Summary of Responses to FDA Docket Opened July 26, 2016: Blood Donor Deferral Policy for Reducing the Risk of HIV Transmission by Blood and Blood Products

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Blood Products Advisory Committee Meeting
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Overview

- Present FDA's current recommendations to reduce the risk of HIV transmission through blood and blood products
- Review the rationale for the recent change to the deferral policy for men who have sex with men (MSM)
- Summarize comments to the public docket opened July 2016 regarding HIV deferral policies
- Share progress on the Transfusion-Transmissible Infections Monitoring System (TTIMS)
- Briefly discuss FDA's future plans

FDA's Current Recommendations

- *Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Components; Guidance for Industry* (December 2015)
- Replaced 1992 Memorandum to Blood Establishments
- Applies to the collection of blood and blood components, including Source Plasma
- Provides FDA's revised recommendations for donor educational materials, donor questioning, deferral, and requalification, as well as blood product management

FDA's Current Recommendations

- Indefinite deferral for history of positive HIV test; exchanged money for sex; injection drug use
  - 12 month deferral for history of sex with an individual having this history
- 12 month deferral for allogenic blood transfusion; blood exposure through needle stick; tattoo, ear or body piercing*
- 12 month deferral following treatment or diagnosis of syphilis or gonorrhea
- 12 month deferral for men who have had sex with another man
  - 12 month deferral for a woman who has had sex with a man having this history

*Except if the tattoo was applied by a state regulated entity with sterile needles and non-reused ink or the piercing was done using single-use equipment.

Revisiting Indefinite Deferral of MSM

- Since testing for HIV first became available in 1985, there have been calls for revising the blood donor deferral policy
- In June 2010 the HHS Advisory Committee on Blood Safety and Availability recommended that the current donor deferral policies are suboptimal, but that "available scientific data are inadequate to support change to a specific alternative policy..." and the Committee recommended research to inform a possible policy change
- Subsequently, the PHS Blood, Organ and Tissue Safety Working Group designed and implemented one operational assessment and three research studies to help inform potential policy change

Data Informing Policy Change

A number of different lines of evidence supported a policy change

- Quarantine Release Error (QRE) Task Force assessment
- Donor History Questionnaire Study
- Retrovirus Epidemiology Donor Study-II (REDS-II)Retrovirus and Hepatitis Virus Rates and Risk Factors Study
- Recipient Epidemiology & Donor Evaluation Study-III (REDS-III) Blood Donation Rules Opinion Study (BloodDROPS)
- Australian experience over 5 years before and 5 years after a change to a 1 year deferral

Recent History of Revised Policy - I

- Results of completed studies were presented to the HHS Advisory Committee for Blood and Tissue Safety and Availability (ACBTSA) in November 2014
  - Voted 16 to 2 to recommend a policy change to a one year MSM deferral
  - Recommended the establishment of a robust system to monitor the safety of the blood supply
  - Recommended a communication plan on the policy change targeted to all stakeholders
- Outcome of the ACBTSA meeting was summarized at the FDA Blood Products Advisory Committee in December 2014
- FDA announced that it would consider a change to a one year deferral policy for MSM in December 2014

Recent History of Revised Policy - II

- FDA issued draft guidance with recommendations for reducing the risk of HIV transmission by blood and blood products in May 2015
  - About 750 comments to the docket
  - Approximately evenly divided between calls for FDA to go further to a shorter deferral or move to individual risk assessment and calls for FDA to leave the policy unchanged
- FDA determined that the best available evidence supported a change to a 12 month deferral for MSM and implementation of the transfusion transmissible infections monitoring system (TTIMS)
- FDA issued final guidance in December 2015

Plans for Further Work on Policy

- When FDA announced the revised blood donor deferral policy in December 2015 it also noted a commitment to continuing to further evaluate and potentially progress policies based upon available scientific evidence
- Collaboration is anticipated with other government agencies and with stakeholders to consider whether emerging scientific evidence and information gained from TTIMS support alternative strategies to time-based behavioral deferrals
  - One strategy to be further explored includes evaluation of use of individual risk assessment questionnaires for all blood donors

Establishment of Public Docket

- Published Federal Register notice in July 2016
- Established a public docket (FDA-2016-N-1502)
  - https://www.regulations.gov/docket?D=FDA-2016-N-1502
- Requested comments, supported by scientific evidence, regarding potential blood donor deferral policy options to reduce the risk of HIV transmission
  - Alternatives to time-based deferral policies and feasibility of individual risk assessment strategies
  - Design of potential scientific studies on feasibility and effectiveness of alternative deferral options
- Posed six questions addressing deferral policies based individual risk assessment

Questions Posed in Public Notice - I

1. What questions would most effectively identify individuals at risk of transmitting HIV through blood donation?
2. Are there specific questions that could be asked that might best capture the recent risk of a donor acquiring HIV infection, such as within the 2 to 4 weeks immediately preceding blood donation?
3. How specific can the questions be regarding sexual practices while remaining understandable and acceptable to all blood donors? For example, could questions about specific sexual behaviors be asked if they helped to identify which donors should be at least temporarily deferred because of risk factors? To the extent the questions are explicit about sexual practices, how willing will donors be to answer such questions accurately?

Questions Posed in Public Notice - II

4. Under what circumstances would a short deferral period for high risk behavior be appropriate? For each short deferral period identified, please specify the duration of the deferral and provide the scientific rationale.
5. What changes might be necessary within blood collection establishments to assure that accurate, individual HIV risk assessments are performed?
6. How best to design a potential study to evaluate the feasibility and effectiveness of alternative deferral options such as individual risk assessment?

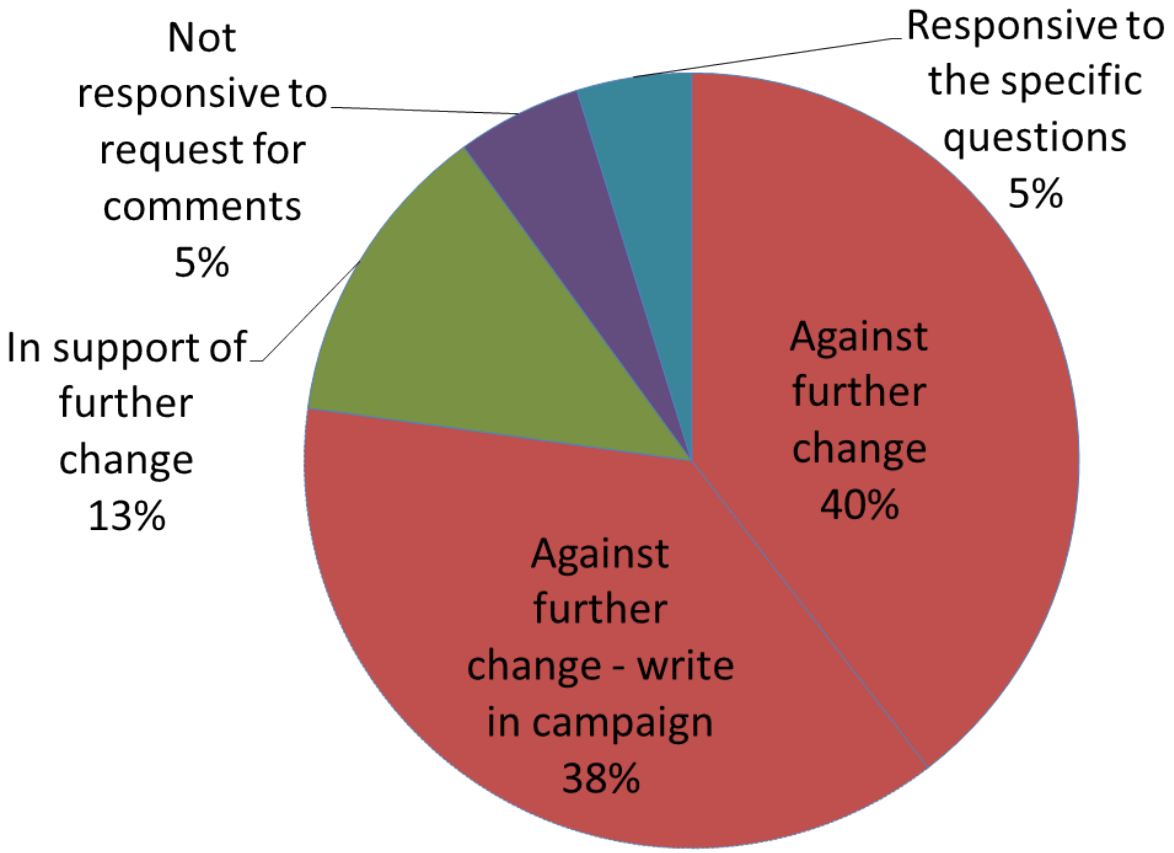
Summary of Comments Received - I

- The docket was opened on July 26, 2016, and closed on November 25, 2016
- A total of 670 non-duplicative responses were received from a variety of stakeholders
  - Individuals
  - Blood donors
  - Advocacy groups
  - Academic and research institutions
  - Health care providers, including HIV physicians
  - Local and state governments, including health departments
  - Medical associations
  - Blood product recipients
  - Blood collection industry and device manufacturers

Summary of Comments Received - II

- The 670 responses can be categorized as follows
  - Against further change in the deferral policy 517
    (252 appear linked to a single write-in campaign)
  - In support of further change in the deferral policy 86
    (includes one petition with 300 signatures)
  - Not responsive to the request for comments 35
  - Responsive to the specific questions 32

Summary of Comments Received - III



Summary of Public Responses to Notice - I

- The policies suggested cover a broad spectrum from no further change (or return to an indefinite deferral) to no deferral for low-risk MSM and a 2 to 3 week deferral for MSM determined to be high-risk
- Multiple commenters noted the need for an improved donor questionnaire for all donors that more accurately assesses risk
  - Note was made about the need for privacy and the potential benefit of electronic responses or specially trained staff
- Several commenters called for continued improvement in donor testing technology to reduce the window period or for the implementation of pathogen reduction technology for blood components

Summary of Public Responses to Notice - II

- Some commenters suggested additional interventions by blood collection establishments
  - Implement rapid HIV test and counsel high risk donors at blood centers
- Responses included a wide range of recommendations
  - Simple versus complex set of questions on the donor history questionnaire for risk assessment
  - One set of questions for all donors versus a customized approach to donor questioning
  - Varying definitions of high-risk MSM activity
- A cross-section of commenters concluded that data are not yet available to evaluate the recent change to a 12 month deferral for MSM

Summary of Public Responses to Question 1

1. What questions would most effectively identify individuals at risk of transmitting HIV through blood donation?
   - Extend questions to all donors
   - Ask questions on monogamy, unprotected sex, new sexual partners, sexual partners of unknown or positive HIV status, specific sexual practices, injection drug use
   - Model questions based on risk index tools developed for health care providers to identify MSM at high risk of HIV
     - Address certain risk factors in last 6 months to one year, such as number of partners, episodes of unprotected sex, use of methamphetamines

Summary of Public Responses to Question 2

2. Are there specific questions that could be asked that might best capture the recent risk of a donor acquiring HIV infection, such as within the 2 to 4 weeks immediately preceding blood donation?
   - Ask all donors about monogamy, number of partners and use of safe sex practices; exposure to blood products, tattoos/piercings; certain medical procedures (in past 3 months); injections drugs (in past year)
   - For MSM, new sexual partners in past 8 weeks
   - Stratify high, medium and low-risk groups based on individual risk assessment as basis for deferral period
     - High – injection drug users; commercial sex workers (longer or indefinite deferral)
     - Medium – MSM with multiple male partners, unprotected sex, $\geq$1 HIV positive partners in the past 2-4 weeks (30 day deferral)
     - Low – MSM with consistent condom use and/or pre-exposure prophylaxis (PrEP) (no deferral)

Summary of Public Responses to Question 3

3. How specific can the questions be regarding sexual practices while remaining understandable and acceptable to all blood donors? For example, could questions about specific sexual behaviors be asked if they helped to identify which donors should be at least temporarily deferred because of risk factors? To the extent the questions are explicit about sexual practices, how willing will donors be to answer such questions accurately?

- Yes/no questions with respect to monogamy, new partners and condom use considered acceptable
- All donors should be asked high-risk questions, but questionnaire could be structured to ask MSM specific risk questions
- Specific questions are likely to result in more accurate responses
- Administer questionnaire electronically and privately

Summary of Public Responses to Question 4

4. Under what circumstances would a short deferral period for high risk behavior be appropriate? For each short deferral period identified, please specify the duration of the deferral and provide the scientific rationale.
   - Three month deferral acceptable for new partner without condom use
   - One month deferral for high risk behavior acceptable given the accuracy of NAT testing

Summary of Public Responses to Question 5

5. What changes might be necessary within blood collection establishments to assure that accurate, individual HIV risk assessments are performed?
   - Questioning in private environment
   - Electronic administration of questionnaire
   - Staff training in cultural competency to ask sensitive questions
   - Include option of responding “I don’t know” to discourage guessing

Summary of Public Responses to Question 6 - I

6. How best to design a potential study to evaluate the feasibility and effectiveness of alternative deferral options such as individual risk assessment?
   - Incidence of HIV infection under current deferral policy should be compared to incidence under a new policy
   - Studies should be conducted to assess feasibility and effectiveness of integrating on-site rapid antibody testing at blood collection sites
   - Pilot study with control arm using current eligibility and deferral criteria and intervention arm (recruit potential MSM donors) that would use individual risk assessment questionnaire and 30 day deferral for those at medium risk. Test all donations using current technology to assess risk of increased HIV risk.
     - Study would also pilot whether the individual risk assessment questions are understood and acceptable to potential donors

Summary of Public Responses to Question 6 - II

6. How best to design a potential study to evaluate the feasibility and effectiveness of alternative deferral options such as individual risk assessment?
   - Four-step study to validate screening questions and their effectiveness in identifying individuals at high risk for HIV
     - Collect blood samples from participants that have been asked specific questions about certain risk activities in last one month;
     - Test sample for HIV;
     - Re-test the participant for HIV in one month;
     - Ask follow up questions depending on whether the second test was positive or negative to help evaluate effectiveness of initial questionnaire

Summary of Public Responses to Question 6 - III

6. How best to design a potential study to evaluate the feasibility and effectiveness of alternative deferral options such as individual risk assessment?
   - Staged approach for research to identify and test new criteria:
     - Conduct research to identify low risk MSM through donor questions and assess whether respondents find questions acceptable and comprehensible
     - Conduct research to understand impact of questions on other donors with respect to a) acceptability and b) eligibility (would currently eligible donors may become ineligible with proposed criteria?)
     - Develop method for testing the safety of the new questions, including testing of BECS to validate controls sufficient to prevent cross-over of study and donor population; establish safeguards to permit study populations to donate (e.g. pathogen reduce donations)

Summary of Public Responses to Question 6 - IV

6. How best to design a potential study to evaluate the feasibility and effectiveness of alternative deferral options such as individual risk assessment?

- Highest priority in study design should be to test the efficacy of classifying MSM donors as low or high-risk; data on non-MSM donors desirable
  - Administer questionnaire to MSM and non-MSM subjects to assess low or high risk for recent HIV infections; subjects would provide blood sample for HIV testing by NAT
  - Follow up test performed at one month to identify subjects who converted from NAT negative to NAT positive
    - Conduct analysis on initial samples to determine whether individual was in the window period or whether new infection

Transfusion Transmissible Infections Monitoring System (TTIMS) - I

- CBER/NIH Joint Program for a long-term representative US blood safety monitoring system that provides information on >50% of the US donor base
- Monitoring HIV, HBV, HCV incidence and prevalence
  - Potential for comparison to data collected in REDS-II in 2011-2013
- Evaluating molecular epidemiology and recency of HIV infection
- Assessing behavioral risk factors

Transfusion Transmissible Infections Monitoring System (TTIMS) - II

- Provides framework for rapid data collection to inform blood safety response to new emerging infectious diseases
- May allow for “alert” levels to indicate if potential blood safety intervention is needed
- Facilitates ongoing data availability to objectively assess the value of new blood safety initiatives including changes to donor deferral policies

TTIMS Progress Update

- Donor Database Coordinating Center
  - Central Database - >50% of US blood supply to monitor HBV, HCV, and HIV in US blood donors
    - Consensus test result definitions
    - Validated data exchange
    - Quarterly Data analysis
      - Prevalence (donors)
      - Prevalence (donations)
      - Incidence

TTIMS Progress Update

- Laboratory and Risk Factor Coordinating Center
  - Will conduct risk factor interviews with all donors that test positive for HIV and repeat donors that are newly positive for HBV or HCV
  - Integrate risk factor data with marker data and compare with control interviews
  - Biospecimen repository
    - Test for recency of HIV infection
    - Perform viral genetic sequence analysis (genotype and drug resistance)

Risk Factor Interviews

- Risk factor questionnaire modeled on REDS-II Risk Factor Study interview, with the following enhancements:
  - Transgender categories
  - Employment
  - Monogamy
  - Specific sexual activities
  - Pre- and post-exposure prophylaxis
  - Antiretroviral therapy
  - On-line administration
  - Spanish translation
- Questionnaire currently under review

Summary of TTIMS Blood Safety-Related Outcome Measures

- Anticipated outcome measures will serve to monitor effects of recent policy changes as well as other potential changes in donor epidemiology and help to inform future blood donor policy decisions
  - Prevalence
  - Incidence estimates
    - NAT yield
    - Database repeat donors
    - HIV recency
  - Risk factor interviews

Potential FDA Next Steps

- Assess the impact of FDA's current donor deferral recommendations, including the change to a 12 month deferral period for MSM
- Consider design of alternative donor history questionnaires
- Study the feasibility, effectiveness and operational impact of individual risk assessment strategies for assessing eligibility of all donors

Principles Moving Forward

- Process will be based on gathering the necessary scientific evidence regarding policy change while ensuring the continued safety of the blood supply
  - Epidemiology (infectious disease and behavioral risks)
  - Laboratory science (NAT and pathogen reduction technology)
  - Social science (donor education and questionnaires)
- Will work to maximize transparency of the process through stakeholder engagement and use of public meetings including scientific workshops and advisory committee meetings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