswered questions for the post-donation testing strategy as are outlined above under the pre-donation testing strategy. In addition, blood establishments would need to maintain stratified and potentially larger quarantine inventories and would incur the costs of discarding all units in quarantine for which a donor failed to return for "post-donation testing."

c) Combined Pre-Donation and Post-Donation Testing

Under this scenario, an MSM donor seeking to donate under modified deferral criteria would be screened with a questionnaire and asked to give a pre-donation testing sample. Assuming the blood sample is negative for infectious markers, and the donor meets all other eligibility criteria, the donor would be invited to return within a defined period to donate a unit of blood. This unit would be placed in quarantine and the donor again would be asked to return, this time for post-donation testing also within a specified time period.

This strategy would provide the strictest control over any increase in risk to the blood supply. Both incident and prevalent infection concerns would be addressed. However, this scenario would require a potential donor meeting the candidate MSM acceptability criteria to make three appearances at a blood collection facility within specified time periods in order to have a donation released for transfusion. Blood establishments would face challenging logistic issues in conducting such a study concurrently with normal, highly standardized blood collection operations.

3) Input is requested on the data that should be gathered and the criteria used to evaluate the results of the pilot operational study. For example, should MSM donors and non-MSM donors be asked to participate in surveys on their understanding of the donor screening questions, their specific sexual behaviors and their motivations to donate blood? Should the study outcome be based on observed markers of transfusion-transmitted infections in MSM donors compared with other donors? Should MSM donors with positive screening tests be interviewed to better understand their risk factors, their understanding of the donor questionnaire and their motivations to donate if they did not appropriately self-defer or disclose their risk?

Requested RFI Responses:

Please comment on each of the above scenarios, or propose additional pilot operational study designs for consideration. In your response, please address each of the following:

- Revised criteria that should be considered to permit blood donation by MSM
- Blood safety considerations and safety mitigations that should be considered
- Impact on blood establishment operations
- Staff training and staff perceptions
- Tracking of pre-donation and/or post- donation test results
- Inventory management
- Donor perceptions regarding the possible changes in deferral policy within the operational study scenarios (including both MSM and non-MSM donors)
- Public reaction, if any, and impact on blood drives
- Potential venues where the study could be conducted
- Study costs

- Willingness of blood organizations to participate in a pilot study
- Data elements that should be gathered during the study, including those that may be associated with future emerging infections
- Criteria for evaluation of the study results and conclusions
- Expected timeframe for each proposed study.

DATED: March 8, 2012

Richard Henry

Deputy Director, Blood Safety & Availability

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