

**FOOD AND DRUG ADMINISTRATION (FDA)
Center for Biologics Evaluation and Research (CBER)
120th Meeting of the Blood Products Advisory Committee**

OPEN PUBLIC MEETING

**FDA White Oak Campus
10903 New Hampshire Avenue
Silver Spring, MD 20993**

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This transcript appears as received from the commercial transcribing service after inclusion of minor corrections to typographical and factual errors as recommended by the DFO.

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1 **CALL TO ORDER AND INTRODUCTION OF COMMITTEE**

2 **DR. KAUFMAN:** My name is Richard Kaufman. I'm
3 the Chair of BPAC. I'd like to welcome members of the
4 committee as well as participants that we'll be hearing
5 from today, members of the public, as well as the
6 audience that may be joining by webcast.

7 Just to start out, I would like to have the
8 members of the committee introduce themselves. Can you
9 please provide your name, institutional affiliation, as
10 well as your expertise? We'll start with Dr.
11 Schreiber.

12 **DR. SCHREIBER:** Martin Schreiber, Oregon
13 Health & Science University, General Surgeon with an
14 interest in novel blood product research.

15 **DR. BLOCH:** Hi. Evan Bloch, the Associate
16 Director of Transfusion Medicine at Johns Hopkins. And
17 my interest is transfusion-transmitted infections.

18 **DR. STAPLETON:** Jack Stapleton, Infectious
19 Disease Professor at University of Iowa. I'm Director
20 of the University Viral HIV Clinic, and my laboratory

1 does HIV flavivirus co-infection work.

2 **DR. DEMARIA:** Al DeMaria. I'm a Medical and
3 Laboratory Consultant at the Massachusetts Department
4 of Public Health in the Bureau of Infectious Disease
5 and Laboratory Sciences, and formally State
6 Epidemiologist for Massachusetts and Medical Director
7 of that bureau.

8 **DR. BRYANT:** I'm Barbara Bryant from the
9 University of Texas Medical Branch in Galveston, Texas.
10 My interest is transfusion medicine. I'm a Transfusion
11 Medicine Medical Director.

12 **MR. TEMPLIN:** Hi, I'm Christopher Templin.
13 I'm the patient rep, personally in Birdsboro,
14 Pennsylvania.

15 **DR. HOLLINGER:** Blaine Hollinger. Baylor
16 College of Medicine in Houston. Professor of Medicine
17 in molecular virology and epidemiology, and interest in
18 bloodborne pathogens.

19 **DR. DEVAN:** Hi, Michael DeVan. I'm the
20 Medical Director for transfusion services at Walter
21 Reed National Military Medical Center.

1 **DR. SHAPIRO:** I'm Amy Shapiro. I'm the
2 Medical Director of the Indiana Hemophilia and
3 Thrombosis Center. My interest is hemostasis and
4 thrombosis and benign hematology.

5 **DR. ORTEL:** Tom Ortel, Chief of Hematology at
6 Duke. My interest is hemostasis and thrombosis.

7 **DR. LEWIS:** Roger Lewis. I'm the Chair of
8 Emergency Medicine at Harbor-UCLA Medical Center in Los
9 Angeles. My interest is in biostatistics clinical
10 trial design.

11 **DR. BASAVARAJU:** Sridhar Basavaraju, Director
12 of the CDC Office of Blood, Organ, and Other Tissue
13 Safety.

14 **DR. KAUFMAN:** And I'm Rick Kaufman. I'm the
15 Medical Director for the Blood Bank at the Brigham and
16 Women's Hospital. My interest is in transfusion
17 medicine.

18 I'd like to also introduce two individuals on
19 the phone. Dr. Stramer, are you there?

20 **DR. STRAMER:** Yes, I am. I'm Susan Stramer.
21 I'm the Vice President of Scientific Affairs at the

1 American Red Cross. My interests are infectious
2 diseases and testing.

3 **DR. KAUFMAN:** And Dr. Chitlur?

4 **DR. ATREYA:** We'll introduce her when she
5 comes.

6 **DR. KAUFMAN:** That's fine. So, at this time,
7 I'd like to ask Dr. Atreya to please read the conflict
8 of interest statement.

9 **CONFLICT OF INTEREST STATEMENT**

10 **DR. ATREYA:** Good morning. This is Prabha
11 Atreya, Designated Federal Officer for the advisory
12 committee. The Committee Management Specialists for
13 this meeting are Ms. Joanne Lipkind and Natalie
14 Mitchell. The Committee Management Officer for this is
15 Marie Keller (phonetic), who assisted in the Conflict
16 of Interest screening and also making travel and/or
17 meeting arrangements. On behalf of FDA and Center for
18 Biologics Evaluation Research and the Blood Products
19 Advisory Committee, we would like to welcome you all.
20 Dr. Judith Baker is the Consumer Rep and she will be
21 here shortly.

1 The press or media person are here, that's
2 Megan McSeveney. She's in the back. Also, Paul
3 Richards in the audience if you have any media
4 questions. I also would like to remind everyone to
5 please check your pagers and cell phones. Please make
6 sure they are either turned off or in silent mode.
7 Also when you make comments, please first state your
8 name and speak up so that your comments are accurately
9 recorded for transcription, and for the benefit of the
10 FDA staff here in the room, and members of the public
11 and those listening via webcast.

12 Now, I'll proceed to read the Conflict of
13 Interest Statement. The Food and Drug Administration
14 is convening today, March 21st, 2019 for the 120th
15 Meeting of the Blood Products Advisory Committee, under
16 the authority of the Federal Advisory Committee Act of
17 1972. Dr. Richard Kaufman is serving as the Chair of
18 the meeting for Topic III.

19 Today, on March 21, 2019, for Topic III, in
20 open session, the committee will discuss blood donation
21 policies regarding men who have sex with men, MSM. The

1 committee will hear an update on donor deferral
2 policies and donor HIV Risk Questionnaire study. Also,
3 an overview of the Transfusion-Transmitted Infections
4 Monitoring System. In addition, the committee will
5 hear presentations and discuss pathogen reduction of
6 platelet donations as an augmented procedure. The
7 topic is determined to be a Particular Matter of
8 General Applicability.

9 Presenters and speakers will provide data on
10 various products or strategies that serve only as
11 examples for the committee to have a scientific
12 discussion while considering various classes or
13 products or strategies related to the topic.

14 This meeting is not being convened to
15 recommend any action against or approval of any
16 specific product or strategy, or to make specific
17 recommendations that may potentially impact any
18 specific party, entity, or individual in a unique way.

19 Similarly, this meeting will not involve
20 approval or disapproval of labeling requirements, post
21 marketing requirements, or related issues regarding the

1 legal status of any specific products and any
2 discussion of individual products will only serve as an
3 example of the product class.

4 With the exception of industry
5 representatives, all participants of the committee
6 around the table are appointed as Special Government
7 Employees, or as regular government employees from
8 other agencies. Hence, they are subjected to federal
9 Conflict of Interest laws and regulations.

10 The following information on the status of
11 this advisory committee's compliance with the Federal
12 Ethics and Conflicts of Interest laws, including but
13 not limited to: 18 U.S. Code 208 is being provided to
14 participants at this meeting and to the public. This
15 Conflict of Interest statement will be available for
16 public viewing at the registration table.

17 Related to discussions at this meeting, all
18 members and SGE consultants of this committee have been
19 screened for potential financial conflicts of interest
20 of their own, as well as those imputed to them,
21 including those of their spouse or minor children and

1 for the purposes of 18 U.S. Code 208 their employers.
2 These interests may include investments, consulting,
3 expert witness testimony, contracts, grants, CRADAs,
4 teaching, speaking, writing, patents, royalties, and
5 primary employment.

6 FDA has determined that all members of this
7 advisory committee are in compliance with Federal
8 Ethics and Conflict of Interest laws. Under 18 U.S.
9 Code 208, Congress has authorized FDA to grant waivers
10 to Special Government Employees and regular government
11 employees who have financial interest conflicts when it
12 is determined that the agency's need for the particular
13 individual's service as a subject matter expert
14 outweighs the concern related to his or her potential
15 conflict of interest. However, based on today's agenda
16 and all financial interests disclosed by members and
17 consultants, no conflict of interest waivers were
18 issued under 18 U.S. Code 208.

19 Dr. Sue Stramer is currently serving as the
20 industry representative to this committee for Topic
21 III. She's Vice President of Scientific Affairs at the

1 American Red Cross. Industry representatives act on
2 behalf of all related industry, and bring general
3 industry perspective to the committee. They are not
4 appointed as special government employees and are non-
5 voting members of the committee. Hence, industry
6 representatives are not screened, and do not
7 participate in the closing sessions, and do not have
8 voting privileges.

9 Dr. Judith Baker is serving as the consumer
10 representative for this committee. Consumer
11 representatives are appointed special government
12 employees and are screened and cleared prior to their
13 participation in the meeting. They are voting-members
14 of the committee, and hence, do have voting privileges.
15 They do participate in the closed sessions if they are
16 held.

17 Mr. Christopher Templin is serving as the
18 Temporary Patient Representative for Topic III of this
19 meeting. He's serving as a member on the board of the
20 Directors of The Committee of Ten thousand. Patient
21 representatives are appointed as special government

1 employees and hence are screened and cleared prior to
2 their participation. They are voting-members of the
3 committee and hence do have voting privileges. They do
4 participate in the closed session if they are held.

5 Dr. Blaine Hollinger serves the committee as a
6 temporary voting member for all topics of the meeting,
7 including today's topic. He's the Director of Eugene
8 B. Casey Hepatitis Research Center, Baylor College of
9 Medicine. And he brings his vast expertise in
10 bloodborne infectious diseases for the benefit of the
11 committee.

12 With regard to external speakers, Dr. John
13 Brooks is employed by the CDC, and serves as one of the
14 speakers for this meeting under Topic III. Dr. Brooks
15 is a regular government employee and has been screened
16 and cleared prior to his participation.

17 At this meeting, there may be other regulated
18 industry speakers or other outside organization
19 speakers making presentations. These participants may
20 have financial interest associated with their employer
21 and with other regulated firms. FDA asks, in the

1 interest of fairness, that they address any current or
2 previous financial involvement with any firms whose
3 product they may wish to comment upon. These
4 individuals were not screened by the FDA for conflict
5 of interest.

6 FDA encourages all of the participants to
7 advise the committee of any financial relationships
8 that they may have with any firms, its products, or if
9 known, the direct competitors.

10 We would like to remind the members and
11 consultants and other participants, that if the
12 discussions involve any of the products or firms not
13 already on the agenda, for which an FDA participant has
14 a personal or imputed financial interest, the
15 participant needs to inform the DFO and exclude
16 themselves from such involvement, and the disclosure
17 will be noted for the record.

18 This concludes the reading of the Conflict of
19 Interest statement for the public record. At this time,
20 I would like to hand over the meeting to Dr. Kaufman.
21 Thank you.

1 policies regarding men who have sex with men, which
2 I'll abbreviate as MSM.

3 In the morning, you'll hear an update on donor
4 deferral policies and a proposal for an HIV Risk
5 Questionnaire study. In the afternoon, you'll hear a
6 proposal for an alternative procedure to donor deferral
7 with the use of pathogen reduction and platelet
8 donations from MSM. I'm going to give a brief history,
9 provide background on the MSM deferral policies. I'll
10 introduce the topics and then the speakers and set up
11 the questions for discussion. There are no voting
12 questions today. We're asking the committee to discuss
13 around the topics that we introduce.

14 FDA is responsible for protecting the safety
15 of the blood supply, which depends on the
16 implementation of donor screening measures based on the
17 available evidence. The AIDS crisis in the 1980s and
18 the recognition that HIV could be transmitted through
19 blood transfusion or plasma derivatives had profound
20 effects on the US blood system.

21 This slide takes liberty to condense 20 years

1 of history onto one slide, so forgive me. But in 1982,
2 the first cases of AIDS from blood transfusion and
3 plasma derivatives were recognized. Although most
4 cases of AIDS occurred in MSM and other risk factors,
5 the recognition of this association with risk factors
6 led FDA to make recommendations early in the '80s for
7 donor education about signs and symptoms of AIDS and
8 asking MSM and other at-risk donors not to donate,
9 excluding them from donation.

10 The identification of the virus, first as
11 HTLV-III, and now, of course, HIV, led up to the first
12 donor screening test for HIV. The antibody test was
13 licensed in 1985. But by the time this test was
14 implemented, thousands of transfusion recipients and
15 people with hemophilia would die from AIDS. In 1992,
16 FDA issued the 1992 Memorandum, which made
17 recommendations for blood donation and direct
18 questioning and indefinite deferral of men who have
19 ever had sex with another man, even once, since 1977,
20 or the MSM Indefinite Deferral Policy, which is
21 abbreviated on the slides.

1 The 1990s would see improvements in
2 technology. In the subsequent generations of HIV,
3 serological tests became increasingly more sensitive.
4 The most sensitive test, nucleic acid testing, was
5 introduced in 2000. Fast forward to present day, an
6 MSM are still a risk group. About 1.1 million people
7 are living with HIV. An estimated 38,700 were infected
8 in 2017. This number has been relatively stable since
9 about 2012. While MSM comprise about 7 percent of the
10 US male population, MSM accounts for over 60 percent of
11 new infections overall, and over 80 percent of
12 infections in men, as you can see on this pie chart.

13 You'll hear much more today about HIV
14 epidemiology in the session this morning. You'll also
15 hear more about FDA regulation of the blood supply,
16 which is summarized on this slide, which depends on
17 multiple layers of protections. First, donor
18 education. Blood centers must provide explanation
19 about readily identifiable risk factors, closely
20 associated with exposure to relevant transfusion-
21 transmitted infections, or RTTIs. Today, we're talking

1 about HIV.

2 They must screen donors with donor history
3 questions and defer those with behaviors associated
4 with RTTIs. Donations are tested. Blood centers must
5 keep donor deferral records so as not to recruit donors
6 who are ineligible, and have procedure for quarantine,
7 recall, and lookback on unsuitable components.
8 Evidence that donor education and donor screening are
9 effective, or at least indirect evidence that donor
10 screening is effective, is shown on this slide.

11 This slide shows HIV and hepatitis rates in
12 blood donors versus the general population -- the rate
13 per 100 thousand for hepatitis B, hepatitis C, and HIV,
14 which we're focusing on today. The rate in the general
15 population, shown in gray, among all donations in red,
16 and among repeat donations in yellow. So, you can see,
17 for HIV, the selection pressure removes about 90
18 percent of the risk upfront before screening. If the
19 education and screening had no effect, the rates would
20 be more similar in the general population compared to
21 blood donors.

1 So why is this important? Why do we still ask
2 questions when we have sensitive tests? The screening
3 tests are extremely sensitive, but they are still not
4 perfect. If a donor population has a higher incidence
5 and prevalence of HIV, there will be a greater chance
6 that more donations will be in the window period and
7 potentially infectious. And this slide provides a
8 schematic illustration of that window period and
9 transfusion risk. The window period is that interval
10 of time after infection. This slide shows the
11 concentration in blood of the different tests and the
12 time after infection.

13 In the window period, the tests are negative,
14 but the virus can still be transmitted through blood.
15 The antibody test has a window period of about 3 weeks.
16 The p24 antigen test, when it was introduced, shortened
17 that window period. But it was soon replaced with
18 nucleic acid testing, which is more sensitive.

19 Depending on which test is used and whether
20 testing is performed in mini pools or individual
21 donations, the window period today has decreased to 7

1 to 10 days. But still, even if the virus is
2 undetected, blood transfusion can still transmit HIV to
3 patients.

4 Since NAT was introduced in 2000, FDA has had
5 public meetings, workshops, and advisory committees to
6 revisit the deferral. This slide highlights key
7 meetings and their outcomes.

8 In June of 2012, an HHS Advisory Committee on
9 Blood Transfusion and Tissue Safety concluded that the
10 indefinite deferral policy was suboptimal but
11 recommended further study to inform a possible change
12 of the indefinite deferral policy. In September 2010,
13 the HHS Blood, Organ, Tissue Safety, or BOTS working
14 group, proposed to design three research studies and an
15 operational assessment of quarantine release errors,
16 which I'll show on the next slide.

17 In November 2014, the results of these studies
18 were presented to the committee, which considered
19 alternative deferral policies such as eliminating the
20 deferral policy altogether, recommending shorter time-
21 based deferrals, or individual risk-based assessment,

1 or pretesting. The committee voted 16 to 2 in support
2 of a policy change from the indefinite deferral policy,
3 to the 12-month deferral policy, and emphasized the
4 importance of having a system for monitoring
5 transfusion-transmissible infections in blood donors.

6 The supporting evidence for that decision is
7 shown on the next two slides. In a study of
8 participants' understanding of the pre-donation history
9 questionnaire, volunteers were recruited from the
10 community -- and MSM were preferentially recruited --
11 to evaluate how donors answered the questions. And
12 donors -- sorry, to understand how the participants in
13 the study understood the question. The studies showed
14 that people understand the questions, but they answered
15 the questions through the filter of, is my blood safe?
16 There was no difference in MSM and non-MSM patterns of
17 response.

18 The Retrovirus Epidemiology Donor Study, or
19 REDS-II, the study of risk factors for retrovirus and
20 hepatitis virus infections, looked at about 196 HIV-
21 positive blood donors and evaluated for their risk

1 factors. So, these were donors who were found to be
2 infected with HIV. MSM had a 60-fold increased risk
3 and was a leading independent risk factor for HIV
4 infection among blood donors. Having multiple sexual
5 partners, in contrast, was a 2.3-fold increased risk.

6 The REDS-III Blood Donation Rules Opinion
7 Study, or BloodDROPS, was a confidential survey of
8 current blood donors -- so these are current blood
9 donors, men who are donating blood -- and found out
10 about 2.6 percent of male donors who are currently
11 donating report MSM. About half of those who were
12 noncompliant indicated, under the indefinite deferral
13 policy, that they would adhere to an MSM-12 policy.

14 An operational assessment of quarantine
15 release errors was also considered. Quarantine release
16 errors is the erroneous release, or the mistaken
17 release, of an unsuitable component before testing is
18 completed or other criteria are met and unsuitable
19 components are distributed. With today's computer
20 systems and blood systems, the risk of a quarantine
21 release error related to a test result is very low.

1 Finally, the Australian Red Cross was the
2 first blood center to report their experience in
3 changing from a 5-year deferral to a 1-year MSM
4 deferral. They reported their experience before and
5 after the change, reporting on 5-year time periods and
6 over 4 million donations in each, before and after the
7 change. They saw no difference in the rate of HIV-
8 positive donations. They also performed a confidential
9 survey and found a very low rate of MSM undisclosed
10 risk of about 0.2 percent.

11 So, in 2015, FDA released final guidance that
12 moved -- that changed MSM from an indefinite deferral
13 to a 12-month deferral. This aligned it with other
14 deferrals for possible sexual exposure to HIV. The
15 other risk groups, or the other indefinite deferrals,
16 did not change. The other 12-month deferrals in this
17 guidance document did not change. Today, we're
18 focusing on the MSM and MSM-related deferrals. FDA is
19 committed to ongoing evaluation of the MSM 12-month
20 deferral policy and potentially advancing the policy
21 based on the available scientific evidence.

1 To this end, in July 2016, a public docket
2 requested comments and supporting scientific evidence
3 regarding potential blood donor deferral policies and
4 asked for comments on alternatives to time-based
5 deferrals and the feasibility of individual risk
6 assessment strategies. The responses were mixed, but a
7 notable cross-section of hospitals, plasma users, blood
8 centers, and advocacy groups commented at that time
9 that data were not yet available to consider a further
10 change of the MSM 12-month deferral policy.

11 In this morning's session, you're going to
12 hear about what other countries do with respect to MSM
13 deferral policies, and the countries that use time-
14 based deferral or shorter time-based deferral than the
15 US uses, countries that use risk-based or individual
16 risk assessments, and countries that use alternative
17 measures, such as quarantine and retest.

18 This morning, you're also going to hear an
19 update of the Transfusion-Transmissible Infections
20 Monitoring System, or TTIMS. TTIMS was launched in
21 2015. It's sponsored by FDA, NHLBI, and HHS. The

1 collaboration comprises more than 60 percent of the US
2 blood supply, with the American Red Cross, Vitalant,
3 the New York Blood Center, and OneBlood. TTIMS
4 collects and analyzes data on the incidence and
5 prevalence of HIV, hepatitis B, hepatitis C, among
6 blood donors, and collects demographic variables,
7 behavioral risk factors, and biorepository samples from
8 seropositive donors.

9 This morning, you're also going to hear about
10 an HIV risk factor questionnaire, which is a research
11 study to assess MSM risk-based questions as an
12 alternative to minimize HIV risk, at least as
13 effectively as the current deferral policy. This is an
14 FDA-sponsored research study developed through
15 collaboration with the Blood Equality Working Group
16 with representatives from advocacy organizations,
17 community health centers, blood collectors, and public
18 health agencies.

19 The speakers and topics for this morning are
20 Dr. Mindy Goldman, who will discuss global developments
21 in MSM deferral; Dr. John Brooks, who will discuss the

1 epidemiology of HIV in the US; Dr. Alan Williams, with
2 FDA and the Office of Biostatistics and Epidemiology,
3 who will give an update on the Transfusion-
4 Transmissible Infections Monitoring System; and Dr.
5 Barbee Whitaker, with FDA in the Office of Blood --
6 Biostatistics and Epidemiology, who will present the
7 HIV risk factor, or HRQ, study.

8 Again, we're not asking you to vote today, but
9 we're asking you to discuss or comment on what has been
10 learned from implementing other MSM policies
11 internationally, such as risk-based deferral methods or
12 quarantine and retest for plasma, and how this
13 information can be used to inform the current US MSM
14 deferral policy. We're also asking you to comment on
15 questions proposed for the study in the HIV Risk
16 Questionnaire and whether there are any additions or
17 modifications to this study in order to best identify
18 behavioral risk questions to predict the rest of HIV
19 transmission in the MSM population.

20 So, with that, I conclude.

21 **DR. KAUFMAN:** Thank you, Dr. Eder. I would

1 like to introduce to our next speaker, Dr. Mindy
2 Goldman from Canadian Blood Services.

3 Actually, before Dr. Goldman gets started, I
4 wanted to note that Dr. Meera Chitlur is now available
5 on the phone. Dr. Chitlur, would you please introduce
6 yourself?

7 **DR. CHITLUR:** Hi. This is Meera Chitlur. I'm
8 a Pediatric Hematologist from Children's Hospital of
9 Michigan and Wayne State University in Detroit. Thank
10 you for having me here today.

11 **DR. KAUFMAN:** Thank you.

12 **DR. GOLDMAN:** Okay, well, I'd like to thank
13 the FDA for inviting me to speak. Rich, did you want
14 to say something else before I get going?

15 **DR. KAUFMAN:** Yes. We have one other member
16 of the committee that I would like to ask for
17 introduction. Dr. Judith Baker?

18 **DR. BAKER:** Thank you. Apologies. Judith
19 Baker with the Center for Inherited Blood Disorders in
20 Orange, California and UCLA -- Pediatric Hematology at
21 UCLA. My background is public health. I work

1 extensively with the US Hemophilia Treatment Center
2 Network and sickle cell disease as well.

3 **DR. KAUFMAN:** Thank you. Dr. Goldman, please.

4 **REVIEW OF GLOBAL DEVELOPMENTS IN MSM DEFERRAL**
5 **POLICIES**

6 **DR. GOLDMAN:** Okay. Around the world in 20
7 minutes, here we go. I don't have any conflicts of
8 interest, but I do have a very definite perspective on
9 this in that I've been involved in formulating and
10 evaluating and thinking about this issue for a long
11 time from the perspective of a medical director of a
12 large blood service in Canada.

13 As you might expect, when you look
14 internationally, there's no general consensus on
15 criteria for MSM. There are various factors that do
16 influence policy, and these include: what is the
17 actual epidemiology of HIV in that country, which can
18 be, of course, quite different from in the US; donor
19 screening methods; regulatory requirements;
20 government decrees; risk analysis and modeling
21 studies; and finally, last but definitely not least,

1 the history of response to threats in the past, which
2 Dr. Eder outlined for the US before. There are
3 basically a couple of main approaches.

4 The first one, which we're all very familiar,
5 is the time-based deferral. So, any MSM in a given
6 time period will lead to a deferral for a given time
7 after last MSM. It's very straight forward. The
8 second group is so-called risk activities based,
9 sometimes called "gender neutral" policies. These
10 policies consider certain sexual behaviors to be high-
11 risk, regardless of whether the partner is the same sex
12 or the opposite sex, in that, usually, there is a given
13 timeframe for that activity and there will be a
14 deferral for a given time after that risk factor. So,
15 that might be a new partner, let's say, or more than
16 one partner.

17 Then, finally, more recently, there's a few
18 countries that have looked at alternative criteria in
19 combination with other safety measures. And the main
20 one will be plasma quarantine and retest. So, as
21 always, with any donor criteria, the problem boils down

1 to how to analyze results. This is always a difficult
2 question. Disease transmission is, thankfully,
3 extremely rare, so that is not the outcome that we're
4 looking at. There's a bunch of kind of surrogates that
5 we use to tell us if what we're doing is safe or not
6 safe.

7 Usually, we look at HIV rates in our donors,
8 incidence rates in repeat donors, anonymous surveys to
9 try and assess compliance with the criteria, and all
10 these factors go into risk modeling studies. The
11 results are going to depend on many factors in addition
12 to the actual criteria themselves. We all know that
13 because our criteria have become more liberal in the
14 last few years, but our HIV rates in our donors are
15 much lower than they were, let's say, 25 years ago.
16 So, clearly, something that had nothing to do with the
17 blood suppliers has happened there. So, there's a lot
18 of factors in the outside world that influence what
19 we're going to see in our donors.

20 Obviously, HIV incidence and prevalence in the
21 general population, public health messaging so people

1 know that they're at risk; they should get tested. And
2 then, if they are tested, how easy is it to go get
3 tested? Then, when you know you're tested, you should
4 know that you shouldn't come in to donate blood. So,
5 all of those things are really not related to what our
6 criteria are at the blood center.

7 At the center, there's different methods of
8 administration of the questionnaire. And then, of
9 course, you're still relying on a human being, the
10 donor, to understand what you're asking and to comply
11 and see the question and answer it the way you would
12 like them to answer it. So, if we look at each of the
13 types of screening, we're starting with time-based
14 deferrals. As Dr. Eder mentioned, from the 1980s until
15 about 2000, many countries had a permanent deferral for
16 MSM "ever, or even once since 1977." Australia was the
17 first country, in 2000, to move to a 12-month deferral.
18 Since about 2011, many countries have moved to shorter
19 deferral periods which range from 3 to 12 months.

20 Why was this done? Some of the countries did
21 risk modeling that suggested that there would really be

1 absence of a significant risk increment if they did
2 move to a shorter deferral period. Of course, all the
3 testing has improved tremendously. And, in terms of
4 the 3-months deferral in the UK, the UK has an
5 independent advisory committee on the Safety of Blood,
6 Tissues, and Organs, called SaBTO, which, a few years
7 ago, had recommended changing from an indefinite to a
8 12-month deferral, and then, more recently recommended
9 moving from a 12-month to a 3-month deferral.

10 As I understand the report, it was mainly
11 based on the virus that had the longest window period
12 for them, which was hepatitis B, nucleic acid testing
13 being done in mini pools, and they arrived at their 3
14 months by taking about double the window period with
15 that test and adding in a few days of pre-infectious
16 period, and deciding that that was about 3 months.

17 So, if we look at where we are in 2019 with
18 these time-based deferrals, we have England, Scotland,
19 and Wales with this 3-month deferral. That was
20 instituted in late 2017. We have the Ministry of
21 Health in Denmark announcing that they will go to a 4-

1 month deferral. I believe that's actually going to
2 happen this summer. And then, we have a large number
3 of countries that are at a 12-month deferral, including
4 Canada, Australia, New Zealand, and a whole host of
5 European countries in addition to the US, obviously.

6 So, what have the results been? Well, the
7 change to a 12-month deferral in countries that have
8 done a careful analysis -- and quite a few actually
9 have -- was not accompanied by an increase in HIV rates
10 in the donors or an increase in NAT-only positive
11 donors, which would be, actually, the donors of most
12 concern because, likely, very recently infected. In
13 these modeling studies that were done in several
14 countries, there was an expected increase in the number
15 of HIV-positive donors and that didn't happen.

16 So, in this review by March Ermere (phonetic),
17 one of the leading modelers, he suggests that actually,
18 probably those studies, which of course are filled with
19 a bunch of estimates, likely were overly conservative.
20 Because what they predicted didn't actually happen.
21 Post-implementation compliance studies, these anonymous

1 surveys of donors, were done in several countries and
2 really did not show any change in non-compliance or, if
3 anything, a slight improvement, because people who had
4 more remote MSM and had been non-compliant with earlier
5 criteria, are now actually compliant because you have a
6 shorter deferral period.

7 We're awaiting publication of UK results with
8 the 3-month deferral. They did present some results at
9 their British Transfusion Medicine Meeting and have
10 told us verbally that their HIV rates have not changed
11 in their donors since they've moved to the 3-month
12 deferral. I think there will be probably some
13 abstracts of ISBT and ABB from the UK.

14 What are the strengths and weaknesses of this
15 approach? Well, we know it well. It's simple and it's
16 similar to the other types of questions that we ask
17 donors, so that's a good thing. It's standardized.
18 For us, standardization is close to godliness. And the
19 changes have enlarged our overall donor pool. So,
20 there's some people who used to be deferred who can now
21 donate, and that's always a good thing because we're

1 always short on donors.

2 What are the negatives here? They, too, I
3 think, are pretty obvious. Well, at some point, you're
4 going to be stuck. Right? Because you're going to be
5 kind of a bit at the limits of your window period, plus
6 a little bit of extra. So, you're not going to be able
7 to shorten the deferral with this approach. Then,
8 another major limitation is that you're still deferring
9 all sexually active MSM, including those who are in a
10 stable monogamous relationship from donating. So, from
11 a justice perspective, or what is the actual lowest
12 risk population of MSM, they are still being deferred
13 using this type of approach.

14 Now, we're going to move over and look at risk
15 activities-based criteria, looking at Italy and Spain.
16 So, here, as I mentioned, donors are asked about sexual
17 partner. It does not matter if this person is of the
18 same sex or of the opposite sex, and they're deferred
19 for what is considered a high-risk sexual behavior.
20 So, that might include a list of things including
21 having a new partner, having more than one partner, or

1 having so-called casual partners. In other words, you
2 and your partner are not in a mutually exclusive
3 relationship.

4 The time period of interest, where you're
5 asking about all these things, could be 4 months in
6 Italy or 12 months in Spain. I just wanted to say
7 that, although we don't have these types of questions
8 in the US or Canada for all donors, in some countries
9 with just trends, they do have some of these broad
10 criteria about a new partner for all donors, in
11 addition to some specific MSM partner deferrals.

12 There are quite a few other differences
13 between Italy and Spain and what we're doing in North
14 America. They are using physicians to screen the
15 donors with the ability to ask additional questions and
16 have, probably, more refined individual risk
17 assessments than we would ever have in our highly
18 regulated manufacturing environment in Canada or the
19 US. There's no national uniform questionnaire, so
20 there's less standardization and more variability
21 between blood centers. So, you end up a little bit

1 with trying to compare apples with oranges, rather than
2 really just looking at the differences in criteria.

3 The results are harder to evaluate on a
4 national level. There has been a study published from
5 Catalonia in Spain, which is where Barcelona is,
6 showing a high HIV rate in the donors, 7.7 out of 100
7 thousand which is quite high. 61 percent of the
8 positivies there were in repeat donors, which is quite
9 unusual. 10 of the 214 positive donors, or 4.7
10 percent, were NAT-only positives. So, likely, infected
11 very recently in the weeks prior to donation. 89
12 percent of positive donors and 90 percent of these NAT-
13 only positives were male donors, with a lot of them
14 having MSM as a risk factor.

15 When you look at European data that have been
16 published, the HIV rates in donors in Spain and Italy
17 are quite a bit higher than other Western European
18 countries. This is not an exhaustive slide; it's just
19 a few studies from the few countries, just looking at
20 HIV rates per 100 thousand NAT-only rates, and then
21 kind of the ratio of positives in first-time versus

1 repeat donors. As Dr. Eder showed you, usually most of
2 the positives are these prevalent infections in our
3 first-time donors. And there's very few positives in
4 repeat donors. So, at the top, you see Catalonia, then
5 you see an Italian study, a US REDS-II study, CBS, and
6 England.

7 So, you can see the HIV rate per 100 thousand
8 and how much higher it is in Catalonia and Italy
9 compared to the US and compared to Canadian Blood
10 Services and England, which are really extremely low.
11 NAT-only rate -- again, you can see how high it is in
12 Catalonia. It's not available in the Italian study.
13 It's quite low in the US, and yield of NAT is
14 approximately zero for Canadian Blood Services and for
15 England, for many, many years. Then, you can look at
16 the ratio first-time to repeat donors.

17 So, you can see, for most countries, it's
18 quite high. In other words, most of the positives are
19 first-time. Like, for that REDS-II study, it's 5.9
20 times higher in first-time versus repeat donors.
21 Interestingly, given that Catalonia and Italy have the

1 same approach, you can see how there's something
2 different happening in those places because, in
3 Catalonia, it's 1.2. In other words, a lot of the HIV-
4 positives are repeat donors. But somehow, Italy,
5 supposedly using the same approach, most of the HIV-
6 positives are first-time donors. So, there's clearly
7 other things other than just the criteria themselves
8 that come into play here.

9 What are the strengths and weaknesses of this
10 approach? Well, for MSM individuals, there's an
11 attempt at a greater categorization of high or low-risk
12 donors. So, an increase in specificity where they're
13 not all thrown into the same high-risk boat. It
14 removes the question and deferral specifically for MSM,
15 so it's reducing perceived stigma and prejudice against
16 gay men. On the negative side, it's a more complex
17 approach and more interpretation is possible for each
18 of those questions. There's a higher residual risk
19 using the data from Spain and Italy. And if you feed
20 those numbers into a modeling study, you will come up
21 with a higher risk than what we have with our approach.

1 As applied in a gender-neutral way, it would
2 substantially increase deferral of currently donating
3 TD marker negative donors. So, if everyone's going to
4 be deferred for having a new partner or more than one
5 partner, we're going to be deferring a lot of donors
6 that are currently happily donating with negative TD
7 markers. So, it would decrease specificity overall
8 and, therefore, may have a negative impact on the
9 adequacy of supply.

10 What about alternative criteria and other
11 safety measures? Additional measures that reduce
12 infectious risk, such as quarantine and retest of
13 donors, may permit adoption of alternative criteria.
14 So, in Israel, there is a program now that is enrolling
15 MSM. Where there is no deferral, people donate whole
16 blood. The plasma is quarantined, and it will be
17 released for transfusion once the donor returns at
18 least 4 months later. Obviously, when they return,
19 they'll be retested. The red cells and platelets will
20 be discarded from that donation. That would never fly
21 where we are. We would not be able to discard two-

1 thirds of the donation. But anyway, that's what
2 they're doing.

3 In France, all donors are asked about if
4 they've had more than one sexual partner in the last 4
5 months, so that's part of their general criteria. They
6 are now allowing MSM who meet that criterion to donate
7 plasma. So, if they have not had more than one sexual
8 partner in the last 4 months, the plasma will be
9 quarantined, and the donor has to return and be
10 retested at least 2 months later. Then, the plasma
11 will be issued for transfusion. So, you could,
12 obviously, also combine this approach with pathogen
13 reduction technology, which is a future topic later
14 today, or with source plasma donation.

15 Strengths and weaknesses of this -- well,
16 maybe the additional steps may compensate for any
17 possible risk increase. We love belt and suspenders
18 and parachuting in the blood sector. You're adding a
19 few things there, so maybe you could give something up.
20 You would get a lot of useful data about eligibility of
21 MSM donors for all our other 65 questions that we ask,

1 information about TD markers, and compliance.

2 That will help you with developing further
3 policy changes, maybe for whole blood donation or other
4 types of donation. It would increase eligibility for
5 MSM, although additional processing requirements, such
6 as quarantine, mean that you're still going to be
7 asking an MSM question. Right? Because you're still
8 going to be treating and processing the blood from
9 those individuals differently than other donors.

10 What about weaknesses? Well, it's going to
11 increase your operational complexity and cost. Just
12 think of that freezer for that quarantine stuff, and
13 then the IT controls for when it comes out of
14 quarantine. All that may lead to increased errors.
15 Quarantine and retest is limited to plasma donation.
16 You can't do that for components that have a short
17 shelf life. And if you have sub-optimal performance of
18 your pathogen reduction technology, you may have an
19 increased risk because you're relying on that to
20 compensate for more liberal criteria in the donors.

21 So, just wanted to mention a little bit about

1 what we're doing in Canada. So, both Canadian Blood
2 Services and Héma-Québec, which are the two blood
3 suppliers in Canada, changed from an indefinite
4 deferral to 5-year deferral in 2013, and then to a 12-
5 month deferral in 2016, after risk modeling and very
6 extensive stakeholder consultations with both patient
7 groups and advocacy groups.

8 There's been no change in our very, very low
9 TD marker rates or in our compliance. And we've done
10 serial anonymous donor surveys. Both organizations
11 have the submission in, now under review, at our
12 regulator Health Canada to change to a 3-month
13 deferral. Many research projects are underway as part
14 of a federally funded research program. You can go to
15 our website to read a lot more about those.

16 In summary, there's no international consensus
17 on MSM policy. There was a trend towards shorter time-
18 based deferrals, with no adverse safety impact to date.
19 Risk behavior-based strategies have shown high HIV
20 rates in donors, although this may be influenced by
21 factors other than the criteria themselves. Quarantine

1 and retest of pathogen reduction steps may mitigate for
2 possible risk increments associated with alternative
3 screening approaches.

4 Thank you very much for your attention.

5 **DR. KAUFMAN:** Thank you, Dr. Goldman. I'd
6 like to introduce our next speaker, Dr. John Brooks
7 from CDC.

8 **EPIDEMIOLOGY OF HIV IN THE UNITED STATES**

9 **DR. BROOKS:** Good morning. I've been asked to
10 join you all this morning to review the epidemiology of
11 HIV in the US in 2019. I work for the Division of
12 HIV/AIDS Prevention at CDC, and I'm the Senior Medical
13 Advisor there presently. I have no relevant financial
14 conflicts of interest to disclose or others. So, let's
15 get started.

16 I just want to open this by showing you what
17 tremendous progress we've made controlling HIV in the
18 United States. Some of you may recall that it peaked
19 in the late 1980s, early 1990s. And it was with the
20 advent of HIV testing and the first drug that was
21 approved that we began to see new infections declining.

1 With the current -- with ongoing improvements in
2 antiretroviral therapy, numbers of infections continue
3 to decline. In the most recent period, from 2009 to
4 2015, we've seen continued declines with the advent of
5 PrEP. I'll review some of the reasons why this is the
6 case later on.

7 But, first, I just wanted to also highlight
8 that we have seen, as a result of these declines,
9 really enormous strides in reductions in death among
10 people who have been diagnosed with HIV infection, as
11 well as increases in the length of life of persons
12 after HIV diagnosis. Deaths have declined by 20 times
13 and length of life has increased by at least 17 years
14 over the period we've been doing surveillance.

15 As a result of that, HIV is no longer a
16 leading cause of death as it was in the early 1990s
17 among people of the highest risk -- young people, age
18 25 to 44. As I mentioned before, this is due
19 predominately to the advent of effective antiretroviral
20 therapy. So, today, among the six leading causes of
21 death, HIV is no longer among them in this group. Let

1 me come back now and look more closely at this more
2 recent period and talk about the HIV epidemiology as we
3 know it today. I'm going to start from the right side
4 of this figure, and the most recent data we have are
5 for the year 2016.

6 First is shown, on the -- on your right side,
7 excuse me. Not the left side. On the right side are
8 HIV diagnoses. And as Dr. Eder mentioned earlier,
9 that's 38,739 were diagnosed in 2016. That's the
10 actual number of infections which had a positive test.
11 But I'll note that the average person has been living
12 with HIV for 3 years before they're diagnosed. That's
13 7 years for people who are African American or black in
14 this country. Using a CD4 depletion model, where we
15 take the CD4 cell count at the time of diagnoses and
16 then work backwards to estimate the likely date on
17 which the infection occurred, we can better infer
18 incidence. That's what's shown on the left.

19 That is the dates at which infections actually
20 occurred. Not surprisingly, it's not that different
21 from diagnoses. But it's 38,700. We like to use

1 incidence because this is usually considered by us when
2 we're looking at trends in what's going on with the new
3 infections -- a more accurate way of looking at the
4 data. What that means is, in the middle, that 1.1
5 million Americans today are estimated to be living with
6 HIV infection of who estimate 1 in 7, or 14 percent, do
7 not know they, yet, have the infection.

8 Annual infections have been declining very
9 steadily since the 1990s. But since 2013, we've begun
10 to see our progress stalling at around this figure of
11 38 thousand to 40 thousand new infections per year.

12 Let me talk a little bit about lifetime risk for HIV
13 diagnoses. I like to talk about it this way because I
14 think it personalizes it more when you're trying to
15 explain to people what risk means. This shows the
16 lifetime risk by age, on the x-axis, over time. Not
17 surprisingly, as people enter sexual debut in their
18 teens and early 20s, lifetime risk increases
19 substantially and then begins to level off in the 50s.

20 Lifetime risk for men is about 4 times that
21 for women. That's also reflected by the prevalence and

1 incidence of HIV infection where there's a ratio of
2 about 1 to 2, for 4 men for every woman who's infected.
3 Because this meeting is concerned with men who have sex
4 with men, I'm going to show you here, now, the
5 estimated incidence among persons who are adults over
6 age 13 by transmission category. You can see, as was
7 described earlier, that among the entire population of
8 people diagnosed with HIV infection, those living with
9 the condition -- those -- sorry. Estimated when
10 infected with HIV in 2016, 68 percent were MSM. And if
11 you looked among men only, it's closer to 80 percent.

12 There is a substantial fraction among
13 heterosexuals -- about one-quarter -- and about 8 to 10
14 percent among persons who inject drugs, either alone or
15 who also are MSM. Looking over time, among MSM, what's
16 been going -- sorry, by risk factor first, what's been
17 going on since 2010. Again, these are incidence data
18 and what I want to apply under a couple of things.
19 Incidence of HIV infection among men who have sex with
20 men has remained stable whereas, among heterosexuals
21 and injection drug users, there have been substantial

1 and significant declines.

2 Now, honing in on men who have sex with men,
3 there also are important differences by race and
4 ethnicity. Black/African American MSM comprises the
5 largest fraction of MSM, and there has been no change
6 over this time period in the incidence in this group.
7 However, among whites, there's been a steady decline.
8 Disturbingly, however -- and this is something that
9 we're very concerned about -- there's been a very
10 substantial and significant increase in incidence among
11 Hispanic and Latino MSM.

12 Looking by age group, there's also an
13 interesting point, which is that, although among older
14 MSM, incidence has remained stable and generally low,
15 there's been a steady increase in the group age 25 to
16 34. Recall that when I showed the diagram earlier of
17 lifetime risk, that's when lifetime risk is
18 accelerating and, generally, greatest. We're pleased
19 to see that there's been a decline in the group age 13
20 to 24. We're looking to understand that better right
21 now.

1 But the point that I want to make here is
2 that, if you combine these two worst categories
3 together and look at black or Latino men who have sex
4 with men in the highest age for risk, 25 to 34, since
5 2010, we've seen a 65 percent overall increase
6 incidence in that particular group. Another way of
7 looking at risk by group is by looking at the lifetime
8 risk in here, by transmission category.

9 Again, MSM have the highest risk, in terms of
10 their lifetime risk, of acquiring HIV infection,
11 followed interestingly by women who inject drugs and
12 men who inject drugs. But heterosexual risk is
13 comparatively quite low. Then, looking at these MSM in
14 particular, again, as I mentioned earlier, the risk is
15 substantially greater for African American MSM, who we
16 estimate may have as high as a 1 in 2 chance in their
17 lifetime of acquiring HIV compared to Hispanic MSM or
18 white MSM.

19 Geographically, risk for HIV is also very
20 different across the United States. In particular, I
21 want to bring your attention to the southern part of

1 the country, which is where the problem is greatest at
2 the present time. Although the southern states in the
3 US depicted here account for only 38 percent of the US
4 population, they bear the highest burden of HIV
5 infection. 51 percent, over half of all new HIV
6 infections, occurred in the South in 2016; 45 percent
7 of persons living with HIV lived in the South; and 50
8 percent of undiagnosed HIV infections were in the
9 South.

10 Looking more broadly, then, and asking, so,
11 what's the lifetime risk geographically -- and this is
12 essentially equivalent to lifetime prevalence because
13 your risk increases by the opportunity to encounter the
14 infection. So, when the prevalence is higher, your
15 likelihood of encountering it is higher and your risk
16 is greater. Again, the South has a very substantial
17 increased risk compared to other parts of the country.
18 Other areas that are notable here are the D.C. Metro
19 area, Maryland, and Delaware, as well as New Jersey and
20 New York.

21 The good news is that effective treatment has

1 done amazing work extending the life of people with HIV
2 infection. Starting in this diagram from the UN AIDS,
3 looking in 1995 up until 2010, with the advent of
4 antiretroviral therapy and its steady improvement, the
5 lifespan that a person could expect to live after
6 diagnoses of HIV has increased steadily, so that in the
7 current Europe, we can say that persons diagnosed in
8 their 20s and given effective antiretroviral therapy
9 can expect to live an essentially normal lifespan.
10 This is due predominately to the advent and changes in
11 the medical therapy used for treating HIV, which is now
12 simple and very effective.

13 As many of you may know, it used to be a
14 complex combination of tablets. This is actually a
15 patient holding the pills that she was given for one
16 day's dose back in the early 1990s. Had limited
17 potency and very high toxicity, which dissuaded people
18 from taking the medication. Today, however, we have at
19 least 7, and soon -- I think -- to be 8, multi-drug
20 combinations available as single tablet regimens that
21 you take once a day. The regimen is very simple. The

1 drugs are more potent now -- in particular, the
2 integrase inhibitors -- and these drugs have very few
3 side effects. It's very easy now to manage HIV
4 infection.

5 Treatment also has another really important
6 benefit that's been brought to everyone's attention by
7 a couple of studies; finally, the last one was
8 published last year. And that is that effective
9 treatment prevents sexual transmission. Shown here are
10 the results of 4 seminal studies looking at sero-
11 different couples, where there was an infected person
12 and their sexual partner was uninfected, and the
13 infected partner took antiretroviral therapy and
14 achieved viral suppression. The uninfected partner
15 used no protection, no condoms, no pre-exposure
16 prophylaxis, no post-exposure prophylaxis.

17 In total, these company's studies included a
18 little over 3,700 couples with a good mix of
19 heterosexual couples and MSM couples. Despite over 125
20 thousand condom-less episodes of vaginal and anal sex,
21 no single transmission of HIV was observed that could

1 be genetically linked between these couples. And I'll
2 just tell you, having been in HIV medicine for 30 years
3 and spending all of my time telling people that you
4 have to be careful, this was a very stunning finding.
5 But I now am certain in my belief that people who
6 achieve and maintain a suppressed viral load have
7 effectively no risk of transmitting HIV infection
8 sexually.

9 But this good news is not reaching all
10 Americans evenly. This shows what we call the cascade
11 of care. Looking at the fraction of persons who have
12 been diagnosed, received, or linked to care, who have
13 been retained in care, and who have achieved viral
14 suppression. I'll bring your attention, first, to the
15 right side of the figure where we show we estimate that
16 no more than 51 percent of Americans have achieved
17 viral suppression.

18 Now, this varies a lot by individual clinic
19 and practice. In the Ryan White AIDS Program here in
20 the United States, they have achieved suppression rates
21 over 85 percent. In the VA system where I see

1 patients, we've also achieved very high rates of
2 suppression. But that's not true for all Americans.
3 The biggest drop-off is in the area from getting
4 diagnosed to staying engaged in care, and that's where
5 we intend to spend most of our effort in the future,
6 trying to make sure that people stay suppressed.

7 Breaking this down by different groups, I just
8 wanted to highlight here that, for MSM, it's about the
9 same. Roughly 50 percent are estimated to not be
10 virally suppressed among those who've been diagnosed
11 and undiagnosed. We also know, from data published
12 earlier this week, that most infections come from
13 persons undiagnosed or not in care. 8 in 10 new
14 infections come from somebody not in HIV care. That
15 fraction of persons who have either been not diagnosed
16 who don't know they have HIV, or who know they have HIV
17 but aren't in care, is only 38 percent of the
18 population of persons we believe have HIV infection.
19 But they account for 81 percent of new infections.

20 I wanted to touch briefly on pre-exposure
21 prophylaxis. This is a single drug combination of the

1 drugs tenofovir and emtricitabine. It's currently the
2 only FDA-approved drug for PrEP in United States. We
3 know that it's greater than 90 percent effective for
4 preventing sexual transmission, and we have a group
5 back in my agency, now, reviewing these data. I
6 believe we're going to come out saying it's probably
7 even more effective. Curiously, the number of
8 Americans that we have estimated who would benefit from
9 pre-exposure prophylaxis happens to be about the same
10 number who we estimate are living with HIV infection,
11 or 1.1 million Americans.

12 These were data presented a couple of weeks
13 ago at the large international HIV conference, looking
14 at PrEP awareness and use among men who have sex with
15 men. These are data from CDC's National HIV Behavioral
16 Surveillance. These are not representative data, but
17 they generally are -- they are taken from a large
18 population of MSM. I say that to caution that I think
19 these data may be over-estimating a little bit. But
20 the trends are important.

21 Right now, we estimate that a very large

1 fraction of MSM have heard of or are aware of PrEP, 90
2 percent on average. But there are important racial and
3 ethnic differences. Whites tend to know more about
4 this or be more aware of it than blacks or Hispanics.
5 And use of PrEP, it defines as "having ever used it at
6 least once" has increased substantially, we think. As
7 high as 35 percent of persons in this survey reporting
8 having ever used PrEP before.

9 For comparison, our last estimate was that --
10 the previous estimate was that only 7 percent of MSM --
11 no, excuse me. I'm going to correct that. Only 7
12 percent of Americans had ever used PrEP, and the
13 fraction of those who were MSM was about the same. So,
14 we think that this is an intervention that's not only
15 important and has a lot of opportunity to prevent new
16 infections but is also getting out there into the
17 public and being used. I don't need to spend too much
18 time talking to this group about HIV testing. I just
19 wanted to point out research we completed about a year
20 and a half ago, looking at how different HIV tests
21 performed.

1 You may be well aware that the antigen
2 antibody-based technologies can detect HIV infection
3 very early. Median, about 18 days. 99th percentile,
4 that is the time at which, if a person tests negative,
5 we would say there's a greater than 99 percent chance
6 that they're uninfected was 44 days. Including in this
7 table now, the Aptima RNA NAT test that was used in
8 this study, the median period is down to about 11 days
9 and the 99th percentile, where 99 percent of people who
10 are tested negative would be considered uninfected, is
11 33 days.

12 With ART, HIV infection in 2019 is a highly
13 preventable and manageable chronic disease. It's
14 important to think that, now, we're near -- or 30 years
15 later, where this infection has become something that's
16 being managed as a chronic disease. I haven't shown
17 you the data about what it's like to live with HIV
18 infection today. But over 50 percent of persons
19 infected are age 50 or greater, and clinicians who are
20 taking care of patients who are receiving good care
21 focus a lot more on the same things that everybody else

1 has to look out for. Don't smoke, manage your weight,
2 get your blood pressure under control, and screen for
3 cancer.

4 They can expect to live a "near normal" life
5 expectancy if treated early and effectively. But this
6 happy state is not easy for everyone to get to. You
7 have to get suppressed, and that requires getting
8 diagnosed and getting into ongoing care. For that
9 reason, these steps and the continuum are a focus for
10 us. Pre-exposure prophylaxis is a potent and very
11 efficacious prevention tool. Although it's rising in
12 use, it's still underutilized by MSM.

13 So, in summary, new HIV diagnoses continue to
14 decline in the United States, although they appear to
15 be flattening in the last few years. And they
16 disproportionately and increasingly affect certain sub-
17 populations which we must prioritize for prevention and
18 treatment efforts. These include MSM, especially young
19 Latino/Hispanic and black/African American MSM, as well
20 as person living in the southern part of the United
21 States.

1 With antiretrovirals, there really is a
2 possibility of true HIV control. And I believe that
3 future of no new HIV infections is fully within our
4 grasp; and that with antigen antibody-based testing,
5 or NAT-based testing, median time from last exposure to
6 reactivity, in the context of testing a person for HIV,
7 is 10 to 20 days -- those kind of liberal boundaries
8 based on the data I showed you before; and that, if a
9 person tests negative at greater than 45 days after
10 last exposure, there's a greater than 99 percent
11 likelihood that they are uninfected.

12 This is my name and contact information, and I
13 think we'll have the questions afterwards. Is that
14 right, Dr. Kaufman? Okay. Great. Thank you very
15 much.

16 **DR. KAUFMAN:** Thank you, Dr. Brooks. Our next
17 speaker is Dr. Alan Williams, from FDA. He'll be
18 providing an overview of the Transfusion-Transmissible
19 Infections Monitoring System, or TTIMS.

1 **DATA FROM THE TRANSFUSION-TRANSMITTED**
2 **INFECTIONS MONITORING SYSTEM (TTIMS)**

3 **DR. WILLIAMS:** Good morning. Thanks very
4 much. As mentioned, I'm with the CBER Office of
5 Biostatistics and Epidemiology. I'm one of the persons
6 who's coordinating the TTIMS program, which has been
7 underway several years. In a long one-sentence
8 definition, TTIMS, or the Transfusion-Transmissible
9 Infections Monitoring System, is a representative and
10 sustainable system initiated in September of 2015 to
11 collect HIV, hepatitis C virus, hepatitis B virus,
12 incidence and prevalence, along with risk factors,
13 advanced laboratory measures, and associated
14 demographic variables among US blood donors.

15 This is reflecting the US blood supply by
16 collecting approximately 60 percent of the total US
17 supply. This program has been discussed in public
18 advisory committees numerous times, including to this
19 committee. December 2015 was the first discussion
20 where we discussed, in depth, recency testing as a
21 potential predictor of incidence in first-time donors.

1 Also, in December of 2016, and then in December 2017,
2 which was the first large data presentation from the
3 program, largely including prevalence from each of the
4 sites. There is a publication which provides
5 background for the program, which is referenced here.

6 In terms of structure and governance, TTIMS is
7 funded by the Food and Drug Administration, by the
8 National Heart, Lung, and Blood Institute, and by the
9 Office of the Assistant Secretary for Health in HHS.
10 Operationally, it's run by two coordinating centers,
11 the Donor Database Coordinating Center, or DDCC. This
12 is a contract to the American Red Cross through 2020.
13 The second coordinating center is the Laboratory and
14 Risk Factor Coordinating Center, or LRCC. And this is
15 a contract through 2021.

16 In terms of internal governance, there's a
17 steering committee, which includes representatives from
18 other vested PHS agencies as well as participants in
19 the program. There's an executive committee that
20 serves as the executive oversight, and there are
21 various analytic workgroups conducting study analysis

1 and proposals.

2 So, to focus, first, on the Donation Database
3 Coordinating Center, this is run by the American Red
4 Cross under Dr. Susan Stramer. The data collection
5 sites, which I report into the coordinating center,
6 include the entire American Red Cross blood systems,
7 Vitalant and each of their blood centers, the New York
8 Blood Center, and OneBlood. And then, all of the
9 laboratory results are coordinated and submitted to a
10 central site from Creative Testing Solutions. In terms
11 of work scope, the DDCC maintains a central database
12 for TTIMS, representing 60 percent of the US blood
13 supply and monitoring for the markers mentioned --
14 mainly hepatitis B, hepatitis C, and HIV.

15 This coordinating center built on the very
16 substantial base established particularly by the REDS-
17 II program and established consensus test result
18 definitions -- because some testing processes do vary
19 between centers -- validated all of the data exchanged
20 within the program between centers and the coordinating
21 center. And the DDCC also conducts quarterly data

1 analysis including prevalence calculations for donors,
2 also for donations, and then ultimately provides
3 incidence estimates which include the NAT yield, which
4 is NAT in the absence of antibody reflecting very early
5 infection, as well as the classic method of assessing
6 repeat donor seroconversion.

7 Then, from these incidence estimates, one can
8 drive residual risk estimates based on the incidence
9 rate times the known window period of infection. Shown
10 here is some of the HIV prevalence data presented by
11 Whitney Steele at the December 2017 BPAC, showing,
12 basically, some variation but largely prevalence of HIV
13 among both first-time and repeat donors from September
14 2015 through July of 2017, which, as you'll note,
15 encompasses the implementation period of the new MSM
16 deferral which occurred throughout 2016. No
17 statistical or measurable difference in prevalence
18 across this time period, with a first-time prevalence
19 of 8.8 per hundred thousand and a repeat donor
20 prevalence of 1.4 per hundred thousand.

21 The second coordinating center is a Laboratory

1 and Risk Factor Coordinating Center. This is conducted
2 by Vitalant Research Institute. Brian Custer is the PI
3 for that program. This similarly uses data and samples
4 contributed by the blood establishment participants,
5 including Vitalant, American Red Cross Blood Services,
6 New York Blood Center, and OneBlood, and the
7 participation of Creative Testing Solutions for lab
8 results.

9 The LRCC work scope includes an important
10 program within this study, which is the design in
11 conduct of the risk factor interviews within the
12 program. And because of the large number of samples
13 involved, interviews are conducted for all HIV-positive
14 individuals, for hepatitis C virus-infected individuals
15 who have yield infections -- in other words, reflecting
16 NAT on the early infection -- and then, similarly, for
17 hepatitis B, yield infection. And then there is a 2 to
18 1 ratio of controls for each of the seropositive
19 subjects. So, a lot of interviews taking place.

20 The LRCC will, in the course of the coming
21 year, integrate the risk factor data with the marker

1 data within the study. Additionally, this group houses
2 a biospecimen repository within the program, which
3 includes HIV, hepatitis C, hepatitis B samples
4 collected within the timeframe of the TTIMS program, as
5 well as historical HIV-positive blood samples from
6 blood donors within the TTIMS sites. LRCC also
7 conducts additional lab studies and is heavily involved
8 in evaluating donor HIV antibodies, using L-Ag avidity
9 tests, which are assays capable of characterizing a
10 recent HIV infection.

11 The period of recency depends on the cut-off
12 used between the assay, but typically, it's in the
13 order of predicting infection within the past 130 days
14 or thereabouts, depending on what cut-off is used. So,
15 the LRCC has been conducting L-Ag avidity testing of
16 stored donor samples to assess performance in blood
17 donation settings, which was a new endeavor for that
18 assay in this country. And then, ultimately, with that
19 testing well underway, these recency data will be
20 modeled to estimate infection incidence in first-time
21 donors. This, of course, increases the power to assess

1 changes in overall HIV incidence over time, and
2 particularly, pre or post any policy change that takes
3 place.

4 The basis of the LAg-avidity assays is that
5 persons with acquired HIV infections typically exhibit
6 HIV-1 specific **IgG** populations with higher proportions
7 of lower antigen-binding strength, also known as
8 avidity. Those with longer term infections typically
9 have higher **LAg** avidity. The mean duration of recent
10 infection, known as MDRI, as I said, can vary, but
11 typically would be something like 130 days and,
12 therefore, reflects fairly recent infection. LAg
13 avidity testing may also soon be available for
14 hepatitis C virus infection and this will also be
15 implemented within the TTIMS program.

16 So, again, just showing some of the early data
17 presented earlier to the committee, from HIV-positive
18 collections from 2010 through 2017, shown here are the
19 numbers tested per year, the number positive, and the
20 percentage. You can see that the percentage varies
21 from the mid-20s up to 32 percent or so, and is

1 relatively stable over time from 2010 to 2017. Indeed,
2 no significant differences by year. Additional
3 research in the Laboratory and Risk Factor Coordinating
4 Center is genetic sequence analysis of viral isolates
5 from HIV, hepatitis B, and hepatitis C. Both provide
6 sequencing data as well as assist drug resistance.

7 This would be a talk in itself; some very nice
8 work by Brian Custer's group and his colleagues. But,
9 in general, the genotypes and drug resistance mutations
10 seen in donors with infection reflect the patterns
11 observed in public health surveillance initiatives in
12 the US general population and, therefore, serve as a
13 representative group reflecting gene sequencing
14 information in other parts of the country, in other
15 populations.

16 In terms of overall accomplishments for TTIMS,
17 as of the end of the year, 2018, TTIMS donation
18 database from the participating vote centers totaled
19 23,982,000. This is from September 2015 through
20 December 2018. December 2018 is an important cut-off
21 because, as I'll talk about in a few slides, this would

1 be the data cut-off for some of the major analyses that
2 are being done in the program, particularly incidence
3 studies. Risk interviews are taking place regularly.
4 All HIV risk interviews for HIV-positive individuals,
5 there have been 144 interviews conducted so far; NAT
6 Yield, for hepatitis C, 28 interviews; for hepatitis B,
7 13 interviews; and all controls, 296.

8 With HIV Recency testing conducted for all of
9 the archive samples, as well as ongoing for the accrued
10 HIV-positive samples in TTIMS, 1,012 tested of which
11 close to 400 have been within the TTIMS time period.
12 So, 2019 is going to build on this success of accruing
13 samples and data and serve as a major analysis year.
14 The major analyses targeted for this year will be based
15 on two years of data and adequate power to assess
16 prevalence and incidence time trends surrounding the
17 MSM 12-month deferral change.

18 So, the pre-MSM 12-month period -- TTIMS
19 defined data are available from September 2015 when the
20 policy change was published through the implementation
21 time period of 2016. This is defined as the blood

1 establishment "pre" period, because the centers changed
2 policy at different times within 2016. Then, the post-
3 MSM period for a 12-month deferral is defined as
4 December 31, 2018. And this establishes a minimum 2-
5 year time period for follow-up after blood
6 establishment implementation at each of the
7 participating sites.

8 That's complex in a verbal description, but
9 shown here is a diagram of implementation of the MSM
10 12-month policy change at the TTIMS sites. The bottom
11 is a timeline for TTIMS with implementation beginning
12 at September 2015 out through the end of 2018. The
13 pre-MSM 12-month policy period really runs through
14 August 8th of 2016 when the New York Blood Center
15 changed policy, followed by Vitalant, OneBlood, and
16 then Red Cross on December 12th, 2016. So, through
17 December 12th, 2016, this comprises the pre-period, and
18 then following that period, then, through the end of
19 2018 is the 2-year post period.

20 So, this was designed to provide adequate data
21 and adequate power to conduct incidence analyses, which

1 is one of the major intents of the program. The
2 analytic strategies for 2019 related to the policy
3 change is, first, to continue the donation prevalence
4 calculations by different strata, including first-time
5 and repeat donors, sex, and US Public Health region.
6 Second is the classical incidence calculations done for
7 repeat donors by two different methods.

8 The first is to use equal MSM pre-
9 implementation periods at each of the centers, along
10 with some stated assumptions as to why this method
11 could potentially result in different results from
12 other methods. Then, the second method is to use
13 modeling to minimize the bias related to the use of the
14 true different policy implementation dates along with
15 certain assumptions.

16 The whole idea of using the two different
17 approaches is to really try to minimize bias because of
18 these staggered implementation times. Since donation
19 intervals are critical to the calculation of incidence
20 -- and these would vary depending on the time periods
21 involved -- it's important to consider this as a

1 potential source of bias when they differ.

2 A third major analysis is estimates of first-
3 time HIV donor incidence by using LAg avidity testing
4 to estimate mean duration of infection. This will be
5 done to determine data for recency of infection, but
6 then modeling will be needed to estimate the HIV
7 incidence as determined in first-time donors. There
8 are discussions underway to determine the best way to
9 conduct this modeling for this particular population.

10 Then, finally, using the resources established
11 as I mentioned, the donor and control risk interviews
12 from the program will be assessed in the context of the
13 marker data and ultimately in comparison with the 2004
14 to 2009 REDS-III data from a very similar question
15 there to look at behavioral risk factors involved with
16 infection and potential trends over time.

17 An initiative developed this past year within
18 the LRCC is to look at pre-exposure prophylaxis and
19 antiretroviral therapy in donated samples from a
20 targeted set of current donors as well as HIV-positive
21 donors for ARV treatment. The reason for this is pre-

1 exposure prophylaxis for high-risk exposure and
2 antiretroviral therapies for HIV infection are highly
3 effective medications. However, dosing compliance
4 failures can result in incomplete protection, and the
5 theoretical possibility of transmissible HIV infection
6 in blood that may not be detected by current blood
7 establishment screening.

8 This is only theoretical. This has not been
9 observed. But TTIMS felt it was important to establish
10 a basis for whether or not some of the HIV seropositive
11 individuals identified were on ARV treatment, or some
12 of the seronegative individuals who are donating are
13 currently using PrEP. So, for the PrEP study, TTIMS is
14 studying PrEP use among current donors.

15 This was in collaboration with the Office of
16 HIV/AIDS at the Centers for Disease Control and
17 Prevention. This uses high-pressure liquid
18 chromatography techniques to assess the presence of
19 PrEP or PrEP metabolites in an initial sample of 1500
20 anonymous but geographically targeted first-time male
21 donors. These are being tested anonymously and this

1 testing is underway.

2 The second program is to study antiretroviral
3 use among HIV-positive donors, also in collaboration
4 with Centers for Disease Control and Prevention. This
5 will use all newly identified HIV-positive samples
6 within TTIMS as well as the archive samples. Results
7 should be available for these studies in the coming
8 year.

9 So, in summary, since its initiation in
10 September 2015, TTIMS has established a comprehensive
11 and sophisticated monitoring capability for the safety
12 of US blood supply. Major analyses are planned for
13 2019 to assist prevalence, incidence, and risk factors
14 for HIV, hepatitis C virus, and hepatitis B virus
15 infection among both first-time and repeat donors, and
16 to assess time trends that may be associated with
17 policy changes, such as the change to an MSM 12-month
18 deferral.

19 TTIMS has been responsive to contemporary
20 needs for data related to pre-exposure prophylaxis and
21 antiretroviral therapy use among individuals who

1 you've made observations about compliance, I was
2 wondering if you knew if there were any similar
3 pressures, I guess, on people to actually answer the
4 questions truthfully.

5 **DR. GOLDMAN:** I'm not sure I'm the best person
6 to answer that question. I mean, many of us have, on
7 our questionnaire, some legalese at the bottom, right?
8 That said that I understood the donor materials, which
9 is the pamphlet, basically, that we have, and I
10 answered the questions to the best of my ability, and
11 I'm aware I could harm somebody if I didn't. So, we do
12 have -- in Canada, for example, we have verbiage around
13 that. And I know Australia has very similar, and so do
14 a lot of other countries. How legally binding that is,
15 I don't know.

16 The compliance studies are usually anonymous
17 and often done by a third party. For example, we use
18 Ipsos Polling to do the compliance study because we
19 don't want our name on it, so we can't really trace
20 back the answers for the compliance study to a given
21 donor. We just ask the donor certain demographic

1 questions on the compliance studies so we can say, oh,
2 well, this was a male first-time donor because they
3 told us that on the study. But we can't link to their
4 blood record.

5 That would be the same with any of the other
6 blood suppliers doing those compliance surveys.
7 They're supposed to be anonymous to encourage people to
8 be more truthful than they, maybe, were when they
9 answered the questionnaire in the donor clinic. I'm
10 not sure that answers your question, but --

11 **DR. KAUFMAN:** Dr. Schreiber.

12 **DR. SCHREIBER:** This is a follow-up question
13 to the last question. I think honesty is one issue,
14 but the other issue is accuracy. I mean, people don't
15 generally keep records of the last time they had sex.
16 It's been a while, yes, but has it been a year? Has it
17 been 2 months? What about accuracy? How do you -- I
18 mean, how is that calculated into the equation? Some
19 people just don't remember the last time.

20 **DR. GOLDMAN:** Yeah, I think that becomes an
21 issue when you're talking about especially more

1 complicated behavior-based questions and you're
2 starting to ask people about how many partners and
3 details about those partners and so on. I think, if
4 you have a very long time period, it really can't be
5 done. You know? So, to ask people, in the last 12
6 months even, about number of partners and were those
7 partners having other partners and everything, I think
8 it gets very sticky. I mean, not if the answer is no
9 and you're talking about boring 50-year-olds. But if
10 you're talking about young people that are getting it
11 on, I think it's not realistic.

12 If you have a shorter period, I think you
13 would get more accurate because people will remember
14 more. We know, even with things like tattoos and
15 piercings, people forget to tell you about ones that
16 happened 11 months ago or even 4 months ago. You
17 shorten your deferral period and you don't have half
18 the number; even your deferral period is half. So why
19 is that? It's because they were telling you about the
20 ones that happened more remotely.

21 So, as the period is shorter, I think people

1 do remember more behaviors. On the other hand, to say
2 exactly when something was, if it was 2 months or 3
3 months, I think that's a problem with all our criteria,
4 that we ask about a lot of time periods and whether
5 people are really doing all that math in their head for
6 all those time periods is probably not that realistic
7 either.

8 **DR. KAUFMAN:** Dr. Baker?

9 **DR. BAKER:** Thank you, and thanks to all the
10 speakers for great presentations. I had a couple
11 questions for Dr. Williams. Thanks. On the TTIMS
12 system, the geographic spread -- can you tell us a bit
13 of -- you know, in light of the FCDC epidemiology of
14 HIV, and happening in the South and to Hispanics and
15 blacks more prominently than other populations, what
16 actually is the geographic coverage of TTIMS? Given
17 that you say that it's 60 percent estimated US
18 population, where exactly in the country?

19 **DR. WILLIAMS:** TTIMS is comprised of major
20 blood systems such as American Red Cross and Vitalant,
21 and these systems tend to be some favoring the

1 different regional representations. But the high
2 prevalence areas, particularly in the South and
3 Florida, are represented within TTIMS. Even, for
4 instance, Vitalant, which is a West Coast operation,
5 has centers throughout the country. So, in terms of
6 population representation of donors within TTIMS, I
7 think we probably need to calculate that a little more
8 finely.

9 On the other hand, I would say the entire
10 country is represented within the program, whether it's
11 an equal numerical representation, I think it needs to
12 be determined.

13 **DR. BAKER:** And the same thing with
14 race/ethnicity, particularly with reference to the
15 South and/or the West?

16 **DR. WILLIAMS:** That would really come along
17 with the demographics. We don't target any certain
18 race or ethnicity within entry into the program. We're
19 covered, certainly, for urban areas and certainly for
20 the Midwest and the coastal regions. But there's no
21 specifically targeting to enhance racial or ethnic

1 subpopulations.

2 **DR. BAKER:** And one more question to clarify -
3 - in terms of governance and public access, for
4 governance, are there any -- can you tell me a bit
5 about any advisory groups or avenues for end user or
6 consumer input?

7 **DR. WILLIAMS:** Well, we certainly have this
8 committee. And I suspect, over the course of time,
9 there will probably be data sharing within the HHS-
10 level advisory committee. Other than that, there's not
11 a formal association with other advisory groups. But
12 certainly, all of the data is presented publicly,
13 generally as soon as it's available.

14 **DR. BAKER:** And one more, if I may. Any
15 thoughts about any discussions internally about plans
16 for some kind of public-facing real-time information
17 about what's happening in TTIMS or a public-facing
18 minimal database -- data visualization about what's
19 going on on a real-time basis?

20 **DR. WILLIAMS:** I guess the core answer is no,
21 that hasn't been discussed. Because real-time, within

1 a large epidemiologic program like this, is relative
2 often by the time the data gets cleaned, available for
3 analysis, needing what you want to obtain for power,
4 your months to year -- you know, a year or so after.
5 So, real-time is relative. But it's certainly
6 something that could be -- you know, see if there are
7 possibilities to do that. There would be an advantage
8 to it.

9 **DR. BAKER:** Thank you.

10 **DR. HOLLINGER:** Can you stay there a minute
11 again? Sorry. Blaine Hollinger. I have about 3
12 questions. What are you anticipating will be the
13 percentage of first-time donors here in these things?
14 20 percent more? Less?

15 **DR. WILLIAMS:** First-time donors overall?

16 **DR. HOLLINGER:** Yep.

17 **DR. WILLIAMS:** A little better than 20
18 percent. Historically, it's been 20; I think that it
19 might be moving a little bit higher.

20 **DR. HOLLINGER:** Yeah. And also, when you were
21 talking about PrEP and antiretroviral use, how many

1 patients actually come in and -- people, donors are
2 coming in and donating that are on PrEP or
3 antiretroviral? That's a little -- that's a pretty
4 high-risk group.

5 **DR. WILLIAMS:** Well, that's not known at this
6 point. That's what the studies are to determine.
7 There's a certain increase to power in using biomarkers
8 to assess a person's individual status in contrast to
9 what answers are given on a questionnaire or other
10 interview format. So, that's exactly what these
11 studies are designed to look at -- ARV use in known
12 HIV-positive individuals who are identified, and PrEP
13 use in a targeted set of individuals who come in,
14 answer the behavioral question, and provide blood
15 samples.

16 **DR. HOLLINGER:** Yeah. And medication use is
17 asked on the questionnaires usually, yeah.

18 **DR. WILLIAMS:** Medication use is asked. These
19 particular drugs are not at this time.

20 **DR. HOLLINGER:** Yeah. And then, the final
21 one, can you tell me after you get this data, and

1 looking at particularly the question about whether the
2 time deferral can change from 12 months to something
3 less or so on, how do you anticipate this data is going
4 to be helpful? I mean, where is it -- what are you
5 looking for to provide that kind of information, if we
6 were trying to say we would -- we're making this
7 decision?

8 **DR. WILLIAMS:** I think it's hard to pin down
9 particular aspects that would strongly influence a
10 policy. I think it's really considering everything --
11 the behavioral risks that are known to continue
12 contributing to ongoing risk coming into the blood
13 centers, what the actual incidence is overall, both in
14 repeat and first-time donors, whether there's any sort
15 of trend associated with that.

16 I think the ARV and pre-exposure prophylaxis
17 data will provide some input in using biomarkers to
18 determine risks that we were otherwise unaware of. I
19 think you really have to consider all aspects and where
20 interventions might still be necessary and where
21 there's been progress.

1 **DR. KAUFMAN:** Okay, thank you. All right.

2 Dr. Lewis?

3 **DR. LEWIS:** Two questions. The first has to
4 do with the study we're using, HPLC, to look for
5 evidence of PrEP among 1500 selected first-time male
6 donors. I was just jotting out the two-by-two table
7 I'd do if I was trying to do a case control study to
8 determine whether PrEP was a risk factor for being in
9 the window versus a protective factor, because it could
10 go either way. In filling out that table, I thought
11 the population you most need to figure out is the
12 population that are HIV infected.

13 So, what I was wondering, was those 1500
14 subjects unselected? Or were those conditioned on
15 being seropositive?

16 **DR. WILLIAMS:** The study of 1500 for pre-
17 exposure prophylaxis are accepted donors. So, those
18 are not seropositive donors -- conditioned on not being
19 seropositive.

20 **DR. LEWIS:** Is there any effort to over-sample
21 those -- because, you know, it's a very small number

1 who are seropositive. I think you probably need to
2 over-sample those.

3 **DR. WILLIAMS:** Yeah. It's true. It's
4 potentially a very rare event and a limited sample.
5 You could consider it almost a pilot study. I think we
6 have an estimated prevalence estimate of between 0.5
7 and 1.5 percent that we can get with a reasonable
8 confidence interval, but we have no idea, at this
9 point, what the prevalence might be. So, this was just
10 an initial pilot effort. We could run larger studies
11 and do over-sampling if we find that's appropriate.

12 **DR. LEWIS:** Do you have access to stored serum
13 or plasma from HIV-positive donors' donations?

14 **DR. WILLIAMS:** Yes. As I mentioned, there are
15 a total of over a thousand.

16 **DR. LEWIS:** That would seem like a wonderful
17 biobank on which to run the HPLC. It helps you with
18 your estimate.

19 **DR. WILLIAMS:** And in fact, we are -- I'm not
20 that familiar with the HPLC, but I think there is a
21 certain amount of overlap between the results between

1 the PrEP therapy and the ARV. So, I assume that can be
2 distinguished at the HPLC level. But I think you
3 wouldn't get a complete negative on one versus the
4 other.

5 **DR. LEWIS:** Okay. And in the answers to the
6 prior -- this is a new question. In the answers to the
7 prior question, you talked about biomarkers. Can you
8 just be more explicit? When you use that term, what
9 are the list of things that are your top 2, 3, 5, 12
10 biomarkers? Hopefully not 12.

11 **DR. WILLIAMS:** Okay. Well, certainly, TTI
12 markers, both antibody and nucleic acid testing. I
13 think any biomarker which could determine the status of
14 an individual from a biological standpoint, and use in
15 comparison with answers given to particular questions
16 which might answers to biomarker.

17 **DR. LEWIS:** I'm asking for specifics.

18 **DR. WILLIAMS:** Specifics, I'm not sure I fully
19 understand.

20 **DR. LEWIS:** Okay. I'll just say, I don't
21 understand what you mean by that phrase, so I'm hoping

1 you're going to help me understand.

2 **DR. WILLIAMS:** I'm talking about a biological
3 marker that's detectable in a validated, reproduceable
4 way in a subject from a biological specimen.

5 **DR. LEWIS:** I know the definition of a
6 biomarker. What I'm asking is what -- in terms of
7 biomarkers that you would measure that would help you
8 understand where there's a disparity between an answer
9 given on a questionnaire and the person's actual
10 behavior, I'd like some examples of those. The
11 presence of a drug, I get. I'm looking for the things
12 farther down the list.

13 **DR. WILLIAMS:** Okay. Perhaps I could give an
14 example.

15 **DR. LEWIS:** Great.

16 **DR. WILLIAMS:** The CDC HIV/AIDS group runs an
17 HIV behavioral survey. They just published a
18 manuscript in AIDS this year that showed of individuals
19 who, when interviewed, indicated that they were
20 negative for HIV or had not been diagnosed. When
21 studied for ARV, half of the individuals were found to

1 be on the ARV treatment. So, that sets up the
2 situation where individuals who indicated that they had
3 not been diagnosed or were negative for HIV had
4 evidence of antiretroviral treatment in their blood,
5 and one needs to figure out that disparity.

6 **DR. LEWIS:** No, I understand that. Other than
7 medications, can you give an example of another
8 biomarker? Because you used a general term, and I'm
9 trying to find out if you just used that to mean drugs,
10 therapeutic drugs that are antiretrovirals or used in
11 PrEP, or you mean something else.

12 **DR. WILLIAMS:** I'm specifically using it to
13 reflect drug, yes.

14 **DR. LEWIS:** Thank you.

15 **DR. WILLIAMS:** Okay.

16 **DR. KAUFMAN:** All right. So, we're going to
17 take a short -- oh, sorry. One last question. Dr.
18 Ortel.

19 **DR. ORTEL:** Hopefully brief, for Dr. Brooks.
20 Just a question about -- you gave us data on incidence
21 and lifetime risk for HIV diagnoses by showing

1 differences in race and ethnicity, and then also in
2 geographic location. Are those considered independent
3 variables? Or do those reflect demographics in those
4 regions?

5 **DR. BROOKS:** Those are -- well, they're --
6 yeah, it's hard to say independent variables because
7 it's not really -- we're not predicting anything. But
8 they are representative of the demography of the
9 populations where this is occurring. Certainly, many
10 people can fulfill multiple criteria. You can have an
11 African American woman living in Alabama. But they're
12 demographic characteristics. And the crossover I
13 showed between race, ethnicity, and age was the one
14 that concerns us the most. Does that help? Yeah?
15 Okay.

16 **DR. KAUFMAN:** Okay. Meera, any questions?

17 **DR. CHITLUR:** No, thank you.

18 **DR. KAUFMAN:** Okay. So we're going to go
19 ahead and take a short break and reconvene at 10:35.
20 Thank you. I'd like to thank all the speakers.

21

1 **BREAK**

2 **PRESENTATION OF THE HIV RISK QUESTIONNAIRE STUDY**

3 **DR. KAUFMAN:** I'd like to ask everyone to
4 please take your seats. Can I get a gavel? All right.
5 Dr. Chitlur and Dr. Stramer, are you able to hear?

6 **DR. CHITLUR:** I'm able to hear. Thank you.

7 **DR. STRAMER:** Yes, I can hear.

8 **DR. KAUFMAN:** Thank you. All right. Just to
9 stay on time, I would like to get going again. And I'm
10 pleased to introduce the next speaker who is Dr. Barbee
11 Whitaker from FDA, and she'll be talking about the
12 donor HIV risk questionnaire study.

13 **DR. WHITAKER:** Good morning. Thank you. I'm
14 Barbee Whitaker with the Office of Biostatistics and
15 Epidemiology, and I will be talking about this donor
16 HIV risk questionnaire study. So, to reiterate, the
17 principles that FDA will use to move forward with the
18 MSM policy are the following. We're committed to an
19 ongoing evaluation of the deferral policy for MSM and
20 to potentially advancing policy based on available
21 scientific evidence. We're also committed to

1 maximizing the transparency of the process through
2 stakeholder engagement and the use of public advisory
3 committees such as this. This process will be based on
4 gathering necessary scientific information while
5 ensuring the continued safety of the blood supply.

6 So, this study that I'm going to talk about
7 today is a pilot study. The idea is to cover, today,
8 the description of the pilot study, the scope of work
9 that will be presented here and then in the future, and
10 looking at gathering population-based risk behavior
11 evidence. I have a little bit of an update on this
12 following bullet, which is that the Sources Sought
13 notice was published on Friday on the FBO.gov site, and
14 it has a deadline -- it was published last Friday,
15 March 15, and it has a deadline of March 29. So, we do
16 have something that has been -- that is available for
17 you to look at on FBO.gov.

18 So, in background, Dr. Eder and others have
19 covered the deferral history, both in the U.S., and Dr.
20 Goldman covered the international background for MSM
21 deferrals and other approaches to MSM safety. And I'd

1 like to remind you that there is non-compliance with
2 the lifetime deferral that was, in the blood drop
3 study, that was about 2.6 percent reported in the
4 United States. And we don't have any updated data for
5 non-compliance in the U.S. since the 12-month deferral
6 was implemented. So, we feel there's a need for
7 population-based evidence on which we can base any
8 further regulatory decisions to be sure that we ensure
9 blood safety.

10 So, I'll go through the details of this HRQ,
11 High Risk Questionnaire, study, including more
12 background on the study, purposes, study design,
13 objectives, and so on. So, the background for this
14 pilot study -- it was designed through a collaborative
15 process to assess potential risk of alternative donor
16 deferral strategies for MSM. It may help determine the
17 feasibility and size of a larger study to assess
18 whether reduction or elimination of the donor deferral
19 interval for MSM is possible in the United States. And
20 the larger study criteria are the identification
21 through this pilot study of a set of behavioral

1 questions and responses associated with the absence of
2 detection of recent HIV infection.

3 The purpose of the study is to provide us with
4 evidence by which to consider these changes to the MSM
5 deferral policy while maintaining the safety of the
6 blood supply. Our primary objective is to assess the
7 discriminate function of a list of behavioral history
8 questions for predicting recent infection with HIV in
9 MSM who wish to donate blood. The secondary objectives
10 include evaluating the recency of HIV infection in
11 those individuals by ID NAT, individual NAT, and/or
12 antibody testing and identifying risk factors
13 associated with recent HIV infection in individuals who
14 are antibody negative yet HIV NAT positive, so the NAT
15 yield donors for -- HIV NAT yield.

16 So, the outcome of this study may be that we
17 can identify certain low risk MSMS -- MSM population
18 that could be blood donors. The primary endpoint is
19 the number of individuals who are HIV NAT positive but
20 antibody negative. Secondary endpoints include the
21 number of overall HIV infections, the number of recent

1 HIV infections, and the correlation of responses to the
2 questions with HIV status.

3 So, we're looking for a study that will
4 include 2,000 men who have had sex with men at least
5 once during the past three months. This sample size
6 was chosen to increase the likelihood that a recent HIV
7 infection will be identified. Subjects will be
8 enrolled from 8 to 12 geographically distributed sites
9 with a high risk of HIV transmission among men who have
10 sex with men and --not the LGBTQ community but men who
11 have sex with men. The sites may be a combination of
12 clinical facilities and venue-based locations.

13 Pilot sites shall be selected from locations
14 in states and cities with the highest new HIV diagnosis
15 rates based on the 2017 CDC HIV epidemiology reports.
16 And some of the sites -- this might include states such
17 as the District of Columbia -- or districts -- Georgia,
18 Louisiana, Florida, and Maryland, which have rates
19 about 20 per 1,000 adults and adolescents of new HIV
20 infections. And the next category might include
21 Nevada, Texas, Mississippi, South Carolina, New York,

1 Alabama, Delaware, and North Carolina, which have rates
2 in the next tier, 15 to 20 per 100,000 adults and
3 adolescents. And then certain cities that have
4 particularly high rates of new infections include
5 Miami; Orlando; Atlanta; New Orleans; Baton Rouge;
6 Jackson; Jacksonville, Florida; Memphis, Tennessee;
7 Columbia, South Carolina; Las Vegas, Nevada; and
8 Baltimore, Maryland. But these are just a sample of
9 potential locations where this study could be carried
10 out.

11 The eligibility criteria -- inclusion criteria
12 -- we're looking for males greater than or equal to 18
13 years of age and able to provide informed consent who
14 have had oral or anal intercourse with a male partner
15 at least once during the past three months. They can
16 answer the study questionnaire, provide a blood sample,
17 and follow the study protocol, and, as I said before,
18 provide informed consent. The exclusion criteria
19 include men who have prior use of injection drugs ever,
20 exchanged sex for money or drugs ever, have a prior
21 documented history of HIV infection, or a diagnosis of

1 syphilis, gonorrhoea, or chlamydia during the three
2 months prior to enrollment. And the point of the
3 venereal disease exclusion is that that would normally
4 be accompanied by HIV testing as part of standard of
5 care and that, if they presented for the study, they
6 would be -- we would be biasing toward a negative
7 result. And that is assuming that they answered the
8 third question accurately.

9 So, for the study, there would be two study
10 encounters. The first would be the initial enrollment
11 materials, completion of the questionnaire, and a
12 collection of a seven-milliliter blood sample for
13 testing. The subject would return within 14 days for a
14 second encounter and receipt of test results, so that
15 would include a second interview, counseling and
16 referral if the subject is HIV positive. Study
17 questionnaire must be translated into Spanish, and OMB
18 and IRB approvals will be required. We can do a nine
19 subject pilot prior to the OMB approval to identify
20 issues associated with the questionnaire, in-person
21 delivery, and data collection methodologies.

1 So, the questionnaire -- we have five
2 questions on our questionnaire, and the first is how
3 many different sexual partners have you had sex with?
4 And that's defined as oral sex or anal intercourse
5 during the past one month, three months, and 12 months.
6 The second question is what kind of sex have you had
7 during the past month? Oral sex, anal penetrative or
8 receptive intercourse, both oral sex and anal
9 intercourse, or not sexually active during the past
10 month. The third question is, to your knowledge, have
11 you had sex with an HIV positive partner during the
12 past 12 months, yes or no? Do you always use condoms,
13 use condoms sometimes, or never use condoms? And the
14 last question is do you take pre-exposure prophylaxis
15 or PrEP? And if the answer is yes to that, when was
16 the last time that you took it?

17 So, these questions will be followed by HIV
18 testing by the investigator, including blood screening
19 for HIV using antibody and individual donor NAT
20 testing. If the subject is HIV positive, then recency
21 testing would be conducted for HIV. At the follow-up

1 visit within 14 days, there will be the interview to
2 collect HIV risk exposure from those who have positive
3 HIV tests of either NAT or antibody and counseling and
4 referral for those HIV positive subjects. There'll be
5 a sample repository established and maintained. The
6 investigator shall submit an analysis plan to the FDA
7 to include proposed data analyses, data specifications,
8 data and table structures, a statistical plan to
9 include any proposed modelling, and data quality
10 control procedures. The investigator should plan to
11 report to the FDA through monthly progress reports,
12 study site selection reports so that we have a good
13 understanding of where the geographic distribution is
14 proposed, a nine subject -- one the pilot for nine
15 subjects has been conducted, a nine subject pilot
16 report, regular test result reports, and then data
17 analysis reports including the mid-point, a draft, and
18 final report, and then -- of the data analysis, and
19 then a draft and final study report.

20 So, as I said before, the Source Sought
21 notification has been published, and that is due by the

1 end of March, March 29 in fact. The RFP will be posted
2 between May and June 2019. An award is expected in
3 fiscal 2019, so that would be by the end of September.
4 OMB and IRB approvals must be maintained. We'll need
5 to initiate enrollment of MSM in late 2019 to early
6 2020, with full enrollment within six months, which
7 would be late 2020, and then data analysis completed by
8 early 2021. I'd like to acknowledge my colleagues in
9 Office of Biostatistics and Epidemiology Anne Sieber
10 and then also the contributions of the Blood Equality
11 Working Group. Thank you.

12

QUESTIONS FOR SPEAKERS

13

14 **DR. KAUFMAN:** All right. Thanks. I'd like to
15 ask the committee if there are questions for the
16 speaker. Dr. Shapiro.

17 **DR. SHAPIRO:** I was just wondering if you had
18 had any focus groups, in the development of these
19 questions, to review them and look at the ability of
20 individuals to understand them, interpret them, and
21 answer them correctly.

1 **DR. WHITAKER:** So yes, there were focus groups
2 conducted, but one of the questions today is to discuss
3 the questions themselves.

4 **DR. SHAPIRO:** Okay. Two other questions. I
5 was wondering if you had considered, besides these
6 specific questions -- which individuals might have some
7 hesitancy to answer -- whether you considered having
8 all of the questions listed and, on the bottom, just
9 say yes or no, qualify or not, in terms of comparing
10 honesty of answers, overall, to the individual
11 questions?

12 **DR. WHITAKER:** I don't know whether that was
13 considered, but I think that there's some question
14 study design methodologies which suggest that each
15 question much be evaluated independently.

16 **DR. SHAPIRO:** Okay. And then, the third
17 comment was you said one of the possibilities for
18 recruitment of individuals might be at bars. I guess I
19 would be a little concerned about the use of alcohol
20 consumption or other drugs that might be prevalent in
21 those areas for recruitment of subjects.

1 **DR. WHITAKER:** Well, I think we're looking for
2 MSM who are interested in donating blood, so there are
3 lots of opportunities -- there could be other events,
4 festivals, gay pride events that might not include
5 consumption of alcohol or other drugs and that it's up
6 to the investigators to propose the way that they will
7 be recruiting their subjects. So, this is just an
8 example of --

9 **DR. SHAPIRO:** -- Right. I just might
10 discourage the use of bars.

11 **DR. KAUFMAN:** Sorry. So, as I understand it,
12 a goal of the study is to try to identify, within the
13 global MSM population, which is currently considered as
14 a single group, is there a low-risk population that can
15 be identified. So, I was wondering if you had
16 considered asking if MSM were married?

17 **DR. WHITAKER:** I don't know whether that was
18 considered, but certainly that's one of the questions
19 that we can discuss today as to whether that would
20 identify a lower risk population.

21 **DR. KAUFMAN:** I speculate that it might, but I

1 have no idea. Dr. Stapleton.

2 **DR. STAPLETON:** Similarly, monogamy would be -
3 - yeah.

4 **DR. WHITAKER:** Well, the number of sexual
5 partners question I think will get at that, so that's
6 one element of it.

7 **DR. KAUFMAN:** Dr. Baker.

8 **DR. BAKER:** Thank you. Can you tell us a
9 little about this Blood Equality Working Group, the
10 composition?

11 **DR. WHITAKER:** So, Dr. Eder had, in a slide
12 earlier on -- so it included representatives from the
13 LGBTQ community as well as blood collectors and public
14 health professionals, as well. And that was a little
15 bit before my time, so I don't know the exact
16 representation on that. But perhaps other could
17 comment.

18 **DR. KAUFMAN:** Can you comment a little about
19 the power calculations and how many individuals with
20 HIV that you anticipate finding -- or with recent HIV,
21 and maybe a little more detail about how you would

1 determine that ability of this questionnaire to
2 discriminate high risk from low risk?

3 **DR. WHITAKER:** Yes. So, hold on a second so I
4 can go to my notes. Okay. The idea is to find at
5 least one person in the high-risk cohort who is HIV NAT
6 positive but antibody negative, so in the HIV window
7 period. And this includes the highest risk incident
8 rate for HIV, which would be African-American MSM, and
9 the window period -- and also the window period
10 calculation, so being the three-day net between NAT and
11 HIV antibody negative -- so NAT positive, antibody
12 positive. Actually, I'm not sure if that three days is
13 completely accurate, but the annual infection incidence
14 for -- whoops -- for the African-American MSM was quite
15 high, about -- I have it here, but I can't read it.

16 **DR. KAUFMAN:** It's okay. I think it was in
17 the range of 20 per 100,000.

18 **DR. WHITAKER:** 20 per 100,000 or maybe even --
19 actually, I think it was 50 per 100,000 for black MSM.
20 So using the highest rate, we calculated that you would
21 have to have 2,000 subjects to be able to identify at

1 least one.

2 **DR. KAUFMAN:** Dr. Basavaraju.

3 **DR. BASAVARAJU:** If the target is only to
4 identify one, is that going to be enough to evaluate
5 whether each question is effective in identifying
6 enough infected MSM?

7 **DR. WHITAKER:** So this is a pilot study. So,
8 if we get any kind of indication that there is an
9 association between the questions and the test results,
10 that's going to give us an indication of whether we
11 should proceed to the full study where we would really
12 have the power to be able to discriminate each of the
13 questions.

14 **DR. KAUFMAN:** Actually, Dr. Bryant and then
15 Dr. DeMaria.

16 **DR. BRYANT:** Thank you for your presentation.
17 The question about the PrEP, will it be just -- is it a
18 yes/no? I think when you went through --

19 **DR. WHITAKER:** -- Yes.

20 **DR. BRYANT:** Are you going to get any
21 additional information if they answer yes, for how long

1 have they been on it or do they just take it
2 occasionally?

3 **DR. WHITAKER:** So, the question is a yes/no
4 question. The follow-up is "When was the last time you
5 took it?" And then, I think the -- so in the follow-up
6 -- 14 days later follow up period, if the subject is
7 HIV positive, either by NAT or by antibody, then there
8 will be additional questions about regular PrEP use and
9 so on -- compliance.

10 **DR. BRYANT:** Okay.

11 **DR. KAUFMAN:** Dr. DeMaria.

12 **DR. DEMARIA:** Probably the most important
13 determinate in terms of risk of exposure to HIV by
14 having a sexual partner who's HIV positive is going to
15 be whether that individual is virally suppressed or
16 not. And obviously, maybe the subject doesn't know
17 that, but it would be good to determine that to sort of
18 put that in the perspective of overall risk.

19 **DR. STAPLETON:** You mentioned that the
20 exclusion for a recent STI was -- one of those was you
21 wanted to not have positive HIV test. But for PrEP

1 recommendations, they also receive HIV testing on a
2 two, three-month basis. So, have you considered that?

3 **DR. WHITAKER:** Excluding for that? No.

4 **DR. STRAMER:** This is Susan Stramer. Can I
5 ask a question?

6 **DR. KAUFMAN:** Yes.

7 **DR. STRAMER:** So, thank you, Barbee. So, for
8 your solicitation, who are you soliciting or expecting
9 to respond to the RSP? Is it groups who have not --
10 who have synergy or who represent MSM population? I'm
11 just looking at who was supposed to respond to this.

12 **DR. WHITAKER:** So, for the Sources Sought,
13 that's the small business set aside approach. Sue, can
14 you mute your phone, please? Thank you. The Sources
15 Sought is directed towards small business and the other
16 categories that are included in that, but, for the next
17 step, we would be looking for community-based
18 organizations and, certainly, LGBT community-based
19 organizations and investigators who might have contacts
20 and good relationships within that community, as well.

21 **DR. KAUFMAN:** Okay. So, any other questions?

1 Dr. Ortel.

2 **DR. ORTEL:** Just a question about the way that
3 you've got your questions written. If the purpose of
4 question one is primarily to tell monogamous versus
5 non-monogamous -- and we've already talked about the
6 difficulty people might have with remembering numbers
7 over the course of a year, so the quality of the data,
8 if you're asking for a number -- would it just be
9 simpler to say one month, three month, 12 months -- one
10 or more than one, and then just have like a quick check
11 box? Or do you really think that putting 8 versus 12,
12 with a 12 month number, is going to give you data that
13 you could use?

14 **DR. WHITAKER:** So, this is -- these questions
15 are the proposed questions, and one of the requests for
16 the -- what we would expect to see in the response to
17 our solicitation request is indication about any
18 suggestions about questions and any further -- how you
19 would present them, what options you would give and so
20 on. So, I think that's still there. Yeah.

21 **DR. STAPLETON:** Sorry to go back to the PrEP

1 question, but since PrEP may also alter serologic and
2 nucleic acid testing results -- and I think we'll
3 probably discuss that more later -- would be my guess -
4 - it does seem maybe not to be a good -- that might be
5 an exclusionary thing you might think about because
6 they should be tested every three months. They are the
7 highest risk, but if they take PrEP, we have good data
8 that it's effective. So that may not -- you might --
9 do you have -- how important do you think that group
10 is, I guess, would be my question?

11 **DR. WHITAKER:** Well, yeah, I think that's to
12 be determined but certainly does give us an indication
13 of risk, perceived risk, and then the follow up
14 interview will provide additional information on the
15 results of the test, as well as the results of the
16 questions.

17 **DR. KAUFMAN:** Dr. Baker.

18 **DR. BAKER:** Hi. Thank you again. This
19 question, then, is for Dr. Eder. Again, this Blood
20 Equality Working Group -- can you give any more
21 information about which advocacy organizations

1 participate?

2 **DR. MARKS:** Hi, Peter Marks, FDA. So, this
3 was a group of a variety of different groups that was
4 put together that included public health
5 representatives from New York Department of Public
6 Health. It included several different advocacy groups
7 from -- with, actually, a national distribution,
8 including G-M-H-C, a couple of other that I can't
9 remember offhand. It included several academic
10 institutions, including people from University of
11 Alabama, University -- actually, from the Harvard
12 system, including some representation from MIT and also
13 from one of the California state universities. And
14 there were probably a mix of others. It was not a
15 deliberately -- one can't say that it was a nationally
16 representative group, but it was a group that came
17 together and discussed these questions. But there was,
18 I think, a -- I think it's safe to say that there was a
19 variety of opinions, in addition to -- it also included
20 certain blood collection -- blood collectors, including
21 representation from individuals from A-D-C and from New

1 York Blood Center. Thanks.

2 **DR. BAKER:** Thanks, and just a brief
3 clarifying. So, was there anybody that you recall, or
4 any groups, who used platelets, plasma products?

5 **DR. MARKS:** There were no users -- blood
6 product users on that group.

7 **DR. KAUFMAN:** Dr. Lewis.

8 **DR. LEWIS:** For Dr. Whitaker, I'm sort of
9 struggling with the -- and this is a hard study to do
10 because you're trying to understand the predictive
11 power of multiple questions that may interact. You're
12 trying to identify predictive power for ruling out a
13 rare event, and it's just tough. It just struck me
14 that, with a sample size of 2,000 patients, there may
15 be an opportunity to use the first 1,000 to figure out
16 what you shouldn't do with the next 1,000. And so what
17 I mean by that is that you may be able to find out from
18 the first 1,000 that there are populations you don't
19 want to include because you're not learning much from
20 them and focus -- I would gently suggest that the
21 agency consider suggesting a step-wise approach where

1 you split the sample and try to use what you learn in
2 the first some percentage of the sample -- to use your
3 resources as effectively as possible in the second half
4 because you're trying to squeeze as much information as
5 possible. And it's going to be very scarce.

6 **DR. WHITAKER:** Thank you.

7 **DR. STRAMER:** This is Sue Stramer, again. I
8 have one other suggestion for Barbee and the
9 questionnaire. There's nothing listed there about
10 querying partners and perhaps including partners in
11 this proposal.

12 **DR. MARKS:** Hi. Peter Marks, again. So that
13 was discussed at length, and the feeling was that that
14 was just not practical because it involves getting
15 someone who is not involved in this. And in addition,
16 in many cases, there're going to be multiple partners,
17 so it's basically trying to overreach and
18 overinterpret. So, we felt that -- the group was
19 pretty unanimous, and this has been discussed both with
20 other government agencies that it's too complex to try
21 to go after the participants' partners. We have to --

1 in the blood donor center, ultimately, the
2 questionnaire will be based on the individual at hand.
3 And so if we were to rely on partners' responses, that
4 could set up, again, something that's not generalizable
5 from the study.

6 **DR. KAUFMAN:** I wanted to ask if you'd
7 crunched the numbers for -- so assuming this study goes
8 forward as a pilot, how big is the anticipated
9 definitive study or larger study?

10 **DR. WHITAKER:** So, Peter's nodding, so the
11 definitive study -- I'm not sure yet.

12 **DR. MARKS:** Sorry. So, the numbers that have
13 been crunched before -- and that's why we need to do a
14 pilot study. It would be a relatively expensive study
15 on the order of something like 150 to 250,000 people,
16 depending on what you see. And I think is well taken
17 about wanting to essentially do this -- to refine
18 things as much as you can, so we appreciate that
19 feedback.

20 **DR. KAUFMAN:** Dr. Shapiro.

21 **DR. SHAPIRO:** Just one question. Is this

1 questionnaire administered in addition to the standard
2 blood donor questionnaire to these individuals in this
3 study?

4 **DR. WHITAKER:** No, it's just these five
5 questions.

6 **DR. SHAPIRO:** So, you're not asking about IV
7 drug use or other illicit drug use, which would also
8 include another high risk population?

9 **DR. WHITAKER:** Well, actually, the exclusion -
10 - so there would have to be some questions to identify
11 that they're appropriate for the study before we get
12 there. So, we're excluding the I-B-D-Us and getting
13 money for sex or drugs. So that would --

14 **DR. SHAPIRO:** -- But you're excluding it base
15 on what? Self-report?

16 **DR. WHITAKER:** Well, I mean, that's all blood
17 donors ever do is self-report.

18 **DR. SHAPIRO:** Right. But if you're looking at
19 specific questions that people either answer truthfully
20 or not and may represent an analysis for this, I think
21 you'd have to include that. Yes? No?

1 **DR. WHITAKER:** Include who? So, the excluded
2 population?

3 **DR. SHAPIRO:** Yes -- that they're self-
4 excluding -- that they're saying they're eligible
5 because they don't use, say, for example, IV drugs.
6 But then, you're going to look at these particular
7 questions, and then that one person who ends up
8 positive -- you may find a particular question -- I
9 don't know how you do that in one patient, but you find
10 power in a few questions. But it's actually a
11 surrogate marker for something else.

12 **DR. WHITAKER:** So that's one of the reasons
13 for the follow-up study, to really dig into how
14 truthful they were, should they have been excluded,
15 what risks do they have for HIV that might not have
16 been identified otherwise. So that second interview is
17 going to be very valuable.

18 **DR. STAPLETON:** Do you have plans to repeat
19 those questions at the 14-day visit, once the person
20 has met you or the questionnaire -- the team and is
21 more comfortable? Because that might be an opportunity

1 to seek out if they feel they were honest.

2 **DR. WHITAKER:** So, the investigator should
3 propose the discussion for the follow-up interview,
4 which would include what additional questions, what
5 kind of discussion, what kind of probing would be done.
6 And I would think that that would be a good approach to
7 make sure that they hadn't lied there or misunderstood
8 the question.

9 **DR. STAPLETON:** And would the people applying
10 for this R-F-P have the opportunity to propose to save
11 samples for future use for --

12 **DR. WHITAKER:** Yes. In fact, that is one of
13 the criteria. Yes.

14 **DR. KAUFMAN:** Dr. Shapiro.

15 **DR. SHAPIRO:** So, are you testing for HCV and
16 HBV in these samples, as well?

17 **DR. WHITAKER:** No, just HIV because that's the
18 population of concern for HIV.

19 **DR. KAUFMAN:** I just want to echo Dr.
20 Stapleton's comment. There was a paper from the
21 Italian group that looked at individuals who had

1 donated, tested HIV positive, and then, on re-
2 interviewing them, there was some really valuable
3 information that was learned about did they interpret
4 the questions right. And it was actually, in that
5 particular study, a fairly high percentage of people
6 didn't feel that some of the questions applied to them.
7 So I think that probably would be a really valuable
8 thing to do.

9 **DR. WHITAKER:** And I think Dr. Eder said this
10 morning that the donors interpret the questions as "Is
11 my blood safe?" not each one of the details of the
12 questions. At least, that's been shown in some of the
13 studies.

14 **DR. KAUFMAN:** Dr. Basavaraju.

15 **DR. BASAVARAJU:** So, I had a question about --
16 in the situation where a person states that they only
17 have one sex partner, have you thought about asking
18 whether they think the sex partner has only one partner
19 as well or whether the partner may have multiple
20 partners, as kind of a marker as to the person they're
21 having sex with is high risk?

1 **DR. WHITAKER:** I don't know whether that was
2 actually considered in the working group, but I think
3 that there are certain questions about trustworthiness
4 and how much can you really ever know -- that, you
5 know, it's the same with a heterosexual couple.

6 **DR. STAPLETON:** But I take -- a lot of my
7 patients say "I'm monogamous, but my partner's not."
8 They're quite open -- people I know well that I've
9 taken care of for years. But yeah.

10 **DR. KAUFMAN:** Dr. Baker.

11 **DR. BAKER:** Thank you. And have you thought
12 about, in the design, to oversample for African-
13 Americans and Hispanics?

14 **DR. WHITAKER:** So, we're asking the
15 investigator to propose high risk populations from
16 which we can capture this, and I would anticipate that
17 that would be the case. And certainly, with the
18 geographic distribution, we would hope to see that.

19 **DR. KAUFMAN:** Dr. DeVan.

20 **DR. DEVAN:** I just have two questions. Do you
21 think you'll need to translate it into any other

1 languages other than just English and Spanish? And
2 then the second question is question 4B to me just
3 seems to be formatted a little differently than
4 question 4A and 4C, just grammatically seems to have
5 the adverb as the end. So maybe just for consistency,
6 you could switch it.

7 **DR. WHITAKER:** Thank you, and regarding the
8 other languages, I mean, I think mostly English and
9 Spanish. And otherwise, that would be an additional
10 exclusionary category.

11 **DR. KAUFMAN:** Can you comment as to whether
12 this type of study has been done elsewhere?

13 **DR. WHITAKER:** Hmm. I don't think so.

14 **DR. STAPLETON:** One last thought. Not having
15 thought through this, I don't have a lot of good
16 suggestions, but since you're going to have this
17 opportunity, will applicants have the opportunity to
18 propose additional questions? Or is this fixed that
19 these will be the five questions that will be asked?

20 **DR. WHITAKER:** It's fixed.

21 **DR. STAPLETON:** It seems like it might be an

1 opportunity to get additional information, so I don't
2 know.

3 **DR. WHITAKER:** I think we'd like to see the
4 follow-up interview really digging into any additional
5 questions and any additional risk factors, and that
6 would be the area where we would see more information
7 coming. And as we said, this is framed as pilot study,
8 so what we learn here could potentially be taken into a
9 larger context.

10 **DR. STAPLETON:** Okay. But the follow-up, 14
11 day, they can ask much more extensive questionnaire.

12 **DR. WHITAKER:** It's more of an interview, a
13 discussion, rather than just a questionnaire.

14 **DR. STAPLETON:** Okay.

15 **DR. KAUFMAN:** Dr. Baker.

16 **DR. BAKER:** But on that follow-up
17 questionnaire, do you have a structured interview
18 already created, and how fixed is that?

19 **DR. WHITAKER:** Not at this time, so that would
20 be part of the proposal.

21 **DR. BAKER:** Thank you.

1 **DR. KAUFMAN:** Dr. Bryant.

2 **DR. BRYANT:** You mentioned that you would go
3 to these areas where you felt like you would be able to
4 recruit the most people to fill out the survey. Are
5 you going to have fliers? Are you going to put it out
6 on some of the websites that might services this
7 community? Or how are you going to --?

8 **DR. WHITAKER:** So that would be up to the
9 investigators' proposal, how they would be recruiting
10 their sample.

11 **DR. KAUFMAN:** Dr. DeMaria.

12 **DR. DEMARIA:** There's been a lot of experience
13 with venue-based recruitments. I think using that --
14 whoever applies for this, probably, will have that kind
15 of experience.

16 **DR. KAUFMAN:** Any further questions from the
17 committee? Dr. Shapiro.

18 **DR. SHAPIRO:** I just wondered if you
19 considered adding a question regarding the use of
20 alcohol or any other agent during sexual encounters
21 because that's a risk factor for lowering inhibitions and

1 breakdown of safe sex practices.

2 **DR. WHITAKER:** I don't think that has been
3 considered. It may have been considered, but it was
4 not suggested by the community -- or the group that
5 recommended the questions.

6 **DR. KAUFMAN:** Dr. Baker.

7 **DR. BAKER:** And was there any discussion about
8 including any questions about donating blood within the
9 scope of the questionnaire?

10 **DR. WHITAKER:** So, the population of interest
11 is MSM who are interested in donating blood, so I think
12 that would be part of the recruitment. You would want
13 to gather information from people who think they would
14 be able to donate, so hopefully, that is a safer
15 population.

16 **DR. KAUFMAN:** Although, I suppose you could
17 ask "Have you donated before?"

18 **DR. WHITAKER:** Mm-hmm. In your recruitment --
19 or as you go through your inclusion subject criteria.

20 **DR. KAUFMAN:** Drs. Chitlur and Stramer, do you
21 have any final questions for the speaker?

1 group that may be affected by the topic of this
2 meeting. If you don't have any such interest, also,
3 FDA encourages you to state that for the record. If
4 you choose not to address this issue of financial
5 relationships at the beginning of your statement, it
6 will not preclude you from speaking, and you may still
7 give your comments. Okay. So, I'd like to invite
8 Richard Benjamin from Cerus to speak.

9 **DR. BENJAMIN:** Thank you, Dr. Kaufman. I was
10 of the impression that my -- that my topic might be
11 better after the MSM -- this afternoon's discussion.

12 **DR. KAUFMAN:** Yeah. That's fine, actually, if
13 you would like to speak after that.

14 **DR. BENJAMIN:** Thank you.

15 **DR. KAUFMAN:** I'd like to ask, then, for
16 Daniel Bruner to speak from Whitman-Walker Clinic in
17 D.C.

18 **MR. BRUNER:** Good morning, Dr. Kaufman and
19 members of the committee. Thank you for this
20 opportunity to address you briefly. My name is Daniel
21 Bruner. I'm the Senior Director of Policy at Whitman-

1 Walker Health here in Washington, D.C., and I have no
2 relevant financial interest or conflicts. Whitman-
3 Walker is a non-profit community-based health system
4 serving the greater Washington, D.C. metropolitan area.
5 We provide outpatient medical and behavioral
6 healthcare, dental care. We have two pharmacies,
7 community health services, youth services, legal
8 services, and other health related services. We have
9 more than 20,000 individuals and families who received
10 those services last year.

11 We specialize in HIV treatment and prevention
12 and the health and wellness needs of the lesbian, gay,
13 and bisexual and transgender community, the LGBT
14 community. Responding to the HIV epidemic has been at
15 the center of our mission for four decades, since the
16 first AIDS cases, even before it was known as AIDS, in
17 Washington, D.C. We currently have more than 3,500 HIV
18 positive patients, including more than 25 percent of
19 all of the people living D.C. with an HIV diagnosis.
20 We provide low barrier HIV and STI testing and
21 counseling services at all of our sites and throughout

1 the metropolitan area, and we operate regular walk-in
2 STI clinics, as well. We have more than 1,000 patients
3 who are currently on PrEP, and we recently instituted a
4 low barrier PrEP clinic to make it easier for
5 individuals who would benefit from PrEP to start and
6 adhere to that therapy. We've also been involved since
7 the 1980s in clinical research of HIV treatment and
8 prevention modalities and issues related to LGBT
9 health.

10 Policies that effect men who have sex with men
11 who identify as gay or bisexual, or otherwise identify
12 as non-heterosexual, have been of great importance to
13 us since the very beginning. Last year, almost 70
14 percent of our male patients who identified their
15 sexual orientation identified as non-heterosexual, gay,
16 homosexual, bisexual, or other. We've followed the MSM
17 blood donation policy since the 1980s, and we were
18 involved in submitting detailed comments in 2015, which
19 resulted in the change of policy to a one-year
20 deferral, and then also in 2016, as well, when the new
21 proceeding was instituted. And we've been an active

1 participant in the Blood Equality Working Group since
2 that was started in 2016 -- the group that's been
3 referenced several times this morning.

4 For many years, the policy of deferring blood
5 donations from all gay and bisexual men who've engaged
6 in any same-sex sexual activity, even decades earlier,
7 regardless of the type of sexual activity or the
8 likelihood of HIV transmission, was widely perceived in
9 the LGBT community as stigmatizing. And although there
10 certainly has been improvement, the current one-year
11 deferral policy still excludes many individuals who
12 pose no risk whatever to the blood supply on the basis
13 of their sexual orientation alone. We certainly
14 support enthusiastically the FDA's efforts to explore
15 how a focus on specific risk related behaviors the
16 individual donors could continue to protect the safety,
17 purity, and potency of the blood supply without
18 labeling people as high risk based only on their sexual
19 orientation. So, we're very excited by the potential
20 of this proposed HIV risk questionnaire study to inform
21 future blood donation policy, and we look forward to

1 opportunities to continue to be of assistance to the
2 agency in this really important endeavor. Thank you.

3

4

OPEN COMMITTEE DISCUSSION

5

6 **DR. KAUFMAN:** Thank you. All right. So, at
7 this time, is there anyone else from the public that
8 would like to make a comment? Okay. So, hearing none.
9 We will now move to an open committee discussion, and
10 really, I'd just like to encourage everyone on the
11 committee to contribute your thoughts to this really
12 complicated area. So, the first question for committee
13 discussion is to comment on what has been learned from
14 implementing other MSM policies internationally, such
15 as risk-based deferral methods or quarantine to retest
16 for plasma, and how this information can inform the
17 current U.S. MSM deferral policy.

18 Why don't I -- I have one thing that I wanted
19 to ask about or maybe just comment on -- is I thought
20 that the approach --the risk-based deferral methods
21 that were put in in Italy and Spain were interesting.

1 These were put in without any data to support them.
2 They were just instituted, and it's only
3 retrospectively or after having done this that it's
4 possible to go back and see how well these approaches
5 have worked or didn't work. One thing that caught my
6 attention was the -- related to something that Dr. Eder
7 talked about at the beginning, which was that the rate
8 of HIV per 100,000 in the general population in the
9 U.S. is pretty high, over 100. I'm not exactly sure
10 what the sort of exact number is. You get about a one
11 log or a ten-fold reduction using the current screening
12 methodology that we're using, such that first time
13 donors have an HIV rate of approximately 8.8, maybe 10
14 per 100,000. And then the rate is about another log
15 lower among repeat donors, since they get tested at the
16 time of their donation. And that will catch most,
17 although not quite all, of HIV infected individuals.

18 So, the thing that caught my attention was in
19 the Spanish study. It looked like the rate in the
20 general population was really not so different than the
21 rate among donors. The authors of this one study --

1 and again, it was just one paper, though, comment that
2 they were concerned that it didn't look like they were
3 getting any real safety benefit from their strategy.
4 So, I don't know if Dr. Goldman will want to maybe
5 comment on that and if that's been seen in any other
6 studies.

7 **DR. GOLDMAN:** Hi. Yeah. I think you've
8 nicely summarized it. If you see the same rate in your
9 first-time donors as in the general population, you
10 have to ask yourself what are you doing with your
11 screening? The other thing that's sort of interesting
12 is we actually defer very few donors for MSM, so most
13 of the screening that's happening is a self-deferral of
14 people who know that they are in a risk group for
15 donation and are just not coming into the clinic. It's
16 not a very common reason for deferral at a blood donor
17 clinic. So, I do think that that's a problem with that
18 Spanish data, and there's not a lot of data.

19 There's that one article from Italy that also
20 seemed to get at individuals not really understanding
21 the questions well. And it's really hard to know what

1 that means in our context, right? They're being
2 screened by a physician. What are they actually being
3 asked? Do they understand what they're being asked?
4 As questions get more complicated, it's harder for
5 people to know what you're asking them about. So, I
6 think that is a valid point, and it's a strength of our
7 system, right, that the rates in our donors are very
8 low. So either they're self-excluding and they're not
9 showing up on the clinics, or we're asking them the
10 right questions and deferring them or, probably, a
11 combination of both.

12 **DR. KAUFMAN:** Dr. DeMaria.

13 **DR. DEMARIA:** I think in terms of the labor
14 intensity of adding that kind of interview to the
15 screening process -- I think with the results that's
16 obtained seems to me to be more than it's worth. In
17 terms of retest for plasma, it seems to me it's just a
18 way of sort of allowing people to donate without really
19 changing anything. You know, it just -- we'll take
20 your plasma and then retest you to see if we should
21 have or not. But I -- that again doesn't really

1 address the underlying issue of blood equality and
2 changing the way we do things to allow people to donate
3 blood but to still maintain the safety of the blood
4 supply.

5 **DR. KAUFMAN:** Dr. Bryant.

6 **DR. BRYANT:** I think one of the things that I
7 keep thinking about is this use of the PrEP. What is
8 this going to do with the window period? We don't
9 really know, in a group of people that are taking this
10 drug, if the detectable limit needs to be change; in
11 other words, their (inaudible) needs to be different on
12 our testing.

13 Or is the window period going to go from 10
14 days to 20 days to 30 days? And then that brings in
15 the question about does retesting of plasma. Would
16 this be the population that we keep the plasma and test
17 them four months later? Maybe the window period is
18 longer. I don't know -- if they're on this drug. And
19 I don't know enough about how this drug works and how
20 the initial studies were done, but obviously, it's an
21 effective drug or combination of drugs that has some

1 benefit. So how does it go about providing this
2 benefit? Is it --?

3 **DR. KAUFMAN:** I think you raised a number of
4 really interesting points. PrEP is -- I find the PrEP
5 thing confusing. As one of the -- I think Dr. Whitaker
6 mentioned it's not clear whether it would be considered
7 a protective factor or a risk factor. Actually, it may
8 have been one of the other speakers. Overall, it's
9 clearly doing good in the world, in society. In this
10 particular case, I don't know, and maybe I could ask
11 one of our epidemiologists to sort of comment on your
12 thoughts about this.

13 **DR. STAPLETON:** As a virologist -- I'm not an
14 epidemiologist, but I think we don't know a lot about
15 how this effects seroconversion. We certainly know it
16 reduces viral loads. And so, you may delay detection
17 of infection, but being a two-drug regimen, if someone
18 becomes infected and stays on that, they're likely to
19 develop resistance, in the majority of people, fairly
20 rapidly, over three to six months. They should be
21 getting tested every three months, as I mentioned. So,

1 I think it does throw a wrench into the works regarding
2 the window period, and I don't think we have enough
3 information. I think -- I know there are people
4 studying this, and some of them might be in the
5 audience, if they'd like to comment on it as well.

6 **DR. KAUFMAN:** Dr. DeMaria.

7 **DR. DEMARIA:** Yeah. I think if the ultimate
8 question we're going to be discussing is going from one
9 year to three months, I think from a public policy
10 standpoint -- you know, we're trying to get everybody
11 at risk, in Massachusetts, on PrEP to reduce HIV
12 transmission. And defining everybody at risk almost
13 excludes them during that three-month period because,
14 if they're really at ongoing risk, they're not going to
15 meet the requirements of not having an exposure during
16 that three months. So, I think, for me, throwing PrEP
17 into the mix of considering this is making it more
18 difficult rather than less difficult to talk about.

19 If we're talking about anybody at risk for HIV
20 infection should be thrown -- well, no. It makes it
21 more difficult. I don't think it's relevant to the

1 discussion of three months versus 12 months because
2 what we foresee is that people at high risk are on PrEP
3 for the time they're at high risk. And not everybody
4 is at high risk for the rest of their lives, so people
5 are going to be going off PrEP because they're changing
6 behavior, usually with getting older -- is going to put
7 them at a less risk situation so that they're not going
8 to get HIV infection. And then, five years later when
9 they don't need to be on PrEP anymore because their
10 risk has changed, they should be eligible to donate
11 blood because they've avoided getting HIV infection.

12 **DR. KAUFMAN:** Dr. Bloch.

13 **DR. BLOCH:** This may be a little bit off
14 topic, but I'm going to interpret that somewhat
15 liberally as looking at risk-based deferral. So, in
16 terms of the leading factor for what's going to impact
17 risk, and one of the input parameters in risk-based
18 deferral is going to be incidence -- in this case,
19 eclipse-based infection. Now, it's a little
20 interesting having today's session back to back with
21 the zika session of yesterday. So yesterday, we voted

1 to be as aggressive as possible for a theoretical risk
2 which effects one subset of the population. And to
3 date, there's never been a clinical case of transfusion
4 transmitted zika. Now, we're arguing to relax policy,
5 which -- so going back, I fully appreciate the
6 historical aspects of this where it really was, in
7 terms of social chastise of it, was totally out of
8 line.

9 Now that has been -- it's fallen in-line with
10 other risk factors, and yet you want to relax -- single
11 this out to relax it even more, despite the evidence
12 which was shown this morning that the epidemiology is
13 still focused in this population. It's not a judgement
14 about sexual orientation. It's purely -- frankly, I
15 don't think it's actually about donor. It's really not
16 a donor problem. It's recipient risk problem. So
17 that's the one piece of it.

18 And then the second thing is -- sorry. Going
19 back to I think Dr. Brooks' talk from this morning
20 where, if you look at -- if we look at donation at the
21 moment, there's really underrepresentation from

1 minority donors, specifically African-Americans and
2 Latino donors. And there's really been effort to
3 engage those donor populations. Well, what he has
4 shown is that there's -- this is one population which
5 is specifically at risk of HIV. So, what we've
6 learned, I think -- it's just interesting that this has
7 been singled out specifically, and yet we know that
8 there is sound medical evidence -- well,
9 epidemiological evidence that this is -- this should
10 not be done.

11 **DR. KAUFMAN:** Mr. Templin.

12 **MR. TEMPLIN:** Thank you. As a person with an
13 arm in the game and a higher demand for a safe blood
14 supply, I'm just concerned with the long-term
15 ramifications of PrEP and all this antiretroviral
16 therapy in the blood supply and how that may ultimately
17 impact the donor health and the recipient health of
18 that blood because, you know, we just don't know. This
19 is such new technology, and people are taking it. And
20 then they're not taking it, and then they're taking it
21 again. I know people that are on antiretroviral

1 therapy, and the medicine itself is pretty hard on
2 these individuals. So, it just concerns me that maybe
3 there's not more studies being done on the long-term
4 ramifications of this stuff. Thank you.

5 **DR. KAUFMAN:** Thanks. I think, in general,
6 the approach that's been taking to individuals who
7 donate who are taking some sort of medicine -- and
8 that's most donors. It's certainly a lot of donors.
9 The general approach that's taken by FDA is to --
10 certainly to exclude donors who are on relatively small
11 number of known teratogens, with concern for the
12 recipients. But for the most part, when individuals
13 are excluded for being on medicines, the main concern
14 is why were you on the drug versus what will it do to
15 the recipient. The assumption is, if you're taking
16 antibiotics, that -- let's say you're taking
17 amoxicillin. The drug will be diluted in the donor's
18 plasma, and then, if a recipient were to receive it, it
19 would be diluted again in the recipient's plasma and
20 probably wouldn't do much to the recipient.

21 But on the other hand, you have to ask the

1 question "Well, why are you taking the amoxicillin?" If
2 you had a bacterial infection that could potentially
3 see the blood product, well, that's a different story.
4 So, for the most part, that's -- anyway, that's how the
5 drug issues are handled. And the PrEP is a whole -- or
6 other antiretrovirals brings up a whole other, you
7 know, kind of range of questions like we've been
8 talking about. But thank you. Sorry. Sridhar.

9 **DR. BASAVARAJU:** So, I just wanted to say
10 something, I guess, to follow up with what Dr. Bloch
11 was just mentioning. So, one thing at CDC that we do
12 is the NBCUS survey, where every other year we estimate
13 how much blood was collected and how much blood was
14 used in the U.S. And what we've noted is that, for
15 several years now, there's actually a declining demand
16 for blood and, therefore, a declining number of
17 collections of blood. But despite that, there's still
18 a surplus. Blood collectors are still collecting more
19 blood products than are used. So there doesn't seem to
20 at least be, nationally -- at least based on evidence
21 that we have -- there's actually a demand for more

1 blood products to be collected, such that you'd have to
2 potentially dip into riskier populations. Which is not
3 the case -- for example, transplants, where there's not
4 enough transplants for people who need them. So,
5 people who want a transplant, for example, would be
6 willing to take on additional risk.

7 **DR. KAUFMAN:** No. I agree with that point. I
8 think collecting blood is difficult. I think it's fair
9 to say, in general, the U.S. has been able to meet the
10 demands year after year. So, I don't think there's
11 really an argument to be made, truthfully, in terms of
12 blood availability. I think the questions related to
13 potential changes in approaches that might allow MSM to
14 donate really are related to issues more of social
15 justice, rather than availability.

16 Having said that, I think, as I mentioned at
17 the beginning, the challenges -- are there ways that
18 donation can be extended to individuals who are
19 currently excluded without changing the level of safety
20 that's been achieved? So, for example, I think it was
21 -- we saw it took quite a while after Australia went

1 from a lifetime deferral to a 12 month -- it took quite
2 a while for other countries to follow suite, and part
3 of that was waiting to see what happened. We know the
4 window period for HIV NAT is somewhere around 10 days,
5 maybe a little less. That's not the same as saying,
6 "Well, if we just defer for 10 days or 12 days, that
7 ought to be completely adequate." What you do in terms
8 of a population with a deferral policy really can have
9 implications that maybe cannot be predicted. And so,
10 anyway, I think that one of the reasons it took so long
11 was just waiting for some data from around the world to
12 see would there be any effect even from that -- what
13 seemed to be quite a modest change. Dr. Hollinger.

14 **DR. HOLLINGER:** Yes. So, part of the issue is
15 this early period, which you might call a window
16 period. Virology might call it an eclipse period.
17 Some other people use the word latency. It's a little
18 difficult term to use virologically, at this stage.
19 But one of the issues is how infectious or what's the
20 data that, during this period of time if there's
21 transmission to someone with a current sensitivity to

1 the assays today. I tried to go back and look at those
2 groups of countries that do not have a time deferral,
3 and it's really hard to find any information about
4 transmission of HIV in those populations. It's either
5 not collected. They don't have good surveillance, a
6 whole lot of reasons.

7 But it is a very important piece of
8 information because if there's going to be -- if the
9 blood's going to be deferred or not utilized -- so it's
10 only really in that one little period there where it's
11 difficult. It has a lot of similarities, in many
12 cases, to even, like, Hepatitis B, for example, in
13 which there's some occult Hepatitis B. Most of the
14 time, in occult Hepatitis B, you can find HPV DNA in
15 the blood, but there are other times when it's just in
16 the liver and it's not in the blood. And these
17 patients do not appear to be infectious.

18 And even at very low levels, we know in many
19 cases that the disease is not transmitted. Most of the
20 disease, whether it's Hepatitis C, Hepatitis B, HIV and
21 so on, there's a relationship between transmission and

1 the level of virus in the blood, so that patients who
2 are treated, for example -- Hepatitis B and treated but
3 may have some virus in their blood do not appear to
4 transmit. So, I think these are the real problems.
5 So, I'd like to know if there is some -- and there are
6 probably some people here who may have that data about
7 transmission during this period of eclipse. That's
8 all.

9 **DR. KAUFMAN:** Just so I understand your
10 question, are you asking about what is the chance that
11 you can donate a unit that's truly infectious a day
12 after acquiring HIV or five days --?

13 **DR. HOLLINGER:** In that seven to ten days.

14 **DR. KAUFMAN:** Yeah. Let me ask Sue Stramer or
15 maybe one of the other people at the table can address
16 that.

17 **DR. STRAMER:** Okay. Yes. Hi, this is Susan.
18 In the United States, since we've implemented either
19 P24 antigen or NAT -- so this is going back to about
20 1999, eight components have been collected from window
21 period donates. And of those eight, five have

1 transmitted. And these all relate to transmission from
2 large plasma containing components, either from FFP or
3 FP24 or platelets in a large volume of plasma. The
4 three that did not transmit were from red cell
5 collections in which there was far less plasma
6 available. So, there is differential transfusion
7 transmission, depending on the plasma volume, that
8 relates to the viral load in the infectious individual.

9 **DR. HOLLINGER:** But Sue, I'm not talking -- so
10 let's get our -- the terms maybe necessary -- the
11 window period. You're talking about NAT positive but
12 antibody negative? Because you often speak of the fact
13 that there hasn't been any transmission of HIV, HPV,
14 HCV since 2015 documented. So, are we talking about
15 NAT positive but antibody negative? Is that what
16 you're talking about in the window period? Or are you
17 talking about that seven to ten-day period where you
18 can't detect anything? And if so, how is it
19 determined, then, that there was transmission?

20 **DR. STRAMER:** I'm talking about the seven to
21 ten days, and let's talk about one agent at a time.

1 So, if we limit this to HIV, we know this from reports
2 of transfusion transmitted HIV and the investigation of
3 co-components from the same donor who was responsible
4 for the transfusion transmitted HIV case. So, from
5 documented transfusion transmissions, there have been
6 co-components, and the co-components that did not
7 transmit were all from red cells.

8 So, the point I'm trying to make within the
9 seven to ten-day window period is viral loads, of
10 course, are dependent on how much plasma, which is
11 where the virus is -- how much plasma is present in the
12 components. So large plasma containing components are
13 more infectious than something like red cells, which
14 only contain a small amount. And we're talking now
15 only about the window period -- the seven to ten days,
16 which, Blaine, to go back and use your definitions,
17 includes an eclipse period in which virus would not be
18 able to be detected by current assays and window period
19 which more sensitive methods of testing may be able to
20 detect low levels of virus.

21 **DR. HOLLINGER:** If I may ask, Dr. Stramer, of

1 those five that transmitted, how many of those were
2 tested with current -- with viral load assays with the
3 sensitivity of 20 -- cutoff of 20 copies per ml?

4 **DR. STRAMER:** Well, we actually use more
5 sensitive assays than quantitative viral load assays,
6 and we do mini pool NATs. And really, the question is
7 what's the differential sensitivity between doing
8 something like ID NAT versus mini pool NAT? So, of the
9 five that I referenced, one was a P24 antigen, a very
10 early transmission, and the others were bi-pool NAT.
11 Now, we don't know in most cases, if we would have done
12 individual donation NAT, if those donors would have
13 been interdicted because then most, if not all cases,
14 residual samples are not available. We don't store
15 samples from all donation, as they do in other
16 countries like Japan, to see if we've had a transfusion
17 transmission that we can go back and test those donors.

18 **DR. HOLLINGER:** So that's essentially my point
19 of what I was bringing up. I'm still trying to look
20 for the issues about the concern in that particular
21 period of time of seven to ten days with individual

1 donations, detection, and so on. And that data's hard
2 to come by. My gut feeling is that it's pretty limited
3 in transmission, but that's the important question, I
4 think, facing us, in terms of when to use a time
5 deferral.

6 **DR. KAUFMAN:** Well, I'm -- I'm sorry. Go
7 ahead, Dr. Bloch.

8 **DR. BLOCH:** But then if one's going to be
9 completely reliant on the testing, then why have any
10 deferral criteria? Why not just accept everyone?

11 **DR. KAUFMAN:** So, I think -- my understanding
12 is that -- so first, if you -- I think the FDA has
13 modeled this, and this is a part of it. We're talking
14 about rates that are low enough that everything becomes
15 really hard to study. So, you end up doing a lot of
16 mathematical modeling. The FDA has modeled what would
17 happen if there were no MSM deferral at all. What is
18 we just got rid of it? And it's not like there would
19 be an enormous number of infectious units entering the
20 blood supply tomorrow, if you did it today.

21 The tests are really, really good, and we're

1 talking about residual risk, which -- and not to really
2 belabor this point, but it's all window period
3 donation. So there really aren't any other, like,
4 meaningful sources of residual risk. But the FDA's
5 modeling did suggest that you would increase the risk
6 from its current level to something like fourfold
7 higher. So, it's still really, really low. You
8 wouldn't notice any day to day change, but the feeling
9 of the agency -- and I think that there's fairly broad
10 agreement -- is that that would not be consistent with
11 what we're trying to do in the (inaudible) community or
12 for the agency.

13 And so, I think that's an important place to
14 start -- that is let's say, as a baseline, I think
15 there should be agreement that we should not do
16 anything that'll make the blood supply less safe. We
17 may choose to do things that make it safer. But in
18 that context, can we change how we do things without
19 affecting safety? So, for example, I will say that
20 England and Japan are going to a shorter deferral
21 period. They're going from 12 months to three,

1 something like that. Will that make any difference in
2 safety? I think it remains to be seen. Although, it
3 sounds like from Dr. Goldman's presentation the data so
4 far would suggest that it's no worse. And maybe you
5 could comment if you thought maybe it was even a little
6 bit better.

7 **DR. GOLDMAN:** I think it's a bitearly days for
8 the data from the UK, but they haven't seen an increase
9 in the HIV rate in their donors. And their HIV rate is
10 really low to start with, with not a lot -- kind of no
11 NAT only positive donors. So, they already are
12 starting from a very low point, and they haven't seen
13 any difference yet. I'm not aware of a lot of data
14 from Japan, so I really couldn't comment on that.

15 **DR. DEMARIA:** Even without the data, I haven't
16 heard anything that was just, biologically, there would
17 be a difference between a year and three months.
18 There's nothing to suggest -- and there is something to
19 suggest you get better history, which is advantageous,
20 at three months versus a year. So, it's hard for me to
21 see that there would be a difference and there might

1 even be a benefit of going to three months.

2 **DR. KAUFMAN:** I think that's right, and I
3 think one of the -- you know, I talked about
4 potentially having things happen after a change is made
5 that you might not be able to anticipate. So, for
6 example, let's say that a country put in -- went from a
7 year to three months. And then what if an unexpected
8 consequence was that individuals who were at higher
9 risk said, "Oh, well, maybe it doesn't matter anymore.
10 They're kind of shortening it, so I don't have to pay
11 attention to screening questions," or that sort of
12 thing. I'm not saying that would happen. I'm just
13 saying that you can't -- we're talking about huge
14 numbers of people, and you can't really accurately
15 predict what everybody's going to do or what the exact
16 effects are going to be. So frankly, I was really --
17 this was the first I had really heard much about the
18 TIMS program.

19 I think having a method that's rigorous that
20 can be used to measure the effect of changes moving
21 forward is incredibly important. So just having that

1 as a -- no matter what you do. Obviously, the number
2 of -- the absolute number of infectious donations is
3 incredibly important stat, but also the ratio of that
4 to what's happening in the general population may also
5 turn out to be -- to matter later if that goes down, in
6 the future -- that sort of thing. Sorry. Dr. Bloch,
7 did you have another comment? Sue, go ahead.

8 **DR. STRAMER:** Oh, sorry. I'm glad you brought
9 up three months. I wanted to bring it up as an
10 industry comment to keep the momentum of change moving
11 forward and to add another potential way that we could
12 decrease, at least, the time-based deferral. Certainly
13 from TTIMS, we haven't fully evaluated it. Allen
14 reviewed the changes in prevalence incidences and other
15 laboratory-based factors that we're looking at. So, we
16 have some time, and over two year -- 2019 to look at
17 what the results of our studies are. But so far, the
18 data, as Allen mentioned, are promising without change,
19 and change hasn't been observed in other countries, as
20 shown from Mindy's presentation. But as we gain
21 experience with three months in Canada, the UK, and

1 Japan, I mean, I think we should look at those data
2 very carefully, as well, because perhaps on our way to
3 behavioral-based deferral, if we ever get there -- I
4 mean, we can go from a 12 month to three months, and
5 the data support that.

6 **DR. KAUFMAN:** Dr. Lewis.

7 **DR. LEWIS:** So, several comments. I've been
8 storing them up, and I apologize. Number one, the
9 comment about the juxtaposition with zika I thought was
10 really interesting. There's a fundamental difference,
11 which is that the epidemiology of zika, both temporally
12 and geographically, is variable and unpredictable;
13 whereas, the epidemiology that we've seen here is
14 actually a lot of things have really stabilized. And
15 there's a huge opportunity in that, in that you
16 actually can study things and gain data that can be
17 useful for estimating risk for implementing a policy
18 change. And with zika, it's exactly the opposite.
19 Studying what happened in 2016 tells us almost nothing
20 about what's going to happen in 2020. So I think
21 there's a real opportunity there that adds appeal to

1 study and then act, as opposed to theoretical things.
2 The second general comment I'll make is that the risk
3 here is really out in the tail, and there was the
4 distribution of the time to detection. I think there
5 was a comment about the 99 percent area under the time
6 to detection under NAT being something like -- how many
7 days is it? Thirty-three days?

8 **DR. KAUFMAN:** Thirty-three.

9 **DR. LEWIS:** And then it was stated by one of
10 the speakers that that meant that, if you're negative
11 at that point, there's a 99 percent probability of
12 something. That was actually, in my view, likely to be
13 an incorrect probability statement. I think that was a
14 99 percent sensitivity mark in time. And it's unclear
15 whether things that might happen, like the use of PrEP
16 or failure to use -- incomplete use of PrEP leading to
17 unexpected seroconversions, might actually change that
18 distribution out in the tail. And the hardest part of
19 a distribution to both estimate and to be stable is out
20 there in the tail on the edges. So, I think there's
21 some uncertainty in that time limit that we just need

1 to be cognizant of.

2 With that said, the third part of my sort of
3 pondering-ness has to do with the social justice blood
4 equality argument. So usually when we talk about
5 justice as one of the principles for consent,
6 distribution of -- say, burden of participation in
7 research, we're worried about the burden and risk of
8 participation in research being borne by a population
9 that will not share in the benefits of that research.
10 And here, it seems just a tiny bit different because we
11 are -- the prior deferrals excluded a population from
12 the opportunity to donate, but that population is not
13 being denied the benefit of the blood supply, given
14 that -- if I understand correctly -- we, at least
15 historically, have an adequate blood supply. So, the
16 justice argument is based on a lack of an opportunity
17 to contribute to a shared resource, but it's not on
18 lack of access to that resource.

19 So, I'm clearly not an ethicist. So, I'm just
20 wondering if there's anybody who can comment just with
21 a little more clarity and precision about the social

1 justice and blood equality argument. What exactly is
2 the harm that is being created by additional
3 prolongation of -- for example, the 12-month deferral?
4 And I did hear very clearly the point about a
5 perception of stigmatization. I'm wondering is there
6 anything other than that that I'm missing?

7 **DR. KAUFMAN:** Dr. DeVan.

8 **DR. DEVAN:** I'm not an ethicist either, and I
9 don't think we should get hung up trying to fit this
10 into one of the seven categories that are from Social
11 Justice 101. I think this is a full participation in
12 society question. I mean, I think we are trying -- we
13 are taking a whole group of people and saying "You may
14 not fully contribute. You may not fully participate in
15 society. Period." And I don't think we know enough
16 about certain risk factors, certain -- I think we just
17 need to dig a little bit more. But for me, you're not
18 benefiting from the blood supply. It's you're being
19 told that you cannot do something that other people can
20 do, potentially unfairly or without good science that
21 blocks you from doing it.

1 **DR. KAUFMAN:** And I think it's complex. That
2 is blood donation is -- it really cannot be conceived
3 of as a civil right, I don't think. We exclude people
4 for many things. I live in Boston. There's a big
5 community of people who've lived in Europe between '80
6 and '96, at a time when there was worry about a variant
7 in CJD. And they're deferred from donating. We defer
8 lots of different people for lots of reasons, and it's
9 not -- with the best of intentions. It's not to be
10 discriminatory. It's to protect the patients. And
11 truly, that's the -- I think that that's really FDA's
12 intent, that is the goal is truly not to discriminate
13 against any group, but rather to reduce risk based on
14 evidence for the safety of patients.

15 And we're kind of at a time when it may be
16 appropriate to reflect on, and potentially change, ways
17 that we have addressed risks to the blood supply, given
18 new testing, new science, and so on. This has been, in
19 the past, of course -- this deferral for MSM has been
20 obviously, I think by many people, viewed as
21 discriminatory. I truly do not believe that it is, but

1 I think, at the same time, it's a worthwhile endeavor
2 to try to see what can be done with the -- anyway, with
3 that in mind, if that makes any sense. Dr. Schreiber.

4 **DR. SCHREIBER:** So, summarizing a little bit,
5 we all agree, I think, that patient safety is
6 paramount, and no decision made any time by the FDA
7 should result in any diminution in the safety of the
8 patient. I think we all agree that anyone should be
9 allowed to donate that does not reduce the safety of a
10 patient, regardless of any other arguments about
11 discrimination. If it's safe for that person to
12 donate, they should be allowed to donate.

13 We're presented with, I think, today, three
14 strategies. The third we'll talk about, which is
15 pathogen reduction, this afternoon. That kind of makes
16 all the rest of this discussion today irrelevant.
17 Because if you can pathogen reduce universally, then
18 the question -- then a lot of these questions become
19 less relevant. But that's for this afternoon.

20 That leaves us two strategies. One is the
21 time-based deferral strategy, and I think that -- I

1 would hope that we would agree that that time-based
2 deferral -- that time should be the minimal amount of
3 time necessary until, essentially, 100 percent of the
4 people who will convert -- or the window period is
5 over. And I think -- it seems to me that a year is too
6 long, and probably three months is adequate for that to
7 occur. And there does not seem to me to be -- I can't
8 think of a biologic or scientific reason that one year
9 is better than three months, right? Because everybody
10 that's going to become positive will do so by three
11 months. And in fact, maybe three months is better
12 because people can remember the last time they had
13 unprotected intercourse or sex better at three months
14 than they can at one year.

15 So, we also have another country, albeit one
16 with a very low incidence, England, who's gone to a
17 three-month period. So, there's a precedent. So, to
18 me, that seems quite reasonable. I think the question
19 of the quarantining -- to me, the issue of quarantining
20 is more of a logistical and economic question. Is that
21 feasible logistically and economically? I have no

1 idea. If it is feasible logistically and economically,
2 then I see no reason not to do that because that seems
3 very safe and won't harm the safety of the patient.
4 So, to me, these are the issues as we're presented at
5 this time.

6 **DR. KAUFMAN:** Thank you. Dr. Marks.

7 **DR. MARKS:** So, we really appreciate the
8 comments. I think -- we understand the issues here. I
9 think one of the issues that we've discussed what the
10 UK has done. And with all due respect to our European
11 colleagues, there's just not data, and the idea here --
12 just to refocus on this study, which will take some
13 time to conduct and which is only a pilot study for
14 potential subsequent study -- is to actually have data.
15 Because when we look at what the United Kingdom did
16 when they made their change -- again, with all due
17 respect to their change process. If you look over the
18 report of a scientific advisory board, it was solely
19 based on, essentially, theoretical considerations, not
20 based on data.

21 We also know that the United States has a very

1 different epidemiology of HIV -- and I think Dr. Brooks
2 could comment more on that -- than the United Kingdom
3 and other places. So I think what we're looking to do
4 here is, I think, think about this pilot study -- and
5 that's what I think we were looking to get comments on
6 -- as a way to try to get some data that could
7 potentially help us see a way forward in the future
8 where you might be able to get away from a time-based
9 deferral.

10 I will tell you from the last docket we had
11 open -- we got feedback to the last docket -- the LGBTQ
12 community in general finds any time-based deferral
13 discriminatory because -- again, we can argue all the
14 aspects of this, but this study is being done -- is
15 being proposed in an effort to find is it possible in
16 the United States, with the existing testing strategy
17 that we have in place -- because I agree that pathogen
18 reduction, potentially, adds a whole new realm to this.
19 But with our existing testing structure, is there a way
20 to come away from this without the need for a time-
21 based deferral? Can you ask questions for at least

1 some subset and not need that deferral? So that's what
2 -- but the discussion here today has been fantastic
3 because it's bringing up the questions and a lot of the
4 issues that we've been grappling with. So, thank you.

5 **DR. KAUFMAN:** Let's put attention then to
6 discussion question two, which is on the screen.
7 Comment on the questions proposed for the study in the
8 HIV risk questionnaire, whether there are any additions
9 or modifications to the study in order to best identify
10 behavioral risk questions to predict the risk of HIV
11 transmission in the MSM population. So, I'll open that
12 up to the committee. Dr. Lewis.

13 **DR. LEWIS:** First of all, to Dr. Marks, that
14 was very helpful. So, I think one of the things we saw
15 from the international experience is that there is
16 geographic heterogeneity in the characteristics, and
17 one of the things we have in the U.S., as you pointed
18 out, is we not only have a very different epidemiology
19 of the epidemic. We actually have heterogeneity within
20 the country. I'm sorry. I don't want to get into
21 Spanish politics, but we have some of the similar

1 divides of different parts of the country seeming like
2 they're different countries.

3 And so one of the things -- and I think this
4 addresses specifically the issue of modifications to
5 the study -- so I think that, even in the very large
6 study that you propose, but certainly in the pilot
7 study, it's going to be difficult to understand whether
8 you would have gotten different results based on the
9 areas in the country in which you sampled. You have a
10 pre-specified approach to sampling particularly high-
11 risk areas that may yield data that are not applicable
12 to other areas of the country that you didn't want to
13 include in your study because you know you would have
14 gotten nothing useful. And so I guess what I'm saying
15 here is that in the pilot study, but also in,
16 especially, the follow up study, trying to capture
17 prospectively measures of differences in the
18 epidemiology of the HIV infected community, or at-risk
19 community, that will help you understand whether, in
20 fact, the non-time-based strategy you ultimately
21 propose needs to be different based on the demographics

1 or the geography in which they are applied. Because it
2 seems very difficult -- just as there's not a one size
3 fits all across Europe -- that there's actually going
4 to be an appropriate one size fits all across the U.S.

5 **DR. KAUFMAN:** Well, maybe we can -- I guess I
6 have some, potentially, more detailed questions just
7 about the pilot study itself. One thing that I would
8 like to ask is what are the main primary -- main
9 outcomes, primary and secondary outcomes from it? That
10 is, many pilots that are done for questions of
11 feasibility. I don't know. Maybe Dr. Marks or Barbee
12 can comment on that. My worry is just that, if it's a
13 big enough study just to catch one recent infection,
14 what can be learned from it?

15 **DR. MARKS:** So, thanks. So, I think Barbee
16 can also answer this. There's a range -- because we
17 don't know exactly what the numbers we're going to
18 actually predict are, depending on how you essentially
19 run your numbers, it could catch at least one. It
20 could catch five. It could catch. We don't know, and
21 that'll depend on -- and I think that last comment

1 about where you are in the country is very key to this.
2 We decided -- we actually went back and forth in
3 thinking about this, whether it made sense to do a more
4 representative sampling upfront or to essentially
5 concentrate on areas. But we thought it would be
6 important to try to at least see if we get a signal
7 first, and then see if there's some correlation that we
8 can make, see if at least the test questions work -- if
9 they're acceptable.

10 It turns out some of these questions may not
11 be fully acceptable in certain regions of the country,
12 but we'll at least get to -- in terms of general use.
13 But at least we'll get a sense of these. It will give
14 us some correlation here. We will have a sample bank,
15 then, afterwards, which will, I think, be useful for
16 being able to go back and try to do some more
17 refinement. So again, we don't know exactly, but this
18 is to catch at least something, hopefully, and get some
19 idea. I mean, I think if we -- the study might be a
20 failure, in one sense, if we catch zero.

21 But I would put it to you that this is a study

1 worth doing, in any case, from the public health
2 perspective because, as we know -- and I guess I'd ask
3 Dr. Brooks -- we know that, depending on where this is
4 done -- and we'd hope it's done in places where there
5 are increasing incidences in some ways of HIV in
6 certain populations -- you are going to identify men
7 who didn't know they were infected. And they will
8 benefit from being identified. And so even if it's a -
9 - I guess this is one where we can fall back on even if
10 the ultimate primary and secondary objectives fail, the
11 tertiary objective not stated will actually be
12 beneficial to participants in some way.

13 **DR. HOLLINGER:** Just a question while you're
14 still up. Doesn't Washington, D.C. have probably the
15 highest risk of HIV in MSM? So that seems like a great
16 place to do a study.

17 **DR. BROOKS:** Washington, D.C. would be an
18 excellent place to do a study, as well.

19 **DR. HOLLINGER:** Yeah. I mean, several pooled
20 hard.

21 **DR. BROOKS:** It's a lot closer, too.

1 **DR. HOLLINGER:** Absolutely.

2 **DR. BROOKS:** I just wanted to add one thing to
3 Dr. Marks' comment, which is one of the reasons -- when
4 we do HIV studies related to prevention, in general, in
5 high prevalence areas is to the point that we want to
6 demonstrate either that you can measure something or
7 that it's effective as quickly as possible. We have no
8 reason to believe that when we translate something
9 we've learned in that circumstance to a low prevalence
10 area that the risks are any different. We may turn up
11 less infection, but there's no reason to believe that
12 anal sex practiced in Georgia is substantially
13 different than that practiced in Montana. So, if we're
14 asking that same question, we would expect to have the
15 same a priori sensitivity -- probably not going to
16 yield as many positives, however.

17 **DR. KAUFMAN:** Dr. Basavaraju.

18 **DR. BASAVARAJU:** So, for Dr. Marks about this
19 plan. So, if you do the pilot and you find zero
20 infections, what are you going to do with that
21 information? Like what does that mean for the larger

1 study? What does that mean for the questionnaire?

2 **DR. MARKS:** It may mean that we go back to the
3 drawing board and bring the advisors together and think
4 more about it. I think it would all depend on what we
5 actually find. Yes. If it was a total no findings,
6 that would be -- we'd have to go back to the drawing
7 board. But I think, from looking at what we've done
8 with the statistics, we think that if we go and do this
9 in the right -- and that's why we're going -- to the
10 idea of going to the Washington, D.C.s, Atlanta, Miami
11 -- I'm sorry to call these -- for the mayors of these
12 cities, I'm sorry to call you out. They've heard it
13 before. Right -- Chicago, Los Angeles -- if you go to
14 those cities, the calculation you can make is that we
15 should at least see one. We've done some calculations
16 where you might see as many as ten, so it just --
17 hopefully, we'll see something. Do we know -- if it's
18 zero, I guess we're back at the drawing board.

19 And then, I would agree with you. We would
20 have wasted this time from the standpoint of advancing
21 the policy. On the other hand, we still would have

1 benefited some people from helping them be diagnosed
2 and also putting together a study infrastructure that
3 might be beneficial in the future to work with.

4 **DR. KAUFMAN:** Dr. Shapiro and then Dr. Lewis.

5 **DR. SHAPIRO:** Thinking about this pilot study,
6 it really seems to me that there's two questions
7 imbedded in this. One is the applicability of these
8 questions in terms of defining risk for a certain
9 population, and then the other is, looking at patients
10 who convert, are they being honest? Are they reporting
11 this information? How likely are you going to be able
12 to use this information for your blood donation policy?

13 It would seem, based on that, then you really
14 need two studies -- two subpopulations to apply this
15 to. One is to an overall MSM population to just look
16 at the questionnaires and do the testing and say are
17 you likely to get honest answers and relevant answers
18 from this. And the other is to look at populations who
19 are antibody-negative NATpositive and to apply this and
20 to determine if any of these particular questions come
21 up as a question that can identify that group more than

1 another question. It just seems like you can't
2 necessarily do both things in one study. Did I explain
3 that or not very well?

4 **DR. MARKS:** Are you trying to say that you
5 would need a study where -- you'd like a study where
6 there would be -- you would actually look for window
7 period or eclipse period individuals and ask these
8 questions of those individuals? I think the problem is
9 that putting that sample together, in retrospect, it's
10 hard to know -- retrospectively, it would be
11 challenging to know that you were getting reliable
12 answers --

13 **DR. SHAPIRO:** -- Not retrospect.

14 **DR. MARKS:** But do it prospectively.

15 **DR. SHAPIRO:** Go to a population where you
16 know you're not going to get one, but if you test 500
17 people, you're going to get 50.

18 **DR. MARKS:** So that's the whole point of this
19 study -- of trying to do this in a population of --
20 we're trying to stilt this population to the highest
21 risk group, so they have to be MSM who are active

1 within the past three months in cities where
2 potentially the risk of transmission is, if anything,
3 stable or increasing. Without just increasing sample
4 size, I'm not sure we can -- to get more in that --
5 maybe I'm misunderstanding you.

6 **DR. SHAPIRO:** If you look at your eligibility
7 and exclusion criteria, if you change that for the two
8 groups that you might study, you would enrich one
9 population. So, you're looking for people who want to
10 donate blood. My question is what difference does it
11 make? If you're looking at the validity of the
12 question to detect a potential seroconversion, it
13 doesn't matter if they want to donate blood or not.

14 **DR. MARKS:** But ultimately, for application of
15 this -- for our purposes -- if you're a person who has
16 sex with other men but you never want to donate blood,
17 then it's not relevant because you're never going to
18 put yourself into the donor pool in the future. So,
19 the idea would be --

20 **DR. SHAPIRO:** -- It is in picking out a
21 question here that may show a seroconversion

1 probability rate. If you just look at these questions
2 in terms of people who want to donate blood, then
3 you'll look at the applicability of those questions to
4 that population, the acceptability and how honest those
5 people are in terms of answering that question.

6 Because you're relying upon two things for this.

7 You're relying upon the testing capability -- the
8 accuracy of the test and the false negative rate. And
9 you're relying upon the honesty of the donor.

10 **DR. MARKS:** Yeah. I guess I'm going to just
11 say something from a practical perspective. I take
12 your point, but I think, from a practical perspective,
13 since no one is actually donating a unit here, the
14 question of whether they'd be willing to donate a unit
15 is quite hypothetical. And how many of them would run
16 away when I come at them with a 19-gauge needle and not
17 donate? We're not going to be actually -- we're not
18 going to be testing that. So, your point's well taken.
19 I just don't know that -- this was felt -- the group
20 felt that this was a way of at least kind of focusing
21 the question. But I think we'll take that back and

1 discuss whether just dropping that as an eligibility
2 criterion may make sense.

3 **DR. SHAPIRO:** I just don't understand, if you
4 get one or ten people here, how you really evaluate any
5 of these questions for applicability to say that that
6 picks out a high-risk group.

7 **DR. MARKS:** I think what it does, at least, is
8 it helps at least start the -- it helps you develop a
9 hypothesis for a larger study as a pilot -- that you at
10 least know how to size the next study, and you might be
11 able to refine these questions further. I think the
12 bottom line is you have to start somewhere, I think.

13 **DR. KAUFMAN:** Sorry. Dr. Lewis and then Dr.
14 Schreiber.

15 **DR. LEWIS:** So I'm increasingly struck by how
16 difficult this problem is, and so I appreciate and
17 fully support the point that you want to make a policy
18 decision based on data. But it sounds like it's going
19 to be impossible to get the data that directly answers
20 the question. Because if I understand correctly, what
21 you're trying to pick up here are -- when you say

1 you're going to try to find one or ten, are they NAT
2 positive, antibody negative? Is that what you're
3 looking -- what is that case you're trying to pick up?

4 **DR. MARKS:** That's correct. NAT positive,
5 antibody negative.

6 **DR. LEWIS:** But we screen the blood supply
7 with NAT, correct? So even that case isn't the case
8 you're really worried about. You're using that as a
9 proxy for the risk of them having been in the window --
10 eclipse, whatever.

11 **DR. MARKS:** That's exactly correct.

12 **DR. LEWIS:** Okay. So, you already have your
13 case defined as something different than what you're
14 really worried about. So that's one area of
15 extrapolation. Then, you're extrapolating from a
16 higher risk population based on practices or geography
17 to try to understand how to screen more globally.
18 That's another area of extrapolation. You're trying to
19 extrapolate from a population who's willing to
20 participate in two interviews and a seven mil draw to a
21 population that will voluntarily donate blood and

1 actually look at 19-gauge needle in the face, which is
2 a very different thing. Okay.

3 And so, there's -- this is -- even though
4 you're trying to get data that will inform the policy
5 decision, at the end of the day, you're going to be
6 making multiple extrapolations and assumptions about
7 the linkages. So where I'm going with that is that it
8 seems to me that the cases -- since you're already
9 going to have to extrapolate from NAT positive,
10 antibody negative back to the risk of having been in
11 the window, that you might as well also take advantage
12 of any other evidence of early infections because the
13 patient who's more early infected, even if they're now
14 antibody positive, also gives you their information.

15 So, believe it or not, this was an incredibly
16 long-winded attempt to answer your question about the
17 endpoint for this. I suggest that you don't define
18 your cases just as NAT positive, antibody negative, but
19 you actually develop an ordinal scale for the interest
20 of the case to you in which that's the highest --
21 that's the most interesting case. The next one is, by

1 other markers, a recent infection.

2 **DR. MARKS:** Keep going. You're right on --
3 we're on the exact same page. Keep going.

4 **DR. LEWIS:** Okay. Well, I may be about to
5 drive off the tracks. Just watch. And the problem
6 with this is that it, if you have a subject you
7 identify who has a relatively recent infection but it
8 would have been picked up by current screening, your
9 time-based questions, in terms of their individual
10 practices, now have to be adjusted for the estimated
11 time of that infection. And that raises a really
12 interesting statistical analysis question. So, my
13 point is to get away from the binary outcome, try to
14 order the importance in terms of their evidence of risk
15 for being in the window of multiple ordinal outcomes,
16 and then try to time adjust your questions so that you
17 can interpret each one of those outcomes as well as
18 possible.

19 **DR. MARKS:** Thanks very much for that, and, in
20 fact, you've -- I really am greatly for that comment
21 because that was something that we'd discussed. And we

1 actually neglected to present that way -- that they're
2 actually -- for instance, the avidity assay will give
3 you another bite at the apple, so to speak. But you're
4 right. We'll have to take into account the other
5 corrects in the statistics.

6 **DR. KAUFMAN:** Thanks. Can I ask those on the
7 phone to please mute their lines? Dr. Schreiber and
8 then Dr. Bloch.

9 **DR. SCHREIBER:** So, I want to make two points.
10 Number one, I believe there to be a problem with the
11 questionnaire in that none of the questions ask about
12 the gender of the partner, which I think is critical
13 and should be included.

14 **DR. MARKS:** The entry criteria is male.

15 **DR. SCHREIBER:** Right. But when you say how
16 many different sexual partners have you had, maybe they
17 had sex with three men and two women.

18 **DR. MARKS:** Point well taken. How many male
19 sexual partners --? Right.

20 **DR. SCHREIBER:** Yeah. So that was point
21 number one. I think that's really critical. The

1 second thing is I wanted to just address a point that
2 you made earlier, which was the issue of the deferral
3 period, and I understand that you would prefer that
4 there be no deferral period. But I think that we get
5 into problems when we talk about having to have data to
6 change rules when the rule itself has no data. So,
7 you've got a one-year rule in place, and, to my
8 knowledge, there's no scientific basis for that one-
9 year rule. And it actually probably doesn't make sense
10 because it's too long. So, could you comment on what
11 is the scientific basis for the one-year rule that we
12 don't want to change to three months because there's no
13 scientific base for the three-month rule, which makes
14 biologic sense?

15 **DR. MARKS:** So, point very well taken. I
16 think what Dr. Kaufman already mentioned, though, is
17 one of the concerns that has been articulated is that
18 when one reduces the questionnaire from a certain
19 length to another time -- and again, with deference to
20 what Canada's done, the question is do you know what
21 that signals to people in terms of their recent

1 behavior? So, will that change at three months? I'm
2 not saying it will or not, and I think points all well
3 taken. We'll be happy to go back and think about this
4 some more.

5 We did go from indefinite to 12 months on the
6 basis of epidemiologic data, and that was because of
7 the desire not to increase risk because we do have to
8 have the end user -- the patient who's going to receive
9 products in mind. So again, I totally take your point,
10 but if we take the natural extension to your point,
11 then we should have a 30-day deferral. And that's been
12 brought up as well. So, I think points all well taken.
13 We can go back and think about this, and I appreciate
14 that.

15 **DR. KAUFMAN:** Thanks. Dr. Bloch. Any other
16 comments on the proposed study? Dr. Baker.

17 **DR. BAKER:** Thank you. Just a general comment
18 that brings in my questions about TIMS, as well as
19 this. Has there been more consideration about
20 communication and dissemination to the public at large
21 about these -- both TIMS and this effort to ultimately

1 demonstrate or increase the blood supply safety -- the
2 safety of the nation's blood supply? I don't think
3 that that's been thought out very well about how that's
4 being communicated to the public -- not just the public
5 community of scientists but just the lay public and the
6 end users.

7 We started BPAC because of blood safety issues
8 affecting the public at large, and, yet, that seems to
9 be a piece that I'm missing. In all of our well-
10 intentioned interest to get the study design correct,
11 is how are we communicating what the important work of
12 TIMS is doing and what this important pilot project
13 will do for -- to try to assure the safety of the
14 nation's blood supply. Not to release data
15 inappropriately, but just I've been doing some internet
16 searches on TIMS. And you really just can't find a
17 more external face of what's going on -- that this
18 exists, why it exists, how it's contributing to the
19 nation's blood supply or what we know about the safety
20 of the nation's blood supply. And the same thing that
21 why we are doing this, there's plasma users and others

1 who rely on blood components, and we want to make sure
2 they're safe. But yet, there's no central place where
3 that information is really out there to the public. So
4 that's a consideration.

5 **DR. MARKS:** This is Peter Marks. So, I
6 appreciate the comment, and I think we can go back
7 again and think about whether we can figure out a place
8 to post this on webpages -- also think about whether a
9 publication in an appropriate journal makes sense.
10 Because there will be publications forthcoming in
11 addition to ones that have appeared.

12 **DR. KAUFMAN:** I was just saying there are
13 groups that are in a position to communicate with the
14 public about these sorts of issues. I'm thinking of
15 the A-B-B, America's blood centers and so on -- I-S-B-
16 T, in addition to the agency itself. So, I think that
17 there are channels available. Dr. Stapleton.

18 **DR. STAPLETON:** I hate to raise whole new
19 study designs, but one of the concerns is that you're
20 not going to have enough endpoints to draw any
21 conclusions. Did you consider doing a rapid testing

1 first visit with a blood draw with the opportunity to
2 schedule a follow-up for the NAT-only positive people?
3 Because then you could do a case control for your
4 cases.

5 **DR. MARKS:** Yeah. So, it's a very good
6 question. It actually was considered, and it just was
7 a matter of thinking about the complexity of trying to
8 have the fewest number of visits to operationally be
9 able to do this because we needed to think about doing
10 this in a way that was not very -- you know, the least
11 expense. But that was absolutely a reasonable thing to
12 consider.

13 **DR. STAPLETON:** Because you would save a lot
14 of second -- if you did case control. And is it too
15 late to -- probably is. But in the RFA, could you give
16 people the opportunity to propose different study
17 design?

18 **DR. MARKS:** It might be a little bit late to
19 be thinking about that, but, you know, it may be that,
20 again -- if this doesn't turn out the way that we would
21 anticipate, that might be another thought to go back

1 and try to get these data that way.

2 **DR. KAUFMAN:** Okay. Any other comments or
3 questions? Okay. Well, thanks very much. So, we will
4 break for lunch, and we will resume with Topic 3B at
5 1:30 p.m. Thank you.

6

7 **LUNCH**

8

9 **INTRODUCTION TO THE TOPIC**

10

11 **DR. KAUFMAN:** This afternoon session, we'll be
12 discussing pathogen reduction of platelet donations as
13 an alternative procedure to MSM donor deferral. I'm
14 pleased to introduce the next speaker, Dr. Carlos
15 Villa, from FDA. He'll be talking about pathogen
16 reduction of platelet donations as an alternative
17 procedure to MSM donor deferral.

18

19 **DR. VILLA:** All set. Thank you. My name is
20 Carlos Villa. I'm the medical officer in the division
21 of blood components and devices in the Office of Blood
Research and Review at CBER. Today, I'll be

1 introducing pathogen reduction of platelet donations as
2 an alternative procedure to MSM donor deferral. I'd
3 like to begin by providing the issues for discussion
4 before the committee today. And these are to discuss
5 the use of pathogen reduction of apheresis platelets as
6 an alternative to the current MSM deferral policy, and
7 to discuss any associated risks and possible
8 mitigations. I will reiterate these issues for
9 discussion at the conclusion of my presentation.

10 I'd like to begin with an outline of what I
11 intend to cover today. First, I'll provide a
12 background, recapping some of what we heard this
13 morning, including FDA's approach to blood safety as
14 well as FDA's current recommendations for MSM donor
15 deferral. Next, I'll introduce the idea of alternative
16 procedures described in the Code of Federal Regulations
17 under 21 CFR 640.120 and describe a particular
18 alternative procedure request to MSM donor deferral
19 that involves the use of pathogen reduction. I'll also
20 provide a bit of background on pathogen reduction
21 technology. Finally, I'll provide some issues for

1 consideration for the committee as they discuss this
2 topic today.

3 FDA's approach to blood safety, as we heard
4 this morning, consists of a multi-layered system of
5 protections for donated blood. These layers of
6 protection include: donor education and screening;
7 donation testing; donor deferral lists; quarantine,
8 recall and lookback for blood components; and systems
9 for investigation, correction, and reporting of
10 problems and deficiencies when they occur in
11 distributed products. It is the first of these layers
12 of safety -- in particular, donor screening -- which
13 are the topic for our discussion today and for which
14 I'd like the committee to focus their discussion.

15 Again, as we heard this morning, FDA's current
16 recommendations for HIV risk deferrals include a number
17 of criteria. But I'd like to reiterate a couple
18 aspects. First, donor deferral recommendations for HIV
19 risk apply to all collections even if the components
20 will be pathogen reduced. Second, among a number of
21 criteria -- the full list which was provided this

1 morning -- are the following specific recommendations
2 for donor deferral. These are to defer for 12 months
3 from the most recent contact a man who has had sex with
4 another man during the past 12 months, and to defer for
5 12 months from the most recent contact a female who has
6 had sex during the past 12 months with a man who has
7 had sex with another man in the past 12 months.

8 These specific criteria I will refer to as the
9 MSM deferral criteria for the remainder of my
10 presentation. And it is these specific criteria for
11 which we are asking the committee to discuss
12 alternative procedures. Alternative procedures are
13 described under 21 CFR 640.120. And under these
14 regulations, FDA may issue an exception or alternative
15 to regulatory requirements, commonly referred to as a
16 variance, regarding blood, blood components, or blood
17 products. FDA's approval of such exceptions or
18 alternatives are based on the availability of adequate
19 information, showing that the alternate process ensures
20 the safety, potency, and purity of the blood component
21 or blood product.

1 FDA has received a request for an alternative
2 procedure to MSM donor deferral per those criteria I
3 mentioned earlier. Under such an alternative
4 procedure, donors will be screened and determined to be
5 otherwise eligible to donate. However, instead of
6 donor deferral per MSM criteria, apheresis platelets
7 will be collected and pathogen reduced using an FDA-
8 approved device according to its instructions for use.
9 Importantly, donations will be tested for all relevant
10 transfusion-transmitted infections, including HIV, as
11 required by the FDA.

12 As this alternative procedure request involves
13 the use of pathogen reduction, I'd like to, next,
14 provide some background on this technology. There is
15 one device, the INTERCEPT Blood System, currently
16 approved by FDA for the treatment of apheresis
17 platelets and plasma. This device is based on
18 Amotosalen/UVA technology, which is depicted on the
19 right-hand side of this slide.

20 In this approach, Amotosalen is added to the
21 blood component. The Amotosalen intercalates within

1 nucleic acids in the blood component. And following
2 UVA elimination, crosslinks are introduced within the
3 nucleic acids. This blocks subsequent replication,
4 transcription, and translation of the nucleic acids,
5 thereby inactivating infectious agents. The device is
6 intended to reduce the risk of transfusion-transmitted
7 infection, including sepsis.

8 The treatment is performed within 24 hours of
9 collection. Following treatment, residual Amotosalen
10 is removed and the component ready for transfusion.
11 The viral reduction of HIV with the INTERCEPT Blood
12 System, according to the package insert for the device,
13 is based on input titer and post-treatment titer. This
14 viral reduction ranges between greater than or equal to
15 2.4 to greater than or equal to 5.6 log₁₀ reduction
16 depending on the viral strain and the suspending media,
17 whether that is platelet added to the solution or
18 plasma.

19 Next, I'll provide the issues for
20 consideration before the committee as they consider
21 this alternative procedure request. These include the

1 extent of HIV log reduction to prevent HIV transmission
2 by transfusion, the possible effect of the variance
3 request on the platelet supply, as well as the
4 manufacturing process for pathogen reduced platelets,
5 which includes the controls necessary to prevent
6 process failures, as well as -- as currently stands --
7 the limitation of pathogen reduction to specific
8 platelet platforms.

9 Additional issues for consideration before the
10 committee include the processes for managing a dual
11 inventory of pathogen reduced and untreated components,
12 as is often the case in blood establishments performing
13 pathogen reduction today. Additionally, adequate
14 measures to prevent release or distribution errors
15 should be considered. For example, the use of blood
16 establishment computer systems, or BECS. Finally, the
17 committee should consider the risks and consequences of
18 biological product deviations. For example, the
19 failure to perform pathogen reduction on a platelet
20 component that was collected from a donor not deferred
21 for MSM deferral criteria.

1 With these issues of consideration, I'll
2 reiterate the issues for discussion before the
3 committee today. And these are to discuss the use of
4 pathogen reduction of apheresis platelets as an
5 alternative to the current MSM deferral policy, and to
6 discuss any associated risks and possible mitigations.
7 I thank the committee and everyone for their time
8 today.

9 **DR. KAUFMAN:** Thank you. I'd like to
10 introduce the next speaker, Dr. Jim AuBuchon, from
11 Bloodworks Northwest. Thank you.

12 **PROPOSAL FOR PATHOGEN REDUCTION OF PLATELET**
13 **DONATIONS FROM MSM**

14 **DR. AUBUCHON:** Thank you, Dr. Kaufman. Across
15 my career, I've had the opportunity to propose a
16 variety of practice and policy changes, but none more
17 historic and significant than this one. I appreciate
18 the agency's invitation to do so today. Just to set
19 the stage, I want to make sure that the committee
20 understands who Bloodworks is. Our not-for-profit
21 mission statement is focused on saving lives, and our

1 vision is one of advancing health and the practice of
2 transfusion and transplantation medicine. And I
3 believe that the steps that I'm going to propose today,
4 indeed, fall in line with those tenants.

5 So, as a quick outline, I'd like to, first,
6 review what we are requesting -- I thank Dr. Villa for
7 doing that already -- tell you why we are doing this,
8 how we think we can go about doing this and maintain
9 the safety of the blood supply, how we're going to
10 manage a very different kind of recruitment of an
11 apheresis platelet donor than what we do today, how we
12 hope to be able to add to knowledge as well as to the
13 platelet supply through this variance request, and then
14 give you some thoughts on where this is all headed.

15 So, in a nutshell, as Dr. Villa stated, we
16 propose to accept, as an apheresis platelet donor,
17 someone who is currently deferred for having sex with
18 another man in the last 12 months or a woman who's had
19 MSM contact in the last 12 months. An apheresis
20 platelet would be collected and, after negative test
21 results, would be converted to an INTERCEPT pathogen

1 reduced platelet. So, in essence, we are proposing
2 applying new technology to offer new donor recruitment
3 and donor inclusion possibilities.

4 Now, how did this all get started? A little
5 over a year ago, I was asked to speak at a seminar, an
6 open session, at Gay City in Seattle. Gay City is an
7 LGBTQ community resource center and there were 50, 60
8 people in attendance. It was known ahead of time that
9 I had been vociferous in advocating for the application
10 of scientific objective evidence in setting all donor
11 deferral criteria. And, because of that, I was willing
12 to accept this invitation and was not pilloried at the
13 meeting. In fact, I was thanked for my advocacy on
14 behalf of the gay community.

15 They wanted to talk more about why this
16 current criterion was in effect, and what had been done
17 and what could be done to change it in the future.
18 Toward the end of that two-hour session, one person
19 stood up, thanked me for my advocacy, and then said,
20 "But what more can you do?" And I didn't have a good
21 answer for that.

1 I'm good at writing letters. I'm good talking
2 with people. But I didn't have another idea in my back
3 pocket. So, I had to punt on the question when it was
4 posed. But it clearly stayed with me. It was only a
5 couple of months later, while sitting with some friends
6 and a glass of wine, that I first had a brainstorm
7 about something we might actually do to change policy.

8 With discussion with other colleagues, other
9 ideas came forward. The first idea we had was to go
10 with a whole blood donation approach for MSM with a
11 quarantine and retest approach. The idea here would be
12 that we would accept an MSM who was currently deferred,
13 collect a unit of whole blood that would, then, be
14 converted into red cells and plasma. But both of those
15 units would be quarantined. We would ask the donor to
16 return 21 days later after the window period for a
17 mini-pool HIV testing for a retest. When that retest
18 showed that all the test results were still negative,
19 the units would be released into inventory. So, this
20 was the first idea that we came up with.

21 There were a couple of concerns that came up,

1 however. One was the donor inconvenience factor
2 because we'd have to expect the donor to show up, not
3 once, but twice before we could use the unit of blood.
4 If the donor didn't show the second time, we would have
5 lost that unit. We were also concerned with some
6 expressions in the scientific literature we were
7 seeing, that when pre-exposure prophylaxis, or PrEP,
8 failed, it yielded a very low level of viremia in the
9 infected individual; so low that we might miss it in
10 HIV NAT testing.

11 So, this was a concern that we might get a
12 false negative when we were depending solely on the
13 test to ensure the safety of the blood supply. And
14 then, also, we would only have half the usual red cell
15 shelf time to use the unit. The other idea that came
16 up in discussion with colleagues was to go with what we
17 ultimately submitted as a variance request -- an
18 apheresis platelet donation with, then, subsequent
19 pathogen inactivation.

20 We recognize there are some concerns about
21 this and we'll be talking more about these, including

1 how would we recruit prior to having any knowledge of
2 the individual's test marker status? And we would be
3 creating a new type of platelet, not just pathogen
4 reduced platelet, but a pathogen reduced platelet from
5 a different donor source than we had used previously,
6 which we have complete confidence in as I hope I will
7 be able to convince you of in the next few minutes.
8 But would the community regard these units, then, as
9 suspect and essentially, perhaps, avoid all pathogen
10 reduced platelet units even though the majority might
11 not come from this source?

12 Both of these approaches require a different
13 treatment for this group of donors, and that's
14 unfortunate. There's no way around that at present.
15 In discussion with various MSM leaders in the Seattle
16 area, the option was clearly for the second approach:
17 using apheresis platelet donation converted to
18 INTERCEPT platelets. So, that's what we have been
19 pursuing since that time.

20 Now, to give you the geography here which
21 relates to the numbers of potential donors, Bloodworks

1 serves the I-5 corridor from the California-Oregon
2 border up to the Canadian border, and then extending up
3 into the panhandle of Alaska. We have 11 different
4 collection centers, plus 15 or 20 mobile blood drives
5 operating daily, and 3 laboratory locations. There are
6 two primary urban centers in this area. But, overall,
7 there are about 6 million people across 45 thousand
8 square miles that we serve with a large number of
9 employees and volunteers in collecting blood from about
10 225 thousand donations annually.

11 In the greater Seattle area, with a population
12 of about 4 million inhabitants, it's estimated that
13 there are about 200 thousand gay males. Whether these
14 would all qualify under MSM criteria as we use that
15 term is not known. But it's a good starting point, an
16 approximation. In the Portland metro area, slightly
17 smaller. There are approximately, it is believed,
18 about 70 thousand gay males. So, that is in the range
19 of a quarter of a million new blood donors that we
20 might ultimately find presenting themselves. Now, how
21 many would actually come and donate blood where the

1 criteria changed is not known.

2 However, recently, Israel opened up the
3 possibility of plasmapheresis donation with a
4 quarantine and retest system, similar to what I
5 described, possibly for whole blood. In that case,
6 they surveyed over 12 hundred MSM and found that almost
7 two-thirds said they would donate. In addition, we
8 know that there are many in the LGBTQ community and
9 their supporters who self-defer, not because they do
10 not meet any qualifications we may have, but they self-
11 defer out of protest over the current requirements.
12 So, the number of donors that we may encounter for the
13 first time could be quite dramatic.

14 Maintaining the safety of the blood supply is
15 absolutely paramount, as was pointed out by the
16 committee in their discussions earlier today. So, I'd
17 like to offer a few comments about the levels and
18 limits of our logic protection, and the process
19 controls that we would use to ensure that we are
20 delivering what we think we are delivering. I'm not
21 going to spend much time talking about bacteriologic

1 safety, but I do want to point out that, although the
2 various pathogen inactivation techniques that have been
3 developed over the last several decades were not
4 focused on bacterial contamination of platelets when
5 they were created.

6 This is the primary reason that many blood
7 bankers are very excited about having PRT platelets
8 available, because we recognize that approximately 1 in
9 every 250 patients who receives platelets -- and most
10 receive multiple units of platelets -- will encounter a
11 bacterially contaminated unit during their course of
12 therapy. And that's scary. So, we are looking forward
13 to using PRT as a simple, quick, and effective means of
14 avoiding this most common form of pathogen transmission
15 in blood transfusion.

16 The limits of detection with the NAT system
17 that we are using have been published, and they are
18 incredibly sensitive. As you can see, the number of
19 copies per mil at the 50 percent limit of detection is
20 very low and the infectious window period that this
21 represents is very short for HIV, HCV, and HBV.

1 Compare these limits of detection with what you have
2 already seen as the probability of a reduction of any
3 viral contamination, and we are looking at multiple
4 orders of magnitude of safety. So, even if an
5 individual is just below the limit of detection in the
6 NAT testing that is currently performed, the INTERCEPT
7 system will be able to produce a unit that has had HIV,
8 HBV, and HCD effectively reduced.

9 Now, there are many process controls that need
10 to be included in this new process that we will be
11 doing. Certainly, we have to make sure that every unit
12 is tested and any unit that is positive in HIV or any
13 of the other tests that we do is appropriately
14 interdicted. But this is standard procedure. This is
15 something that we do every day anyway. So, this is not
16 new. It does not require any new approaches.

17 We have to make sure, though, that we identify
18 who is an MSM and capture that information in our
19 system so that we handle them and their unit
20 appropriately; have to make sure that we don't create
21 any other components that could not be pathogen reduced

1 through the process; and that we manage any units that
2 are unsuitable for the INTERCEPT system.

3 So, how would we do that? Well, today, if a
4 donor comes in and donates and answers yes to one of
5 the MSM questions, this yields an automatic deferral
6 and no collection of any blood component is possible.
7 But, in the future, if this variance is authorized, we
8 have to have our BECS system be able to accept them as
9 a donor, but only for apheresis platelet collection,
10 and then further require that that unit is converted to
11 INTERCEPT platelets before the unit is released. This
12 will be handled after examination of our computer
13 system and how it's structured.

14 With the step that -- when the deferral, which
15 is now automatic for positive response to the MSM
16 question, is overridden, that will cause an attribute
17 to be created, related to that donation, which is
18 automatically applied. The attribute will only allow
19 apheresis platelets to be collected and will require
20 conversion to INTERCEPT platelets before release of the
21 unit. This is absolutely key and will be automated.

1 When the unit is collected, it will, then, proceed to
2 the laboratory as do all the other apheresis platelet
3 units. It has to be found within certain platelet
4 content and volume limits in order to be handled
5 through the INTERCEPT system, meeting the so-called
6 guard band requirements.

7 When these have been verified as having been
8 met, the unit would be treated in the INTERCEPT system
9 and could be labeled, then, as a pathogen reduced
10 apheresis platelet unit. The BECS system is in control
11 of this and, obviously, is interfaced with the systems
12 to make sure that the unit has actually passed through
13 the eliminator and has received the Amotosalen and that
14 everything has been handled according to package insert
15 requirements before the unit can be labeled and then
16 released. It would be released into our inventory, and
17 we receive orders against that inventory from hospitals
18 as they need their platelets.

19 This is not a matter of a new product creating
20 a dual inventory. As you can see, we have multiple
21 flavors of platelets already on the shelf. We have

1 apheresis platelets that we will soon be converting, if
2 they're not pathogen reduced, to a large volume delayed
3 sampling approach. We provide individual whole blood
4 platelet units for pediatric platelet transfusions. We
5 provide pre-storage pooled platelets from whole blood
6 donations. And any of these forms of platelets may be
7 requested to be irradiated.

8 So, as you see, there are many different forms
9 of platelets. And having one new form from a new
10 source is not really any change to our operations. If
11 the unit, when it reaches the laboratory, is found not
12 to have appropriate content or volume, it cannot be
13 processed through the INTERCEPT system. It would be
14 quarantined and discarded. Again, because the BECS
15 would require that the unit be treated through the
16 INTERCEPT system and have a pathogen reduced label
17 before being able to be released, the unit would not be
18 able to be released for transfusion. So, the process
19 controlled through the BECS is very important.

20 Picking up test positive units, picking up the
21 unit or any portion of the unit that hadn't been

1 INTERCEPT treated, and if any co-component were created
2 -- and the system wouldn't allow for that, but if it
3 would, it, too, would not have passed through the
4 INTERCEPT system and could not be labeled and released.
5 Now, the donor recruitment for this process is going to
6 be different than what we do today. We recruit, as
7 plateletpheresis donors, individuals who have given
8 multiple whole blood units already. We are looking for
9 a level of commitment. Because when we need platelet
10 donors, we need them. We need them to show up and we
11 need them to be reliable. We need to know that they
12 live close to somewhere where we routinely collect
13 platelets.

14 Although we do have mobile platelet
15 collections, most all of our apheresis platelets are
16 collected in our fixed collection sites, so they can't
17 live a great distance from there. We know their test
18 results; they've donated on multiple occasions. We
19 know their infectious disease test results are
20 negative. We know their blood type, which also would
21 steer us toward collecting platelets from certain types

1 and not others. And, importantly, we know their
2 platelet count, because we would rather have an
3 apheresis platelet donor with a higher platelet count.
4 With all of that information, we can make the decision
5 to recruit them as an apheresis platelet donor.

6 That has worked very well for us and is
7 similar to what many other blood collectors use. In
8 this situation, however, we're going to be dealing with
9 a donor that we don't know. We don't know any of that
10 information when they first present for donation.
11 We're going to be approaching recruitment in two
12 different ways. One, something that we do already, is
13 we recruit MSM to donate through our in vitro research
14 product program. We have a large biologic products
15 division that collects blood that is usually used for
16 in vitro research. And when it is used in vitro
17 research, we don't apply the MSM deferral criteria.
18 When it's used in some in vivo method, then, of course,
19 we do apply that.

20 So, we have the opportunity to meet these
21 donors ahead of time, make sure that their donor

1 questionnaire responses are all acceptable other than
2 the MSM question, and that their test results will be
3 satisfactory. If someone walks in and says, I'd like
4 to donate in your new program, we would give them a
5 complete donor history questionnaire to fill out and we
6 would draw a sample to be run through all of the
7 standard infectious disease tests to ensure
8 acceptability of the donor before we commit a slot on
9 our platelet collection schedule, an apheresis
10 collection kit, and potentially even an INTERCEPT
11 system -- an INTERCEPT kit. So, once we know the donor
12 would be acceptable, we would, then, set an appointment
13 for their donation and then recruit them.

14 Also, as part of this, we would create what's
15 called a donor profile, or donation profile, that would
16 restrict them to this system. So, the only thing that
17 would be able to be collected from them would be
18 apheresis platelets and the only thing that would be
19 able to be generated from that donor would be an
20 INTERCEPT platelet.

21 So, this is a second layer of safety in the

1 variance request that goes along with the donation
2 attribute that I talked about earlier that would be
3 invoked when an MSM deferral was overridden after the
4 MSM question was answered with a yes. So, we have two
5 different BECS systems that will both ensure that only
6 the right component is collected and a right component,
7 ultimately, is produced.

8 Now, this morning, you heard Dr. Whitaker
9 talking about a study to gather more information about
10 the sexual practices of potential MSM donors. The
11 agency has asked if we would be willing to consider
12 participating in that. The idea is that an MSM donor,
13 after donating apheresis platelets, would participate
14 in a study, giving written informed consent to provide
15 some information that would allow us to correlate their
16 sexual practices with a infectious disease test result.

17 This would be optional. It's not required.
18 And it would be an IRB-approved research study that
19 would attempt to associate certain sexual practices
20 with donation proclivity and testing results. We would
21 intend to use the same questions that the FDA-sponsored

1 study would be using.

2 I hasten to add, however, that the collection
3 in transfusion of PRT platelets is not a study. We
4 would be generating a licensed PRT platelet unit as a
5 result of being granted the variance. This would be an
6 additional study. It would be a research study that
7 donors may decide to participate in, if they would like
8 to give us additional information. That would help the
9 FDA ultimately see if there are some risk-based
10 questions that could be used rather than asking a
11 question about membership in a group.

12 So where is this all headed? Well, we began
13 several months ago, shortly after we submitted the
14 variance request to the agency with partnership with
15 the LGBTQIA community for potential recruitment of
16 donors and publicity in the gay community about this
17 process once it's been approved. We have approached
18 them already about participating in research product
19 donation, and they are very interested in helping us
20 get the word out in the future about platelet donation.

21 We're also preparing our hospitals for PRT

1 platelets. We have not seen the uptake that we would
2 like in interest in PRT platelets, but several
3 hospitals have indicated that they are interested and
4 willing to use PRT platelets. We believe that it
5 increases recipient safety, and that is the primary
6 reason that we should be using PRT platelets -- to
7 avoid the bacterial complications. As hospitals become
8 more aware of the complicated processes they may be
9 required to follow in the future if a unit is not
10 pathogen reduced, in order to mitigate the bacterial
11 risk, they may become more interested in using this
12 simple approach.

13 We believe that this approach also provides a
14 new means to bring additional diversity into the blood
15 supply. We struggle with the fact, as all blood
16 collectors do, that all minorities are underrepresented
17 in our donor lines. We would like to have the support
18 of all communities, and for no other reason than we
19 certainly attempt to provide blood to all those
20 communities, but the dispersion of different red cell
21 anagens are not equal across different ethnic lines.

1 So, we need all communities to participate so that we
2 have the ability to have the blood available to make
3 sure all can be supported.

4 We are very interested to find out what
5 recipients of platelets feel about this variance
6 request. We are working with a local company that
7 works for a number of pharmaceutical companies in
8 putting together patient focus groups, and patients who
9 appear in commercials and appear before other groups of
10 patients. We're using them to see if we can put
11 together groups of patients who have received or
12 continue to receive platelets to get their impact to
13 make sure that we are crafting our messages to the
14 community about the safety of this approach in a manner
15 that patients are not concerned. We have also begun
16 some internal preparations in the hope of ultimately
17 having this variance be approved.

18 Developing appropriate SOPs, making sure that
19 the BECS system is appropriately programmed and
20 validated to operate in the manner in which we believe
21 it needs to, making sure that the staff is

1 appropriately trained. In knowing that this meeting
2 was a public meeting and not knowing how well it would
3 be covered by the media, we have to be prepared for MSM
4 showing up tomorrow at our donor centers, wanting to
5 donate blood. So, we have already created a system to
6 not only advise our staff of this variance request, but
7 to create a system to capture the interest expressed by
8 MSM donors before we can actually take them as regular
9 blood donors.

10 We believe that this approach is essentially
11 analogous to the approach which the agency has already
12 approved for one blood collector, and that is the
13 ability to accept donors who are current -- or have
14 otherwise currently been deferred for travel to malaria
15 areas or having been born in malarial endemic areas,
16 providing that the apheresis platelet is treated with
17 the INTERCEPT system.

18 So, the idea is that, again, we can apply new
19 technology to expand the diversity of our donor pool.
20 Because, in the end, it is all about diversity. It's
21 about supporting the community that we support. We

1 depend on the community's support in order to be
2 successful, and we believe that it is appropriate for
3 us to seek social justice and provide an equitable
4 approach to blood donation while maintaining safety --
5 you could even argue improved safety -- with an
6 increased availability of PRT platelets, having a boost
7 to our donor recruitment.

8 There were some discussions earlier today
9 about whether or not there was enough blood in the
10 country. And I would just caution the committee about
11 looking at annualized data about collections and
12 assuming that there's enough blood. Because, on a day
13 to day basis, I can tell you that many blood centers,
14 strictly those in larger cities, are exceedingly
15 pressed to make sure there is enough blood on the
16 shelves.

17 We are all spending additional time,
18 additional resources -- that is, additional money in
19 recruiting in a new sociologic framework, in a new
20 demographic distribution of our population. And it is
21 exceedingly difficult to keep enough donors coming

1 through the door, even if not as many red cells are
2 being used as in the past.

3 In this variance request, we're talking about
4 platelets. Our platelet utilization continues to
5 climb. It's gone up 15 percent in the last 4 years.
6 We are looking at the future of a likely bacterial risk
7 mitigation guidance from the agency that will probably
8 put whole blood platelets out of business. That's
9 unfortunate in our opinion, but we understand the
10 rationales. So, we are going to have to turn more to
11 apheresis platelets. 25 percent of all of our platelet
12 doses today come from whole blood derived platelets.
13 That's going to decline in the future, and we need to
14 find more donors to provide those platelets. Because,
15 today, we just don't have them.

16 So, for all those reasons, we are very excited
17 about this proposal to the agency. I look forward to
18 hearing what the committee has to say about it. Thank
19 you.

20

QUESTIONS FOR SPEAKERS

21

1 **DR. KAUFMAN:** All right. Thank you very much,
2 Dr. AuBuchon. I'd like to ask if there are any
3 questions from the committee for both Jim AuBuchon and
4 Carlos Villa. Dr. Schreiber?

5 **DR. SCHREIBER:** I'm curious to why the
6 discussion is limited to just platelets. Pathogen
7 reduction for plasma is approved as well and your
8 platelets are suspended in plasma, if I am correct.
9 Why not -- one of your last statements were, you know,
10 we're worried about the shortage of blood, so we could
11 also make -- potentially make plasma available this
12 way. Why is that not in the discussion?

13 **DR. AUBUCHON:** You are correct. It certainly
14 is possible. A couple reasons: one, we don't have a
15 shortage of plasma. Occasionally, we are a bit short
16 on AB plasma. We do have an AB donor plasmapheresis
17 program, so I suppose we could certainly use some MSM
18 donors in that and treat them in the same manner.
19 That's possible. I think the reason we didn't propose
20 it initially is because the primary impetus, primary
21 driver, for adoption of PRT is avoidance of bacterial

1 risk. And that just isn't present in platelets.

2 So, if the agency likes our proposal here for
3 platelets, we certainly could consider applying it to
4 plasma. We would probably only use it for AB MSM
5 donors, but then, we rarely have enough AB platelets
6 anyway. So, any AB donor that we found through this
7 program, we'd probably want to collect platelets from
8 them anyway.

9 **DR. KAUFMAN:** Dr. Shapiro?

10 **DR. SHAPIRO:** Did I understand you correctly
11 that you're only going to apply the PRT technology to
12 MSM donations and not to the general pool of donors?

13 **DR. AUBUCHON:** Thank you for the opportunity
14 to clarify that. No, that is not the case.

15 **DR. SHAPIRO:** Okay.

16 **DR. AUBUCHON:** I don't know how many MSM
17 donors are going to present, but I am expecting that
18 the vast majority of our PRT platelet units that we
19 produce will come from our regular donor pool. The MSM
20 donors will augment that, but I -- unless we receive a
21 far stronger outpouring than I could imagine, it'll

1 probably be mostly from the regular donor pool.

2 **DR. SHAPIRO:** So, they're using the technology
3 on all the pheresis platelet --

4 **DR. AUBUCHON:** Now, we are not yet providing
5 PRT platelets to any hospital. Truth in advertising
6 here, several hospitals are getting ready for that. We
7 have done all of our validation work with the INTERCEPT
8 system. So, we're ready to produce INTERCEPT
9 platelets; we just have to get some hospitals to be
10 able to use them. It's complicated. The committee may
11 wonder, well, if they like it, why don't they just use
12 it?

13 One of the problems is that the hospitals are
14 interested in using PRT to avoid the need to irradiate
15 the platelets. But that means they have to make some
16 fairly substantial changes in their hospital laboratory
17 information system, so that a unit that comes into
18 their inventory as a PRT platelet is regarded as the
19 equivalent of an irradiated platelet. And that is
20 causing them some difficulties.

21 **DR. SHAPIRO:** Another question I had about

1 this is the website for this agent says that it's very
2 effective in a susceptible pathogen. What constitutes
3 a susceptible pathogen versus an unsusceptible
4 pathogen?

5 **DR. AUBUCHON:** I will defer to an expert
6 sitting in the audience, Dr. Richard Benjamin, if the
7 committee would like to hear him speak to that.

8 **DR. BENJAMIN:** Hi. Richard Benjamin, Chief
9 Medical Officer for Cerus Corporation, the manufacturer
10 of the INTERCEPT system. Our pathogen set describes a
11 broad-spectrum ability to kill pathogens across
12 enveloped and nonenveloped viruses, bacteria,
13 parasites, and leukocytes. But, like any pathogen
14 reduction system, we do not claim that it inactivates
15 all pathogens and there are some specific pathogens
16 that we are less effective at killing. Specifically,
17 spores or bacteria such as bacillus and some of the
18 small nonenveloped viruses, such as hepatitis A and
19 hepatitis E, are not effectively killed as HIV is. So,
20 we need to be very careful about what our claims are.

21 **DR. KAUFMAN:** Dr. Basavaraju?

1 **DR. BASAVARAJU:** So, you know in
2 transplantation when a transplant recipient is offered
3 an organ from a donor who is at increased risk for HIV?
4 Even when that infectious disease testing is negative,
5 the recipient is still told of the donor risk factors
6 and subjected to informed consent. Do you have a plan or
7 are you planning to have an informed consent process
8 for recipients who might receive these products or
9 hospitals that might buy them?

10 **DR. AUBUCHON:** No. We believe that we can
11 make a strong case to the public and to our hospital-
12 based colleagues that these units will be absolutely
13 safe and that there is no increased risk to the
14 recipient. In fact, we believe that by having these
15 additional donors, we will be able to provide more PRT
16 platelets than we would otherwise. Therefore, we will
17 be providing a platelet inventory of increased safety,
18 not decreased.

19 **DR. KAUFMAN:** Dr. Lewis?

20 **DR. LEWIS:** So, following up on that question,
21 I want to try to understand the quantification to the

1 extent that we can about the potential risks. There
2 are two changes that are being made. One is you are
3 expanding your donor pool criteria. So, potentially,
4 your donor pool will have some increased risk of being
5 in that very short window before the NAT testing is
6 positive.

7 **DR. AUBUCHON:** That's correct.

8 **DR. LEWIS:** That's the increase before
9 treatment. And that's being counterbalanced -- if I
10 understand your prior comment, you believe more than
11 counterbalanced -- by the two or more log reduction
12 associated with the treatment of the platelets. Is
13 that correct?

14 **DR. AUBUCHON:** That's correct.

15 **DR. LEWIS:** So, to argue that the net effect
16 is an increase in safety, that means that you believe
17 that the increase in risk of being in the window period
18 is less than a couple of logs?

19 **DR. AUBUCHON:** No. I use the term "increase
20 safety" in relation to reduce bacterial risk, because
21 we know that our current culture methods are only

1 approximately 50 percent sensitive in detecting
2 bacterial contamination. And 1 in every 1500 units, or
3 1 in every 250 platelet recipients, is receiving a unit
4 that has bacteria in it. I don't like that and I would
5 like to get away from that.

6 So, as we make more PRT platelets and have
7 them become a larger proportion of the entire
8 inventory, the safety of the recipients will increase.
9 By increasing the donor pool, particularly those people
10 who have to have their platelets go to PRT platelets,
11 we will be ultimately increasing the safety of the
12 blood supply.

13 **DR. LEWIS:** Okay. So, you're making one of
14 the changes to increase the donor pool; could at least,
15 theoretically, increase the risk of HIV not detected in
16 the -- because it's in the window period. But you --
17 but the in vitro work demonstrates that the pathogen
18 reduction gives more than a 2-log reduction of that
19 pathogen. But, overall, you're arguing the safety is
20 based on the increased safety with a stricter bacterial
21 contamination?

1 **DR. AUBUCHON:** That's correct.

2 **DR. LEWIS:** Okay.

3 **DR. KAUFMAN:** Dr. Schreiber, and then coming
4 from Dr. Benjamin.

5 **DR. SCHREIBER:** So, I think the -- using more
6 platelets to 5-day shelf life, which is very short, is
7 limited by the potential bacterial contamination. Does
8 this process potentially lengthen the lifespan of the
9 donated platelets?

10 **DR. AUBUCHON:** Some countries are using
11 INTERCEPT platelets for storage up to 7 days. That's
12 not currently approved in this country. One benefit
13 from using INTERCEPT treatment as opposed to the
14 culturing approaches that have been proposed is that
15 the effective useful storage period for the platelet
16 increases. Because the processing to INTERCEPT
17 platelets is done within 24 hours of collection and
18 since the infectious disease test results come back
19 within that window period as well, the unit can be
20 released on day 1. And that's not the case for the
21 large volume delayed sampling.

1 Although that has been discussed as possibly
2 leading to a 7-day storage period, it won't be possible
3 to get those platelets out into the market, get them
4 out into inventory and distribution, until probably day
5 3 of their lifespan. So, the effective amount of time
6 that the unit is available when it's an INTERCEPT
7 platelet will probably be greater than when it's
8 handled with the new culture systems that are being
9 proposed.

10 **DR. KAUFMAN:** Dr. Benjamin?

11 **DR. BENJAMIN:** Richard Benjamin, Cerus
12 Corporation. I'd just like to clarify something about
13 the 2-log cure for HIV that you saw on the two clinical
14 isolates. All of those strains, you'll have seen a
15 greater than or equals to sign before the number, which
16 signifies that we've cured the -- or we've activated
17 the virus, but to the limit of detection. So, we are
18 constrained, then, about how much virus we can put into
19 the product. And those clinical isolates do not grow
20 to high concentrations. So, the maximum amount of
21 virus we could put in was only 2 to 3 logs.

1 For the laboratory strains, we could grow them
2 to higher concentrations and you would've seen a 4.7 or
3 5 logs. But again, it was to the limit of detection.
4 So, I wouldn't get focused on the 2 logs as we have not
5 seen heterogeneity in our ability to cure different
6 strains of a virus. When I see 4.7 or 5 logs, I think
7 that's probably the more realistic minimum number for
8 cure rate on HIV.

9 **DR. KAUFMAN:** Dr. Bryant?

10 **DR. BRYANT:** In your presentation, you talked
11 about the safety engagement with the recipient groups.
12 Are you referring to patient groups or are you
13 referring to hospital customers?

14 **DR. AUBUCHON:** I'm specifically referring to
15 patient groups. We'd like to hear directly from
16 patients. We are pursuing getting those groups set up
17 right now. We are working with our hospitals as well.
18 We have made known to them this presentation today and
19 what we are asking the agency to approve. But we look
20 forward to further engagement with them and discussions
21 with them. We've had many meetings with our hospitals

1 over the last year and a half, talking about PRT
2 platelets and their advantages. They appear to be
3 well-accepted theoretically. The problem comes down to
4 cost.

5 **DR. KAUFMAN:** Dr. Shapiro?

6 **DR. SHAPIRO:** I just want to clarify if I
7 understood what you said in your presentation. You
8 said you were going to be using the questionnaire that
9 the FDA developed in MSM individuals who were donating
10 for platelets, but are not these individuals already
11 testing negative for HIV so you already know their
12 status?

13 **DR. AUBUCHON:** Yes. It is true that we will
14 already know that these individuals are negative in all
15 infectious disease tests before they ever come in to
16 donate. At the break I was talking with Dr. Whitaker,
17 saying that perhaps if we participate in this, we
18 should apply the questionnaire to all those individuals
19 who present with interest to donate so that we can
20 capture some who, perhaps, are test-positive.

21 **DR. SHAPIRO:** Okay. Okay. Thank you.

1 **DR. HOLLINGER:** So, Jim, just a question
2 again. Is -- so, with the current techniques that are
3 used, there's some benefits you see with the pathogen
4 reduction in terms of bacterial contamination
5 potentially and other things. But what has been the
6 risk with the current -- forget the pathogen reduction.
7 But what is currently available for looking for
8 bacterial contamination for serology and everything
9 else? Has there been a problem with that that you can
10 see? And I can understand the practice eclipse phase.
11 If you figure that some patient who is in this eclipse
12 phase actually is expressing virus in the blood, which
13 that is going to come out in the donation, it'll be a -
14 - should be a very low titer. But can you give me some
15 idea about risk?

16 **DR. AUBUCHON:** Well, I'm not the expert in
17 that field of transfusion medicine. But as the
18 committee has already discussed today, the risk of HIV
19 or hepatitis transmission currently through the blood
20 supply is unseeable and occurs very infrequently. It's
21 one per millions of units transfused and it is very

1 difficult to quantitate because it is so low.

2 Bacterial risk is much higher.

3 Now, I don't know if it's the clean living of
4 the people who live in the Pacific Northwest or not,
5 but we have not had the magnitude of bacterial
6 contamination cases that other collectors have seen.
7 I'm grateful for that, but I also know the literature
8 that says, still, 1 in every 1500 units is contaminated
9 with bacteria.

10 So, I don't go to sleep at night worried about
11 HIV or hepatitis transmission because, effectively, it
12 does not exist in our blood supply at present. If
13 someone from the public asked me, "Is the blood supply
14 safe?", I'm very quick to give an unequipped glance or,
15 "Yes, it is safe." And I want to keep it that way.

16 **DR. HOLLINGER:** So, just a follow-up, maybe
17 somebody in the blood banking community can tell me,
18 which is what -- how many deaths have occurred each
19 year with the bacterial contamination from platelets?

20 **DR. BENJAMIN:** Just the FDA fatality rates, I
21 believe it's two to three a year -- is the number that

1 appeared.

2 **DR. AUBUCHON:** That's recorded.

3 **DR. BENJAMIN:** That's recorded by -- the FDA
4 can talk to that.

5 **DR. HADDAD:** Based on the estimate and based
6 on the rate of contamination and how many contaminated
7 units actually lead to a septic reaction and to death,
8 you really can estimate between 10 and 20 death a year.

9 **DR. HOLLINGER:** All right. Thank you.

10 **DR. KAUFMAN:** And with -- and just to follow
11 up on that, there are -- this pathogen reduction
12 technology has been used nationwide in some places.
13 Switzerland, they've had zero septic reactions since
14 implementation over a period of some years. So, it is
15 quite effective for them.

16 I had a question. And this, as you stated,
17 would not itself be a study. That is, you'd end up at
18 the end with a -- I assume the label would be exactly
19 the same.

20 **DR. AUBUCHON:** Correct. These units would not
21 be distinguished in any manner.

1 **DR. KAUFMAN:** But at the same time, I was
2 wondering if you were interested in capturing -- kind
3 of processing information or some data about the
4 logistics of the process. How many units, for example,
5 above expectation were you able to get? Or how many
6 did not meet the guard bands? Or things of that
7 nature.

8 **DR. AUBUCHON:** Oh, absolutely. I mean, we
9 will set up to make sure that we are able to track all
10 of these units and understand not only the donors and
11 how frequently they've come to donate, but how
12 successful we are with collecting the units, what
13 impact they make on the overall supply, and if we're
14 able to collect, within the guard bands, better with
15 them than other units -- other donors perhaps. I don't
16 know.

17 **DR. KAUFMAN:** All right. Dr. Bryant?

18 **DR. BRYANT:** Jim, will the donor be -- in your
19 computer system, will it be per donation? In other
20 words, when they answer the question yes, that's when
21 it tags that donation. Or will the donor carry a tag

1 as well?

2 **DR. AUBUCHON:** The answer to both of those
3 options is yes. The donor will carry a tag, if you
4 will --

5 **DR. BRYANT:** Notation. Notation.

6 **DR. AUBUCHON:** -- indicating that they can
7 only donate apheresis platelets and only INTERCEPT
8 platelets can be made from their donations. And then,
9 whenever the MSM deferral, which is automatically
10 imposed when someone answers yes to that question --
11 whenever that deferral is removed or overridden, then
12 an attribute is added to that donation that requires a
13 donation to be apheresis platelets and the ultimate
14 unit produced to be INTERCEPT platelets.

15 **DR. BRYANT:** So, if the donor answers no, they
16 would still be tagged for --

17 **DR. AUBUCHON:** That's correct. If a donor
18 came in and answered no to the MSM question, the same
19 requirements would still be placed on them. Now, we
20 may have to ultimately work out a system if we find
21 that there are donors who previously were MSM with a

1 12-month deferral, and then they say, well, I've been
2 abstinent for 14 months. And they would, then, qualify
3 as a regular donor. Or if the time deferral were to
4 shift from 12 months to something shorter, then perhaps
5 some of these gentlemen would, then, not be caught by
6 that new question. We'll come to that, and we'll deal
7 with that when we come to it.

8 **DR. BRYANT:** Okay.

9 **DR. KAUFMAN:** Dr. Stramer, did you have a
10 question or comment?

11 **DR. STRAMER:** Yes. Actually -- can you hear
12 me?

13 **DR. KAUFMAN:** Yes. Go ahead.

14 **DR. STRAMER:** Okay. Jim, thank you. Have you
15 discussed with the advocacy groups that you've been
16 working with that via the guard bands, you probably
17 won't be able to pathogen inactivate all units, and
18 perhaps 50 percent of them, from donors who you will be
19 accepting as MSM, will not be acceptable for
20 distribution; unlike donors who won't be MSM who we can
21 apply different bacterial mitigation sets to? And what

1 was their reaction to that?

2 **DR. AUBUCHON:** We do not yet have the
3 collection experience that your system has, so we will
4 be devoting a lot of attention to the platelet count in
5 these donors and exactly how much we collect from them.
6 Because, if we don't produce a PRT platelet, we're not
7 producing anything from them. And that's obviously a
8 large expense that is lost.

9 So, we are looking to gain more experience in
10 how to collect platelets within the guard bands for all
11 donations. But in particular, for these donors, we
12 will have to be very careful to make sure that we get
13 it right, otherwise we've lost all of our investment.

14 **DR. KAUFMAN:** Dr. Lewis, and then Dr. Ortel.

15 **DR. LEWIS:** I'm sorry. I want to come back to
16 this issue of the two different possible effects on the
17 overall safety of the platelets that are provided. So,
18 in principle -- and don't interpret this question as my
19 advocating for this approach. But, in principle, you
20 could institute the pathogen reduction with your
21 current donor pool which would gain you the increase in

1 safety associated with the bacterial contaminant
2 reduction without expanding your donor criteria.

3 **DR. AUBUCHON:** That's a logical and reasonable
4 question, but not exactly. First, we have the problem
5 of the 25 percent of our platelets that are produced
6 through whole blood donations. There is no pathogen
7 reduction system available for them, so we have to
8 collect more apheresis platelets in order to do the
9 full conversion, I think, as you're talking about.

10 Now, we have the additional problem that Dr.
11 Stramer was just mentioning, that the guard bands are
12 tight. We are hoping that Cerus will be able to submit
13 data to the agency to expand those guard bands. But
14 not every unit that's collected can be converted, by
15 product insert, to INTERCEPT platelets.

16 So, we know that the discard rate becomes
17 higher or the split rate goes down. That is what
18 might, today, be regarded as a double unit collection.
19 It could only be a single unit INTERCEPT unit. So, we
20 anticipate we are going to have to collect more units
21 of platelets to, someday, convert to 100 percent PRT.

1 And we don't have those donors today.

2 **DR. LEWIS:** Okay. So, the connection you're
3 making between the expansion of the -- or making the
4 donor requirements less restrictive is because the use
5 of the pathogen reduction technology will cause other
6 issues that may decrease the actual availability of
7 platelets?

8 **DR. AUBUCHON:** I would agree with you, but I
9 wouldn't regard what we are proposing as making it less
10 restrictive. I just say that we would be avoiding an
11 unnecessary deferral.

12 **DR. LEWIS:** Eliminating a deferral?

13 **DR. AUBUCHON:** Correct.

14 **DR. LEWIS:** Okay. And then, just to quantify
15 for a second, the numbers that you gave on the map for
16 the estimated MSM population in your collection area
17 was about 5 percent of the whole population.

18 **DR. AUBUCHON:** Correct. It's slightly higher
19 in Seattle than Portland. But yeah, that's
20 approximately correct.

21 **DR. LEWIS:** How does that 5 percent potential

1 increase in the population -- knowing that the
2 population doesn't necessarily translate to the
3 fraction that are enthusiastic about becoming platelet
4 donors, how does that 5 percent compare to the
5 potential loss in units associated with this additional
6 safety procedure?

7 **DR. AUBUCHON:** I don't have enough experience
8 in collecting platelets for the INTERCEPT process to be
9 able to answer that question. I would hope that we
10 would get good enough so that we would come out ahead
11 in that equation -- good enough in terms of collecting
12 the right volume and the right platelet content. But I
13 don't have the experience to answer that yet.

14 **DR. LEWIS:** Okay. Thank you.

15 **DR. BASAVARAJU:** Do you plan on asking MSM
16 donors potentially about their use as PrEP? Because
17 that may cause false negative NAT results.

18 **DR. AUBUCHON:** We were not planning on asking
19 platelet MSM donors about PrEP. Because, although PrEP
20 may cause a false negative because of very low viremia,
21 that would be no different than the situation of

1 someone being in the window period and being missed by
2 current NAT testing. And that level of viremia would
3 be well taken care of through the INTERCEPT process.
4 We were anticipating asking questions about PrEP for
5 those donors who wish to participate in the FDA study,
6 but that's a different, separate issue.

7 **DR. KAUFMAN:** Dr. Ortel?

8 **DR. ORTEL:** Yeah. This might be a question
9 more for the FDA. If this is a request for approval
10 for variance, I'm just curious, what kind of oversight
11 or what kind of supervision does this get approved
12 with? Or is it -- what's the next steps, for example?

13 **DR. AUBUCHON:** I'm very interested in the
14 answer to that question also.

15 **DR. ILLOH:** This is Orieji Illoh from DBCD. I
16 think, generally, when we receive variance requests,
17 like Dr. Villa mentioned, we look at the supporting
18 data to ensure that whatever changes will maintain the
19 safety, purity, and buoyancy of the product. So, we
20 will be taking away the discussions from today and any
21 available data to consider that decision.

1 **DR. ORTEL:** But is there -- do you, then, come
2 back with a plan that you want to see a certain follow-
3 up data in 6 months? Or is there something that's
4 developed with the applicant?

5 **DR. ILLOH:** So, depending on the request,
6 there are times that we might request for additional
7 data. Sometimes we grant what we call time-limited
8 variances or we put some conditions with the variance
9 to say you have to do this study or follow up with some
10 data for us to reconsider our variance approval.

11 **DR. KAUFMAN:** Dr. Stapleton?

12 **DR. STAPLETON:** So, this may reflect my
13 ignorance of the technology, but are there internal
14 controls to document the inactivation? And what sorts
15 of QA, CLIA type things are set up for -- since this
16 system isn't used many places?

17 **DR. AUBUCHON:** I'm not understanding the
18 question completely. Are you talking about the use of
19 the INTERCEPT system?

20 **DR. STAPLETON:** Yes.

21 **DR. AUBUCHON:** Ah, okay. Perhaps I should

1 defer to Dr. Benjamin on that.

2 **DR. BENJAMIN:** Yes, Richard Benjamin, Cerus
3 Corporation. They process controls in the way that --
4 the process of doing the inactivation, where you scan
5 the product into the machine; you scan them out. Time
6 and length of elimination is recorded. And that's kept
7 in the BECS system as a permanent record of
8 elimination. So, yeah, there are process controls for
9 every step. We do start off by sterile docking your
10 platelet onto the product, and there are usually ways
11 of documenting that so it's an input and an output at
12 the end. So, yes. You use your BECS system to
13 document the process.

14 **DR. BLOCH:** Is there a failure rate?

15 **DR. BENJAMIN:** Is there a failure rate?

16 **DR. BLOCH:** Yeah.

17 **DR. BENJAMIN:** I'm not sure what you mean by
18 failure rate.

19 **DR. BLOCH:** How frequently does it fail?

20 **DR. BENJAMIN:** I'm not understanding what you
21 mean by fail.

1 **DR. BLOCH:** If there's an assay that -- there
2 are always cases which are going to escape detection
3 because of whatever reason.

4 **DR. BENJAMIN:** We have discussed the relative
5 pathogens that might be resistant to the pathogen
6 inactivation process already. Since this is a manual
7 process where you take a platelet manually through a
8 sterile docking elimination, the whole process, as in
9 any manufacturing environment, things are apparent that
10 your sterile docking may not work. There may be leaks
11 in the bag, there may be defects, et cetera. And the
12 staff are, like any process, trained to look for those.
13 It's no different to any other blood banking process
14 that is currently used today.

15 **DR. AUBUCHON:** Please correct me if I'm wrong,
16 Richard. But if, for example, the ultraviolet source
17 did not turn on during the presumed elimination period,
18 then the eliminator would identify that as a failed
19 run.

20 **DR. BENJAMIN:** So, I think -- yes.
21 Absolutely, there is a sensor for the elimination. The

1 way the bag is designed, you're guaranteed to add the
2 Amotosalen. You cannot fail to add the Amotosalen
3 since it's a flow-through system where the platelet
4 runs through a bag containing the Amotosalen into the
5 first bag. So, you are guaranteed to have added the
6 Amotosalen as a control for the actual elimination
7 occurring. There's a control for placing the product
8 into the eliminator and taking it out of the
9 eliminator. So, yes, there's process control, like
10 everything we do in blood banking.

11 **DR. STAPLETON:** And I'm sure there are UV
12 light source requirements that are maintained, that
13 sort of thing; as far as duration. Yeah.

14 **DR. BENJAMIN:** Absolutely. These lamps have
15 lifespans, and there's a counter and number of times
16 it's been used. The maintenance requirements, et
17 cetera, are all documented and inspected and
18 maintained.

19 **DR. AUBUCHON:** I appreciate Dr. Benjamin's
20 assistance in responding to your questions. I should
21 also make it known to the committee that neither I nor

1 Bloodworks are receiving any monetary support, and we
2 are not engaged in any research studies with Cerus.
3 This is imperially on our own volition.

4 **DR. KAUFMAN:** All right. Dr. Bryant?

5 **DR. BRYANT:** The variance will be for MSM.
6 Will it be for men who have had -- deferred for 12
7 months from the most recent contact with a female who
8 had sex during the past 12 months with a man who had
9 sex with another man in the 12 months?

10 **DR. AUBUCHON:** Yes.

11 **DR. BRYANT:** That will happen as well? Okay.
12 And are you looking at, possibly, any other high-risk
13 groups?

14 **DR. AUBUCHON:** We have also submitted a
15 variance request to allow to take donors who are
16 currently deferred for malaria. We have many tens of
17 thousands of Asian and South Asian immigrants in the
18 Seattle area who frequently -- well, they have been in
19 the U.S. for longer than three years, often. But they
20 came from a malarial area and they go home to visit
21 friends and relatives and keep getting deferred.

1 We would love to have them as blood donors --
2 as platelet donors in the same kind of approach. And
3 it would be easy to adapt the same process controls
4 that we would use with MSM for those individuals.

5 **DR. BRYANT:** Are you looking at possible
6 tattoos, ear piercing, body piercing, or needle sticks?
7 Just curious.

8 **DR. AUBUCHON:** We don't lose many donors for
9 tattooing in Washington and Oregon because tattoo
10 establishments are licensed by the state, and we allow
11 those individuals to donate. Our main problem is
12 making the young adult population aware that, after
13 they have been tattooed in one of these establishments,
14 they can still donate blood. So, that's our challenge
15 there rather than the actual deferrals.

16 **DR. KAUFMAN:** All right. So, if there are no
17 other questions from the committee, thank you very
18 much. We're going to take a short break. We'll take a
19 10-minute break and come back at ten to.

20

21 **BREAK**

1 you choose not to address this issue of financial
2 relationships at the beginning of your statement, it
3 will not preclude you from speaking and you may still
4 give your comments.

5 So, we have one person on the list from this
6 morning, Dr. Richard Benjamin.

7 **DR. BENJAMIN:** Good afternoon again. Dr.
8 Richard Benjamin, chief medical officer from Cerus
9 Corporation. I am an employee and a stockholder in the
10 company. Really a pleasure to present in support of
11 Dr. AuBuchon's variance application. I want to
12 reiterate what he said was that we were pleasantly
13 surprised to see that his variance request was being
14 considered by BPAC and, really, there was no collusion.
15 We had let it known in our own talks that we thought
16 this was a possibility, but we did not encourage him to
17 submit the variance application. We're very glad that
18 he did.

19 Okay. So, what I thought I'd do is just to
20 run through the submission that Cerus made in 2016 to
21 the FDA's request for comments at that time around

1 blood donor deferral policy for reducing the risk of
2 HIV virus transmission by blood and blood products.
3 Because, in November of that year, we submitted -- and
4 that submission is in the committee's review packet and
5 available outside on the table for anyone who wants to
6 see it.

7 In that submission, we pointed out that -- in
8 our executive summary -- that the availability of
9 pathogen reduction using the FDA-approved INTERCEPT
10 Blood System for platelets and plasma provides an
11 additional layer of safety to help protect patients
12 from transfusion-transmitted infections. For blood
13 collectors to use pathogen reduction, individual
14 behavioral risk assessment independent of sexual
15 orientation could be implemented immediately for
16 platelet and plasma donors, addressing the major
17 concerns of the regulatory agencies of possible
18 increase for recipient risk.

19 Any resulting change in the donor population
20 could be assessed by the means of terms and rights to
21 studies in anticipation of the availability of approved

1 systems for red cells that might allow universal
2 pathogen behavior-based deferrals. So, it's good to
3 see, now, two and a half years later, that we're
4 discussing it in public.

5 You have already seen this table of claims.
6 Let's see. This is the one table that refers to viral
7 reduction and there's another that refers to bacterial
8 reduction capacity of the system. And I pointed out
9 earlier that the greater than or equal to signs do mean
10 that we inactivated to the limit of detection and that
11 the clinical isolates of HIV really could not be grown
12 above 2 to 3 logs, and that's the limitation there.

13 We have every reason to believe that they
14 would've cured at least 5.4 or 5.6 logs, if not more.
15 And it's our belief that the combination of mini-pool
16 NAT and pathogen reduction actually makes a very
17 powerful multilayer safety system for blood products,
18 and believe that, actually, we will continue to perform
19 NAT testing even one day when we have universal
20 pathogen reduction available.

21 Why do I believe this? Well, a good case,

1 which is impressed today in transfusion, online early,
2 illustrating the capacity of intercept system. This is
3 a French case report that just got published. In
4 France, they introduced individual donor nucleic acid
5 testing in 2010. And the residual risk of HIV is two
6 to three times lower than it is in the U.S., at 1 in 6
7 million.

8 Nevertheless, they recalled, back in September
9 2017, a repeat whole blood donor who seroconverted, was
10 HIV antibody and NAT positive. When they did a look
11 back to four months earlier to his prior donation that
12 had tested antibody and NAT negative -- I.D. NAT
13 negative -- they had his sample on hand and were able
14 to detect very low levels of viremia in that donation,
15 less than 34 CP per mil.

16 So, they looked at the recipients of those
17 blood products. The plasma had gone to fractionation
18 and could not be traced further. The red cells had
19 been given to a patient who died within six days, and
20 so they had no follow-up on that patient. But the
21 platelet, which was a platelet in pass, had been

1 transfused to a patient. They did do a follow-up six
2 months after transfusion, and the patient remained
3 seronegative for HIV, to everyone's relief.

4 The good news is that that platelet had been
5 INTERCEPT treatment. France introduced universal
6 INTERCEPT platelet pathogen reduction in November 2017.
7 This was in about May 2017. So, they were on the ramp-
8 up phase of introducing INTERCEPT at the time. And
9 actually, this particular platelet had been pathogen
10 reduced. We don't know that the low levels of virus in
11 that platelet would have been infectious, but I'm
12 certain that everyone was very reassured that, in fact,
13 it had been.

14 So, then, the landscape for removing the MSM
15 deferral question and the one-year deferral --
16 apheresis platelets are a particularly attractive
17 population to lead this change, because there is a
18 robust pathogen reduction process available and in use,
19 there is outpatient reimbursement in place today in the
20 U.S., and platelets are always in short supply. Red
21 cells, it may have been a decline of 30 percent over

1 the last 10 years in use. But platelet use continues
2 to be stable or increasing year to year. And because
3 of the 5-day shelf life, there are always local
4 shortages of platelets. So, an increase in donors and
5 supplier is needed for platelets.

6 Finally, the apheresis collection process
7 lends itself to this question. It encourages repeat
8 donation over time, allows longitudinal assessment of
9 individual risks over time, and tends, in the fixed-
10 site setting, to be separate in some way from whole
11 blood donation. So, if you're going to have a
12 different process, apheresis platelet donation is a
13 good place to do it because it's not happening out on
14 the drives and you can do it in a controlled
15 environment. The requirements would include the use of
16 routine donor screening, conventional testing, pathogen
17 reduction, and adequate BECS controls to deploy.

18 This could be done, as Dr. AuBuchon suggested,
19 at the individual donation level. And you could use
20 the "yes" answer to the MSM question as it triggers to
21 track and treat that donation. An alternative way of

1 doing it might be to do it either at the donation
2 center level, blood center level, and maybe one day at
3 the universal pathogen reduction level for the whole
4 country. Because, then, you would cover things like
5 noncompliant donors -- donors who don't admit -- say
6 yes to the MSM question. In fact, I would suggest that
7 you can, then, remove the question completely and start
8 to ask questions around behavioral deferrals.

9 So, in that setting, the current deferral
10 could possibly be removed and you could start to ask
11 behavioral questions in the setting of pathogen
12 reduction plus nucleic acid testing. And I would
13 venture that we really need to be asking both
14 heterosexual and MSM behavioral risk factors, and
15 things like substance abuse and alcohol abuse and sex
16 with alcohol.

17 Questions that are asked today when they look
18 at HIV vaccines for risk factors; we should look at
19 those questions and ask whether they would apply to
20 blood donation. Of course, now we've heard that we
21 already have systems in place to track the incidence

1 and prevalence of viral markers through TTIMS REDS-IV.
2 We have the mechanisms to actually look at changes in
3 the donor population over time with pathogen reduction.

4 Now, this is an important question: is it
5 feasible? We heard the comment that only 50 percent
6 could meet the guard bands. I venture that that's
7 completely incorrect -- that, today, you could treat
8 100 percent of collections from these donors. How can
9 I say that? Well, today, 100 percent of collections in
10 France -- 330 thousand per year, that's quite a large
11 number -- are treated. 70 thousand collections in
12 Belgium, 30 thousand donations in Switzerland; all 100
13 percent treated.

14 So, how do you get there? Simply, today, in
15 apheresis collections, you set your machines for the
16 volume and concentration of platelets you want to
17 collect. There are settings today that you could set
18 to collect double or single, triple platelet
19 collections to make sure that they are 100 percent
20 treatable. Remember that these are all additional
21 collections. You're not taking somebody who gives a

1 triple and moving them down to a double. These are all
2 additional new collections. You can aim for double
3 collections and make sure they're 100 percent
4 treatable.

5 Alternatively, you could collect your triples.
6 But, then, you would need to manipulate the product
7 after collection. Split a triple into a single and a
8 double, and treat them separately. The other
9 alternative, with time, is Cerus is working on a triple
10 collection set which is licensed and approved today in
11 Europe. So, we have every confidence that we will get
12 that process available in the U.S. There's a process
13 we have to go through to finally get FDA approvals, and
14 we are highly engaged in moving that forward.

15 So, while today, blood centers struggle to get
16 to 100 percent or even 75 percent compatibility, that's
17 with the constraint that they do not want to change
18 their split rates. Right? If the focus of blood
19 centers today is to maximize and improve their platelet
20 split rates for economical reasons, if they are
21 prepared to put safety -- as in the MSM situation,

1 where you'd put safety first, you can get to 100
2 percent today.

3 Moving on. One day, when we actually have
4 universal pathogen reduction, we actually have the
5 opportunity to study over a million platelet donations
6 from both heterosexual and MSM donors in the U.S. I
7 would venture that, if we're going to do behavioral
8 questionnaires, you actually want to look at a
9 population that wants to give platelets or wants to
10 give blood. And this is probably the best way to do
11 it, because they've already shown the interest and
12 eagerness to give blood donation. They're in the
13 chair. And they're probably the best population to
14 study.

15 So, finally, I think we're all on the same
16 page. Every patient deserves safe platelets. This
17 committee has discussed bacterial contamination in
18 great depth, and the top photographs are related to
19 bacteria. But pathogen reduction does provide a
20 comprehensive solution, not only for HIV, but also
21 bacteria, virus and emerging pathogens, parasites, T-

1 cell contamination, and does provide an opportunity to
2 reduce discrimination and to provide social equity
3 while enhancing patient safety. So, with that, thank
4 you and I'd be happy to take any questions.

5 Maybe I can just stress one thing before I --
6 and 7-day platelets came up in discussion. There are
7 two things about 7-day platelets. One, are they that
8 safe from bacteria? And I think pathogen inactivation
9 or pathogen reduction provides the safety you need to
10 get to seven days. And two, are the 7-day-old
11 platelets viable and active and effective? For that
12 second part, the agency requires recovery and survival
13 studies to be performed.

14 Cerus is in the process of performing those
15 studies to meet the FDA's requirements. So, we know
16 today that in Switzerland and some other countries,
17 they use 7-day platelets routinely. And the
18 hemovigilance data we get from those countries shows,
19 quite convincingly, that those platelets are effective
20 and, in fact, do not require more platelets per patient
21 in use. So, we're confident that we will get there in

1 the U.S. Thank you.

2 **DR. KAUFMAN:** All right. Thank you, Dr.
3 Benjamin. Do we have any other representatives from
4 the public that would like to make a comment? Please.

5 **DR. HERSHMAN:** Good afternoon. My name is Dr.
6 Janet Hershman, and I'm the medical director for
7 BioLife Plasma. We are part of Takeda. And I would
8 like to speak on behalf of the PPTA, our industry
9 representative. PPTA is the Plasma Protein
10 Therapeutics Association. We would like to speak on
11 topics 3A and B related to this MSM donation. We are
12 the international trade association and we set the
13 standard for the major producers of plasma-derived and
14 recombinant analog therapies. We produce about 80
15 percent of the world's needs for source plasma and 60
16 percent for plasma protein therapies.

17 As you know, these are for individuals with
18 clotting disorders, immunoglobulins, for those who are
19 immune deficient, some people with neurologic disorders
20 as well as patients with Alpha-1 antitrypsin
21 deficiencies. We also produce albumin, which is used

1 in emergency rooms and for individuals with shock. Of
2 course, our goal is to produce safe and available
3 medically needed therapies which are plasma-derived.

4 The PPTA does agree with the FDA's overall
5 stated concept of looking at these policies, monitoring
6 the effective policies and evaluating future policy
7 alternative, including the MSM deferral. Although we
8 agree with the overall changes, we do wish to address a
9 few points that were provided in the FDA's issue
10 summary. The first one is with respect to topic 3A.
11 As you know, PPTA -- our companies operate about 760
12 U.S.-licensed plasma collection centers in the U.S.
13 And in 2018, we collected 48 million donations of
14 source plasma.

15 As PPA [sic] stated to the BPAC in 2014, at
16 which time the committee considered the change in
17 deferral policy from a lifelong deferral to the current
18 12-month deferral, source plasma is marketed globally.
19 And we have to adhere not only to the FDA standards,
20 but to policies beyond the FDA, some of which do not
21 conform with what the FDA's current policies are with

1 respect to the 12-month deferral. Notwithstanding
2 these changes in the donor policies, are they
3 [00:19:54] generally applied broadly in both donations
4 of blood and plasma.

5 Without the plasma industry's participation
6 and the design of this study that was discussed this
7 morning, incorporating an additional donor history
8 questionnaire for donors that may be at higher risk of
9 HIV -- which, again, that was discussed this morning --
10 it is unknown whether the results of such a study could
11 be transferred to source plasma as our collection does
12 differ in several methods from, for example, whole
13 blood. We only have fixed locations. We don't have
14 mobile locations. We have a much higher degree of
15 automation and donor selection and monitoring that
16 could affect the operational applicability to the
17 source plasma industry.

18 With respect to topic 3B, certainly the PPTA
19 is committed to providing safe and effective therapies.
20 Our patients who receive our therapies made from
21 plasma, as we mentioned, have very chronic and life-

1 threatening illnesses. Donor selection is certainly
2 one of our layers of safety. We acknowledge that we do
3 have a robust manufacturing processes and a lot of
4 dedicated manufacturing steps. We have complex
5 purification processes in viral removal as well as
6 viral inactivation.

7 We can tell you that, over the past two
8 decades, there have been no documented transmissions of
9 HIV or hepatitis B or C. Almost all products imply two
10 orthogonal methods for pathogen reduction. The log
11 reduction is generally higher than those achieved with
12 the methods being used for pathogen reduction in
13 transfusable products, and this addresses both
14 enveloped and nonenveloped viruses.

15 Despite the remarkable safety for final plasma
16 protein therapies, the PPTA members have retained donor
17 selection and donation testing as key quality
18 management tools within our construct, again, of layers
19 of safety. The FDA regulations include the assessment
20 of behaviors associated with the relevant transfusion-
21 transmitted infection and deferral of donors with

1 behavioral risk factors. PPTA opposes an ad hoc
2 variance approval that includes a specific set of risk
3 factors in a specific indication -- for example,
4 pathogen reduced apheresis platelets.

5 PPTA and its member companies welcome a
6 broader discussion of the value of behavioral risk
7 assessments and other current requirements in the face
8 of robust pathogen reduction processes. Thank you.

9 **DR. KAUFMAN:** Thank you. Is there anyone else
10 from the public that wishes to speak? All right.
11 Thank you. So, I'd like to ask the committee if you
12 have any questions or comments related to what we've
13 just heard during the open public hearing. Dr. Lewis?

14 **DR. LEWIS:** Referring back to one of the early
15 slides presented by Cerus, it talked about the desire
16 to move to a place where we could individualize risk
17 assessments of the donor to avoid painting people with
18 overly broad brushes -- for example, based simply on
19 sexual preference. And yet, this seems a teeny bit
20 different to me from the request for the variance,
21 which is to eliminate completely an entire set of

1 behavioral risk assessments that have to do with
2 behavior.

3 So, I'm wondering if someone can sort of
4 address how we got from the original text from 2016,
5 which seemed circumspect, and it's asked to something
6 that seems quite a bit more extreme.

7 **DR. BENJAMIN:** Maybe I can talk to my slide.
8 That slide was aspirational. It definitely is where we
9 think we could get to. I don't think it's necessarily
10 where we are at the moment. And it's certainly not the
11 request that's on the table for variance from Dr.
12 AuBuchon, which is a more limiting scope. So, I think
13 we could get there.

14 **DR. LEWIS:** So, I may have spoken unclearly or
15 we're seeing things quite a bit differently. If we
16 could show your slide -- I'm not sure if it was the
17 second slide. It showed -- it was full of text. It
18 had to do with your 2016 submission, if I understand
19 correctly. While we're waiting for that, where I'm
20 trying to get to is I can see very strong arguments for
21 using a different additional information that we have

1 available to us, based on epidemiology and other
2 sources, to try to be as discriminating as possible in
3 identifying the probability that an individual donor is
4 likely to be in the window.

5 I interpreted the phrase "individual
6 behavioral risk assessment independent of sexual
7 orientation" as moving away from simply asking whether
8 there has been MSM behavior over the last 12 months or
9 some period to one of asking whether or not the
10 behaviors, regardless of sexual orientation, are
11 behaviors that we know, epidemiologically, are
12 associated with risk of recent transmission. In fact,
13 I tried, in one of the breaks, to look up to see if I
14 could find a current questionnaire that's used to
15 identify patients eligible for HIV vaccine trials
16 because that really is attempts to find the exact same
17 population.

18 In that case, you're trying to recruit a
19 population at risk for acquisition. And here, we're
20 trying to avoid a population at risk for being in the
21 window associated with acquisition. I was unable to

1 find something. But, to me, those are very analogous
2 things. But there, you talk about individual
3 behavioral risk assessment and yet the variance request
4 said no risk assessment associated with MSM behavior,
5 that those -- that entire line of questioning would be
6 removed. And those seem quite a bit different --
7 qualitatively different.

8 **DR. BENJAMIN:** Indeed. The way it could is
9 aspirational -- could be implemented or you could do
10 this. In prior discussions, both in this BPAC and at
11 the Advisory Committee for Blood Tissue Safety and
12 Availability, the voice has been patrolled by the MSM
13 groups that their aspiration is to do away with the
14 question completely and to look at both heterosexual
15 and MSM risk factors. I think, in this 2016
16 submission, that's what we were attempting to address.

17 **DR. LEWIS:** And when you say "do away with the
18 question completely", which question are you referring
19 to?

20 **DR. BENJAMIN:** Are you a male that has had sex
21 with a man? Right now, it's for 12 months. At the

1 time -- three years ago, I can't remember if this was
2 before or after it changed to 12 months. But
3 certainly, it was indefinite at one point. It used to
4 say "since 1977".

5 **OPEN COMMITTEE DISCUSSION/QUESTIONS FOR THE**
6 **COMMITTEE**

7 **DR. KAUFMAN:** Okay. Thank you. All right.
8 So why don't we move on to the open committee
9 discussion? And maybe we can have the question up for
10 the group. Issues for discussion -- we want to discuss
11 the use of pathogen reduction of apheresis platelets as
12 an alternative to the current MSM deferral policy and
13 discuss any associated risks and possible mitigations.
14 So, let me open this up to the committee. Sridhar?

15 **DR. BASAVARAJU:** So, it seemed to me that much
16 of the risk reduction in blood safety actually occurs
17 because of the donor deferral process. So, by the time
18 a donor is deemed to be eligible to donate blood, it's
19 because they are at lower risk. And I think that's
20 evidenced by the fact that the proportion of total
21 donors who are found to be HIV positive during blood

1 donor screenings is substantially lower than the
2 population prevalence.

3 So, if you take that out and then you
4 introduce a population who is known to have the
5 highest, I guess, risk of having incident HIV
6 infection, it would seem that you would have window
7 period cases that are tested and found to be negative
8 even though they could be infected. And then, you
9 would apply a technology that's pathogen reduction.
10 It's not pathogen elimination.

11 So, presumably, there's still at least some
12 risk. So, it would seem that this -- I think the idea
13 of saying, could we talk about reducing the 12-month
14 period or something like that, I think that's
15 reasonable. But, to say we're going to just stop
16 asking at all, that seems a little extreme.

17 **DR. KAUFMAN:** Dr. DeMaria?

18 **DR. DEMARIA:** My question would be, is
19 pathogen reduction more or less reliable than the
20 history that we're getting from the donor? Because the
21 deferral depends on the history we're getting from the

1 donor. And presumably, the residual risk is in people
2 who are not providing an accurate description of what
3 their risk is and, therefore, turn out to be positive.
4 So, it is a balance between that history and the
5 pathogen reduction addition to the safety, it seems to
6 me.

7 **DR. KAUFMAN:** Dr. Shapiro?

8 **DR. SHAPIRO:** From a standpoint of patients
9 with bleeding disorders who utilize plasma-based
10 products, we, as providers, look at the products. What
11 we want from them is we want donor testing, and we want
12 two viral inactivation methods to assure that the
13 products are likely safe. Now, again, those are larger
14 pool products and it's different than this, but -- and
15 I think this technology's wonderful. I think that I
16 view it as your using of the donor testing and a viral
17 inactivation process, which will help make the blood
18 supply safer to the recipients.

19 The total elimination of risk questions seems
20 a little premature in light of the discussion when
21 you're considering going from one-year deferral to a

1 shorter period of time and being totally reliant upon
2 one inactivation technology. And it's not just the
3 risk of what we know; it's the risk of what can appear.
4 This doesn't get every virus.

5 **DR. KAUFMAN:** Dr. Bloch?

6 **DR. BLOCH:** So, you know, I totally agree with
7 you. I'm really struggling with this because, on the
8 one hand, really, are proponents of pathogen reduction
9 which I see as transformative because it's protecting
10 against emerging, remerging, as well as established
11 pathogens. I also agree with what has been said in
12 terms of the platelet inventory, particularly HLA-
13 compatible products. There's really -- while red cell
14 utilization has gone down, I think that there
15 definitely is a need for platelets.

16 But the premise for this seems to be -- there
17 seems to be a disconnect. Because we're arguing for
18 eliminating something which we know potentially has
19 established benefit in favor of pathogen reduction
20 because of the bacterial benefit. It's just, in a way,
21 kind of comparing apples with oranges. Is this a real

1 need to abandon -- we've singled out the highest risk
2 factor, almost arbitrarily. There's no need to abandon
3 the risk factor just to bring in pathogen reduction.

4 **DR. KAUFMAN:** I think that -- if I've
5 interpreted Dr. AuBuchon's presentation correctly, I
6 think the bacterial benefit is more of a side thing and
7 not at all the focus to this. And I would like to keep
8 the discussion really focused around HIV for this.

9 **DR. BLOCH:** Again, it's kind of selective --
10 we're arguing selectively. I think that the real
11 benefit is actually the bacterial protection. And then
12 -- because no -- I'm just trying to understand why one
13 would abandon the donor inquiry when we know that
14 that's potentially offering benefits.

15 So, in terms of precedent with laboratory
16 testing as we mentioned this morning -- well, actually,
17 yesterday -- the only test which have -- where they've
18 given something up was where they had something which
19 improved upon it, whereas this is not really -- it
20 definitely offers a completely different layer of
21 safety. But it's not necessarily in line. It's not --

1 we didn't go from p24 antigen to NAT testing. They're
2 two different sources of benefit.

3 **DR. KAUFMAN:** I think I don't exactly agree.
4 Well -- so what I would say is that it's not possible
5 to get rid of the window. So, we can kind of hammer
6 down the risk by shrinking the window with incredibly
7 sensitive tests. And we may be about as -- where we
8 can be. Maybe there's a way to get it down another
9 couple of days. I don't know. And there's probably a
10 period immediately after infection where something's
11 not infectious; there's not enough virus. But I think
12 that that risk continues to exist that is -- if you're
13 relying on testing and whatever else you do, I think
14 that risk exists.

15 Pathogen reduction, essentially, can take care
16 of that residual risk which is, again, really what
17 we're talking about. So, even though, yes, I agree
18 with your point that you're actually actively inviting
19 donors who, as a group, have -- at least at the group
20 level, have a higher risk of HIV. That's not
21 debatable. But you're still using NAT with this very

1 small window. So, what's left is still really quite a
2 low risk.

3 And then, I think you can essentially, with a
4 -- what could only be a recent infection and a very low
5 level of viremia, I think you're really talking about a
6 zero risk essentially, with pathogen reduction in that
7 setting.

8 **DR. BASAVARAJU:** I don't think it'd be zero,
9 right? I mean, I don't -- I think that none of the
10 mitigation strategy is at zero. Even PRT, I don't
11 think -- even Dr. Benjamin wasn't claiming it's zero.
12 So I think you -- I mean, you have a lower pathogen
13 load, by virtue of it being subjected to PRT, but if
14 you're having more people who are acutely infected,
15 then you would presume that some of those people would
16 be potentially not.

17 **DR. KAUFMAN:** Dr. Stapleton.

18 **DR. STAPLETON:** I think, theoretically, it is
19 zero. Because if you're talking about missing it on
20 NAT testing that has a very high sensitivity -- so the
21 amount of virus in that product is less than a few

1 copies per mil, and the volume is less than two liters
2 and you've got five logs of reduction, you've gotten
3 rid of every -- you've inactivated every virus in
4 there. So, theoretically -- nothing is zero. But,
5 theoretically, it's zero.

6 **DR. STRAMER:** May I say something?

7 **DR. KAUFMAN:** Yes, Sue.

8 **DR. STRAMER:** So the combination of testing
9 and donor selection obviously doesn't work perfectly,
10 because we have positive donors for all markers we test
11 for. The FDA authority allowed pathogen inactivation
12 to serve as a substitute for bacterial mitigation for
13 Zika and in the plasma industry for many other markers
14 that they don't test for that we do. The pools that we
15 do for NAT in whole blood -- for instance, in the
16 plasma industry -- are much smaller. The donor
17 demographics are very different.

18 So, I would position pathogen inactivation as
19 an indiscriminate method of the eliminating pathogens.
20 Perhaps not all pathogens, but certainly those envelope
21 pathogens that we're very familiar with in MSM and

1 other individuals with sexual risk factors. So, I
2 think, if we're trying to compare one-year deferral or
3 two, three-month deferral or donor retest, it's really
4 -- as others have said, it's an unfair comparison
5 because pathogen inactivation is much more robust. It
6 may not be zero, but it's certainly more robust than
7 the other technologies we talked about earlier today.

8 **DR. KAUFMAN:** Thank you, Sue. Dr. Lewis?

9 **DR. LEWIS:** I, perhaps, like Dr. Bloch -- I'm
10 really disturbed about the structure of the argument.
11 I don't see any connection between reduction of
12 bacterial contamination risk and the question about the
13 deferral question.

14 Because if, in fact, our concern was about the
15 safety of the platelet supply with respect to the most
16 common pathogens which are bacterial, then we would be
17 discussing widespread use of this pathogen reduction
18 technology along with concomitant strategies to
19 increase the donor pool broadly since it's a very small
20 fraction of the population that donates platelets.
21 These things have nothing to do with each other, and

1 I'm personally bothered by the attempt to link them and
2 defend that linkage. That's the first point.

3 The second point is that -- was, I've been
4 going to my logarithmic math in my head, as Dr.
5 Stapleton has as well, and I agree with you that it is
6 likely that the risk is very, very, very close to zero.
7 There's actually no data provided to us or the agency
8 regarding the incidence of folks in the window that
9 would be associated with reduction of those screening
10 questions.

11 Unlike some things where you have to replace
12 one technology with another technology -- and for some
13 reason, they're mutually incompatible -- in this case,
14 there's nothing that says you can't ask some questions
15 and then also treat the platelet with pathogen
16 reduction. Again, it's a false choice. So, I believe
17 that Dr. Stapleton's math is probably correct. I
18 believe there's no data to support it other than just
19 sort of conjecture about what we believe about the
20 population.

21 I think that the linkage of questions that

1 should not be linked is something that we should call
2 out, and that it is perfectly reasonable to recommend
3 that one pathogen reduction technology be used because
4 it does increase the safety of the platelet supply;
5 that broad approaches to increasing the population that
6 provides platelets to the nation's platelet supply be
7 pursued because it will be some loss of efficiency
8 that's the cost of that additional safety; and that
9 the real issue with the MSM question is that it paints
10 an overly broad brush that is, therefore, offensive
11 because people know it is not sexual orientation or it
12 is not a monogamous relationship that places you at
13 risk.

14 And the question, now, inappropriately
15 captures that. What we should focus on is trying to
16 figure out what the questions are that capture the risk
17 so that we don't appear discriminatory as we try to
18 distinguish levels of risk.

19 **DR. STAPLETON:** I agree with that. And I
20 think that the participation in the study and at the
21 time of screening is very appropriate.

1 **DR. BAKER:** A general lending of support to
2 Dr. Lewis' statements.

3 **DR. KAUFMAN:** Mr. Templin.

4 **MR. TEMPLIN:** Personally, I think the whole
5 question entered needs to be revisited. And maybe more
6 people should be deferred in other risk categories.
7 But, because of the short shelf life of these
8 platelets, I would think if there's at all a
9 possibility that this technology could harm -- because
10 it could let something go through that isn't being
11 inactivated other than HIV -- these folks that are
12 receiving these platelets would be in more danger.

13 Going to listen to what PPTA says, their
14 product is held in inventory for a long while. It's
15 not just used within a few days. So, I just wanted to
16 add that.

17 **DR. KAUFMAN:** I think those are -- well, a
18 couple of different points. Obviously, the
19 consideration for a donation in testing and then to
20 come back and retest the donor strategy truly can only
21 be applied for products with longer storage. So, for

1 platelets, at least as they're currently collected,
2 it's just completely not viable. I do think that from
3 a -- strictly from a pathogen -- from the potential for
4 a platelet unit to transmit any pathogen, a pathogen
5 reduced unit is considered to be the safest that is
6 available.

7 So, it's -- one of the things that we were
8 kind of talking about a little bit today, a little bit
9 more in the morning, is, well, when you ask questions,
10 do people understand them? Do they answer accurately?
11 Do they remember? Do they not remember? You know?
12 And then, ultimately, you're left with, okay, so, now
13 we think we have someone who's incredibly low risk;
14 they're in a monogamous relationship. And the truth
15 is, you can never be 100 percent sure about monogamy.
16 There's just no way around that.

17 One of the, I think, attractions of an
18 approach like pathogen reduction is, because it's
19 completely different, none of that matters. So, while
20 you may, as part of a multilayered approach, be able to
21 drive risk down, it does allow to cover up for

1 potential limitations for some of these other
2 approaches, like risk questions.

3 **DR. TEMPLIN:** I think if, with this
4 technology, you get rid of bacteria, that's great and
5 it should probably be used for that purpose. But I
6 would rather have a product that was solvent/detergent
7 treated that have filtered in a multiple-step approach.
8 I also think, too -- I know, personally, people who
9 have told me they lied on the questionnaire for
10 whatever reason they did.

11 It's heartbreaking because I would want that
12 person to have a unit of whatever that was perfectly
13 clean at any time. Everybody should have the right to
14 have safe blood or any kind of medication period. So,
15 it is sad when people say they would only donate now
16 because they can't. But if they had the opportunity to
17 donate, they would. So, it is just sad to hear.

18 **DR. KAUFMAN:** Well, and with respect to the
19 other products -- plasma drive clotting factors, for
20 example. So, here, we're talking about acellular
21 products that can be more intensively processed and

1 that sort of thing.

2 **DR. SHAPIRO:** Right. So, cellular products.

3 **DR. KAUFMAN:** Right. For cellular products,
4 it is different. I will say, again -- and I have no
5 financial conflict of any sorts, but I will say that
6 one of the advantages that we've seen with pathogen
7 reduction is, even with these large pools, these
8 approaches, somewhat different -- solvent/detergent,
9 ultrafiltration, and so on -- were applied to factory
10 products, for example. So, when West Nile Virus, for
11 example, came to the U.S., it was a nonproblem. It is
12 sort of already had been taken care of.

13 Anyway, so, it's another argument for a
14 pathogen reduction approach versus a, "Did you travel
15 somewhere where there's West Nile?" or that sort of
16 thing.

17 **DR. SHAPIRO:** I wasn't arguing against
18 pathogen reduction; I was arguing for it for these
19 products, just not necessarily elimination of
20 assessment of risk through questionnaires.

21 **DR. KAUFMAN:** Dr. Demaria?

1 **DR. DEMARIA:** I think -- well, you know, to
2 get back at why we're here discussing this is that the
3 -- and people may or may not agree, but the reason we
4 are discussing this is because there's a perception
5 that the way we do it now is not equitable or just in
6 terms of eliminating people purely on their sexual
7 orientation, not what they actually do or do not do
8 that may put them at risk or not put them at risk. And
9 there are ways to address that.

10 I like the Bloodworks Northwest approach; I
11 feel that it's a safe approach and that it's preferable
12 to the approach of quarantining plasma, which we don't
13 really need the plasma. It's just being done as a
14 concession to make up for the fact that we have this
15 policy in place whereas the platelets are really
16 needed, and it could enhance overall health by
17 providing more platelet products for people who really
18 need them.

19 So, I think, looking at it from that
20 standpoint, there's not one solution to all of this.
21 But there is an exploration of various solutions. And

1 I still think, if you can find that technological fix
2 that gets around the fact that people many not always
3 tell you what behavior they're participating in, that
4 is preferable to depending on that kind of history.

5 **DR. CHITLUR:** This is Meera. Can I ask a
6 question?

7 **DR. KAUFMAN:** Yes. Please go ahead.

8 **DR. CHITLUR:** The Bloodworks Northwest
9 approach of considering doing a PRT for all platelet
10 donations coming from MSMs -- did I understand that
11 right? Is that what they were saying, that they will
12 consider PRT for those units?

13 **DR. KAUFMAN:** I'm going to try to say this
14 correctly. So, their approach will be, if, in the
15 course of a routine screening, an individual answers
16 yes to one of the MSM questions, they would
17 automatically be restricted just to donating apheresis
18 platelets. Those apheresis platelets would be
19 automatically restricted to be pathogen reduced, and
20 then have to meet the guard bands on sort of
21 manufacturing steps necessary to ensure inactivation of

1 the units.

2 The donors would be tested by the usual
3 nucleic acid test, and the product at the end would be
4 essentially considered to be equivalent as any of their
5 pathogen reduced apheresis platelets currently in
6 inventory.

7 **DR. CHITLUR:** Is there any reason to think
8 that -- I don't know if this is even right. But if --
9 considering that we have some information, does the
10 recipient have to somehow -- I know at the end, I
11 guess, they're all equivalent. Am I right? So, it
12 does not -- that information up front that we got does
13 not necessarily have to reach the consumer at the end.

14 **DR. KAUFMAN:** Yes, that's correct. The label
15 of the product would be exactly the same, and there
16 would be nothing different from the hospital that got
17 this. From their perspective, it would be the same as
18 every other platelet. And really, that's, I guess, one
19 of the questions the group is being asked to
20 contemplate is, does that sound reasonable? That is,
21 could the product be considered as safe as every other

1 product? I personally think that the answer to that
2 question is yes.

3 Sorry. Dr. DeVan? Dr. Bryant?

4 **DR. BRYANT:** I agree with you, Dr. Kaufman. I
5 look at this and think, okay, what could go wrong? A
6 donor comes in; answers a question yes for MSM. Then,
7 they'd be tested anyway for infectious disease, right?
8 So, worst case scenario, in a window period or maybe on
9 PrEP, and viral load's really low and not getting
10 picked up. But then you're going to go through
11 pathogen reduction. So, you're going to be covered
12 with that.

13 I think that's a safe alternative to our
14 current policy. As long as there's -- have all the
15 stopgaps to make sure that you're not going to have a
16 problem with the eliminator being turned on or the
17 Amotosalen being added. And those are things that are
18 built into the system that that wouldn't pass; I mean,
19 there would be a big flag that's -- that product would
20 not get through the processing. As long as a computer
21 system's picking this up and flags the patient that

1 this unit of platelets would need to go and be -- we
2 could only collect platelets and it would, then, become
3 pathogen reduced.

4 So, I think, if everything is in place, it
5 would make sense. And it actually would probably be a
6 better product than possibly a three-month deferral or
7 maybe even a year. I mean, I don't know. Especially
8 since we've got the added PrEP in place. We don't know
9 what that means. Is that going to delay the window for
10 how many weeks? So, pathogen reduction, I think, is a
11 good option.

12 **DR. KAUFMAN:** Yeah. And just a couple of
13 points; I think, what you talked about at the end --
14 would everything work right? I think that is really
15 kind of the risk. On the other hand, those are the
16 sorts of risks that blood centers have to deal with
17 continuously. Did you get the correct result matched
18 to the correct donor? And was the NAT test done
19 properly? All I can say is it's a industry that deals
20 with risk. And I forget who said it; maybe it was Dr.
21 Goldman earlier, like, "Standardization is next to

1 godliness."

2 So that is a question, but that is a practical
3 logistical question for Dr. AuBuchon and the blood
4 center. I thought the way that he laid it out in his
5 presentation, where, sure, it's a different pathway;
6 they have some different products in their inventory.
7 But the pathway that he laid out wasn't radically
8 different from how they're making other PRT platelets.
9 In the absence of a computer system to handle a lot of
10 the sorting of a product, I would be much more
11 concerned about the logistics. But for the same reason
12 that, for example -- I don't know -- electric
13 crossmatch works, that sort of thing, to me, it seems
14 okay is my feeling.

15 Dr. DeVan?

16 **DR. DEVAN:** This -- along the same lines of
17 your thinking "what could go wrong?", I was wondering
18 about, during the process, the phlebotomy of a donor
19 that comes in the phlebotomy -- the removal of the unit
20 before it's gone through the Amotosalen processing.
21 Does that increase any risk if we do accept donors from

1 a higher risk pool? And does -- should that play any
2 role? Does that play a role or should that play any
3 role? A patient that comes in from a higher risk
4 population and the phlebotomy, the removal of the unit
5 itself before it's gone through the inactivation
6 process.

7 **DR. STAPLETON:** I don't know if you're talking
8 about transmission or to the donor.

9 **DR. DEVAN:** I'm thinking of a potential risk
10 to the phlebotomist.

11 **DR. STAPLETON:** I have a number of patients
12 with hemochromatosis and HIV, and before they were on
13 HIV meds, we sent them for a phlebotomy. And that's
14 not considered a dangerous procedure other than -- more
15 so than using universal precautions. So, I would not
16 think so, but others could argue with me if they want.

17 **DR. STRAMER:** This is Sue Stramer. I mean,
18 that risk exists today when we collect from any -- from
19 a donor who may be in the window period as HIV positive
20 and before we even know the test results. So, those
21 risks occur now with HIV positive. 62 percent, as we

1 heard earlier, come from donors who have MSM.

2 The real question today is, you have two
3 choices for platelets. One are platelets the way they
4 are today, with the 12-month deferral for MSM,
5 accepting a 7 to 10-day window period, knowing that our
6 residual risks for HIV are somewhere in the 1 to 2, to
7 1 to 3 million range -- probably lower for platelets
8 because they're so pedigreed -- versus accepting the
9 same testing that we do today and substituting the MSM
10 question with its flaws, the noncompliance, and other
11 issues we've talked about. But the technology that
12 especially, within the window period, is fairly robust.

13 And for those viruses that may present an MSM,
14 we know they're very susceptible to pathogen reduction.
15 The agents that Dr. Benjamin mentioned of bacterial
16 spores, bacillus, or HIV or HAV possibly, but those are
17 not the agents you would expect today to be in a
18 presenting MSM donor.

19 **DR. KAUFMAN:** Dr. Lewis?

20 **DR. LEWIS:** But I think there is a third
21 option. I think we get different answers depending on

1 -- for each of us, we can pick two options and make a
2 choice between them, but we all get to pick which two
3 we want to choose between. The third option that the
4 previous speaker didn't mention is the option of adding
5 the pathogen reduction, which everybody is unanimous
6 about its merits, but retaining some level of
7 behavioral risk stratification as well.

8 And I just don't see why we tie the addition
9 of this additional layer of safety necessarily with
10 elimination of a different layer of safety about whose
11 removal we've actually been seeing no data in terms of
12 what it does to, I guess, the prevalence of donors
13 being in the window. And I agree with everybody's math
14 that the risks here are very, very low. But we should
15 structure our argument accurately.

16 **DR. KAUFMAN:** Oh, sorry. Mr. Templin?

17 **MR. TEMPLIN:** I'm all for the safety of blood
18 supply, I don't want anybody to be discriminated. I
19 want social justice, everybody to be happy. Yes, the
20 industry takes risks, but also the recipient of the
21 products take risk. And I get some infected products

1 and nobody compensates me because there is no
2 compensation. The blood share laws protect these
3 products.

4 So, maybe a Vaccine Injury Act for blood would
5 be something that should be created because, if I get a
6 vaccine and something happens, somebody takes care of
7 me. I'm all for the industry taking risks, but if I
8 need some sort of product, I'm taking a risk too.
9 Unfortunately, some people have to take more risk than
10 others.

11 **DR. KAUFMAN:** I think you're at one of the
12 most risk-adverse places in the country. That is, I
13 think that, truly, we -- I'm very proud of the fact
14 that blood has gotten so safe. I don't think anyone
15 could've imagined blood could be this safe in the
16 1980s. It's gotten amazingly safe relative to how it
17 used to be, even before there was HIV in the U.S.
18 Again, we've kind of -- I've kind of said this before,
19 but I think that the general theme is we want to try to
20 maintain that safety. That is the primary mission.
21 That is not something that I don't think anyone is

1 talking about compromising.

2 So, having that as a first and immutable goal,
3 the next question is, can we meet that in different
4 ways that might allow more people to donate? And I
5 think that's kind of the crux of it. So, I guess I
6 don't frame it as, well, let's pick a flyer on this
7 approach or that. And I think Dr. Marks said it as
8 well. And again, the FDA, in this instance, after much
9 deliberation, went from a permanent deferral for MSM to
10 12-month, and that's where it's staying for the time
11 being without further data. He made that very clear.

12 And then, I think the question is sort of one
13 -- truly an exploratory effort that we talked about
14 this morning is a study that may or may not lead to
15 further changes, and then this other approach, which --
16 frankly, because it offers a completely different way
17 of making blood safe, you end up discussing some -- I
18 don't know -- different sorts of possibilities, is what
19 I would say.

20 Dr. Stapleton?

21 **DR. STAPLETON:** Dr. Schreiber may not have

1 appreciated my taking his comments this morning, but I
2 thought his comments about, "What was the evidence for
3 going to 12 months as opposed to 3 months or 2 years?"
4 The exclusion doesn't apply to heterosexuals who don't
5 answer the questionnaire honestly either. So, there is
6 that social justice issue. And those at-risk people
7 will still be donating, and they'll be excluded from
8 the PRT. So, if they get platelets, actually, those
9 units will still be there.

10 I think, on balance, there is a more
11 biological support for this approach, even dropping the
12 three-month window, than there is for -- well, than
13 there would be for the blood supply. And the other
14 thing that will happen is we will collect -- we should
15 generate good evidence and data on this group of people
16 over the next few years that will help us in
17 understanding about blood transfusion.

18 **DR. KAUFMAN:** Sridhar?

19 **DR. BASAVARAJU:** So, we haven't seen any data
20 here, right? So, we don't know how many MSM will show
21 up to donate apheresis platelets. We don't know how

1 many of those would be acutely infected. And we don't
2 know how many of those would be acutely infected on
3 PrEP, let's say. Then, let's say that there are those
4 people we don't know necessarily how much of this will
5 be eliminated by PRT, right? We haven't seen data on
6 that because I don't think that they have that data.
7 But we're going to give it to recipients without
8 telling the recipients we don't know any of this
9 information. Right?

10 **DR. STAPLETON:** I don't -- we do that with
11 heterosexual people who have risk as well, who lie on
12 the questionnaire.

13 **DR. KAUFMAN:** And I will say there is a lot of
14 published data over many years, both in vitro and in
15 vivo related to PRT. It was not presented today. I
16 think that's fair.

17 **DR. SHAPIRO:** I mean, you're right that we do
18 that with heterosexual people who do not tell the truth
19 on the questionnaire, but not knowingly.

20 **DR. STAPLETON:** So, I guess you could argue,
21 how do you knowingly know that a homosexual man is

1 lying on the questionnaire versus a heterosexual? And
2 so --

3 **DR. SHAPIRO:** No, you don't. I mean, both
4 groups lie a certain percent. I mean --

5 **DR. STAPLETON:** So, the beauty of the PRT is
6 that it takes away that.

7 **DR. SHAPIRO:** I'm not arguing against PRT.
8 I'm talking about dropping of risk questions on the
9 questionnaire and not informing the recipients of those
10 products that you've dropped a level of what was
11 considered safety by the public.

12 **DR. STAPLETON:** Would -- I guess it would be
13 publicized that this was happening in Seattle. I would
14 assume it.

15 **DR. SHAPIRO:** I wouldn't guess. I would ask.

16 **DR. STAPLETON:** Yeah. That's -- yeah. I
17 would -- yeah.

18 **DR. KAUFMAN:** I don't know, maybe Dr. AuBuchon
19 can -- if you -- maybe you want to comment a little bit
20 about that, because that's something we haven't talked
21 about. How would the hospitals feel about it? How

1 would the public feel about it?

2 **DR. AUBUCHON:** I can assure you that, if this
3 variance is granted and the program begins, it will be
4 front page news in the Seattle Times. And it will be
5 well-known across the community. It is our opinion
6 that -- well, it's not my opinion. It is the data that
7 any donor who tests negative in NAT will have any HIV
8 or hepatitis B or C inactivated through the INTERCEPT
9 process. The data are well established, by orders of
10 magnitude, for that safety.

11 Therefore, we feel there is no reason to raise
12 unnecessary concern in the recipient population that
13 these products are somehow less safe. That is just not
14 true. In fact, were there a requirement misguided, in
15 my opinion, that we get informed consent, this program
16 has zero chance of ever getting off the ground.
17 Because the assumption will be, from the recipient,
18 that it is a less safe unit and they will not want it.
19 I do not believe the data supports that assertion.

20 **DR. KAUFMAN:** Dr. Marks?

21 **DR. MARKS:** Can I just formally, for the

1 record, just make sure that we understand -- because I
2 seem to be thinking there's some question here. The
3 remainder of the donor questionnaire questions will be
4 asked for these units, so it's -- the only question
5 that is not in play here is the one by definition,
6 because it's the MSM question, right? All the other
7 questions are being asked. Is that correct?

8 **DR. AUBUCHON:** That's correct.

9 **DR. MARKS:** Okay. Thank you.

10 **DR. LEWIS:** So -- I'm sorry. That's different
11 than how I interpreted one of your slides. And I think
12 this is a --

13 **DR. MARKS:** That's why I was a little worried.
14 I was worried that's -- with some of the questioning,
15 that's why we were worried.

16 **DR. LEWIS:** Yeah. So, in one of your -- the
17 slides, it was presented early on. It says -- when
18 you're going through what is being requested, it said,
19 eliminate all then something questions. And maybe you
20 could explain that to make sure that we're at least
21 debating the same issue, the same request.

1 **DR. AUBUCHON:** This variance request applies
2 only to two questions on the donor history
3 questionnaire. Actually, one question per donor
4 because one question would be asked of women; the other
5 of men. But it pertains to whether or not a man has
6 had sex with another man in the last 12 months --
7 that's the male question -- or whether a woman has had
8 sex, within the last 12 months, with a man who's had
9 sex with a man in 12 months. So, that's the only
10 question that would still be asked, but would not lead
11 to an immediate deferral and asking the donor to leave.

12 **DR. LEWIS:** And then, for the sake of
13 completeness, could you just go through the other
14 questions that would be asked about recent sexual
15 practices that would remain on the questionnaire?

16 **DR. AUBUCHON:** There are no questions, at the
17 moment, that are asked of donors about particular
18 sexual practices. There are those in the gay community
19 who feel we should be asking heterosexuals the same
20 kinds of questions about sexual activities leading to
21 increased risk that is presumed to occur in the MSM

1 population. But, at the moment, there are no such
2 questions.

3 **DR. STAPLETON:** There is a paying for sex
4 question. Correct?

5 **DR. AUBUCHON:** Oh, I'm sorry. That is --
6 there is a prostitution question. You are correct.
7 Thank you. That would still be asked and would still
8 lead to a deferral.

9 **DR. LEWIS:** And no questions about multiple
10 partners or new partners?

11 **DR. AUBUCHON:** No. There are no questions
12 about numbers of partners or new partners. There's a
13 question about having recently been incarcerated, but
14 that would still stand.

15 **DR. LEWIS:** As I said, question --

16 **DR. AUBUCHON:** Yes, and there's still a
17 question regarding syphilis and gonorrhoea. Thank you.
18 I don't have all the questions in front of me. But all
19 other questions would stand. It's just the MSM
20 question.

21 **DR. KAUFMAN:** Dr. Bloch.

1 **DR. BLOCH:** Just to clarify something.

2 **DR. VERDUN:** Sorry.

3 **DR. KAUFMAN:** Oh, sorry.

4 **DR. VERDUN:** No, while you're there, can you
5 comment on the part of the question that someone asked
6 about what the hospitals think or any conversations
7 you've had?

8 **DR. AUBUCHON:** Our hospitals have only
9 recently been informed of our interest in this
10 approach. We have not had detailed discussions with
11 them. Informal discussions with some transfusion
12 medicine physicians in the community has yielded no
13 concern whatsoever. We'll obviously be having more
14 conversations with them as this process proceeds.

15 **DR. SHAPIRO:** So, could I ask one question?
16 Would you accept, as a donor, an individual who was on
17 PrEP because they were in a relationship with someone
18 who was HIV-infected?

19 **DR. AUBUCHON:** There is already a question in
20 the questionnaire whether or not you have had sex with
21 anyone who has HIV. That would still be a deferral

1 criterion.

2 **DR. KAUFMAN:** Dr. Bloch?

3 **DR. BLOCH:** So -- not to revisit this again
4 and again, but this is where I'm completely torn in
5 that I actually think that the risk is really -- I
6 can't say negligible, but it really is theoretical.
7 So, by putting in that layer of safety when really --
8 when it's achieving, really, a safe product.

9 The problem is the approach where, if this was
10 sold as -- one wanted to increase the inventory of safe
11 platelets or increase the access to platelets, and then
12 it was kind of a broad-based approach where one looked
13 at all the risk factors together and, essentially, it's
14 just kept them all out. But it's really so selective.
15 One went to one and one -- one actually went to the
16 highest risk first, which doesn't make any sense.

17 So, on the one hand, it doesn't really
18 matter because that's kind of academic. Because, if
19 your product is safe when achieved, achieve that
20 anywhere. But I just -- the whole sell. This doesn't
21 make any sense to me.

1 **DR. KAUFMAN:** Dr. Baker?

2 **DR. BAKER:** Thank you. Following up with that
3 point, if it doesn't make sense to some of us around
4 the table and we have these questions, I wish to go
5 back and ask what proactive steps are being taken to
6 have structured communications now with the leaders of
7 the hemophilia -- you know, the platelet community, the
8 people who are end users, to discuss this in a
9 proactive fashion. Because they will begin to get
10 questions if it, indeed, gets on the headlines of the
11 Seattle news.

12 **DR. AUBUCHON:** We intend to have those
13 discussions as we proceed through this process toward
14 implementing the variance, if granted. We haven't
15 completed that process obviously. We have a long ways
16 to go. So, if the agency is taking additional months
17 to consider our request, we will be putting that to
18 good use. The hemophilia community, rightly, is very
19 concerned about the safety of transfusion in general,
20 but they're particularly focused on the products they
21 receive. And, for the most part, those are not

1 platelets.

2 That's why we have been attempting to pull
3 together a group to get input from patients so that we
4 can structure our media releases, structure our public
5 education campaigns, as we move toward implementation
6 to address concerns that they may have. Admittedly, we
7 are working from a belief that this proposal is safe.
8 If we did not believe that, we would not have presented
9 it to you for consideration. We feel, with appropriate
10 information, that a reasonable person will come to the
11 same conclusion.

12 However, we haven't tested the exact messages
13 that we will be using yet, but we do intend to do that.
14 We will continue to have discussions with our hospitals
15 because those hospitals that depend on their own
16 physicians and their own transfusion service to lead
17 the patient care in their institution will have to
18 field those questions first, likely. And we want to
19 make sure that those people are informed and are also
20 comfortable with our approach.

21 But again, we've got time before we roll that

1 out. We have not rolled that out. We didn't put that
2 at the front of our process because we are anxious, not
3 to create undue desire in the MSM community to donate;
4 it's not that we're keeping it quiet in order to do
5 something nefarious. We just feel that we don't want
6 to make this a public discussion on the front page of
7 the newspaper before we actually have a process that we
8 can offer those donors who would be affected.

9 **DR. KAUFMAN:** All right. Well, why don't we
10 just go around -- I'm sorry. Dr. Bryant?

11 **DR. BRYANT:** I have a billing question. I
12 don't know if this is appropriate. But I -- I just
13 want to throw this out there. If you have an apheresis
14 donor who's answered all the questions correctly and is
15 not an MSM, and then you decide to pathogen reduce that
16 platelet, then that platelet is sold to the community
17 as a apheresis platelet and there's a charge for the
18 fact that it's pathogen-activated.

19 On the other hand, if it's an MSM -- and for
20 you to get that platelet to market, you've got to
21 pathogen-reduce it. Is that cost of pathogen reduction

1 -- will that be passed on to the consumer? Because
2 it's what the blood center has to take on to get it to
3 be marketable. I'm just kind of curious; will that set
4 up a -- will you have double population of billing of
5 these products, or will you just treat them all the
6 same?

7 **DR. AUBUCHON:** All units with the same product
8 code would be charged out similarly. And the units
9 that would come from donors previously deferred under
10 MSM deferral criteria would not be distinguished in any
11 way. But the same token, however, we would not attempt
12 to recover the additional costs associated with opening
13 up donation to MSM donors.

14 For example, all of the hours -- and there are
15 hundreds of hours that have already gone into thinking
16 about this -- the additional cost of recruiting an
17 entirely new donor population, the pre-testing involved
18 to make sure that the donors will be appropriate for a
19 donation -- none of that would be charged out. So, as
20 I said at the beginning, every unit would be handled
21 the same way. And the source of the donation would not

1 distinguish it at any manner.

2 **DR. KAUFMAN:** So, I thought we can just go
3 around to kind of wrap this up, and I'm going to -- not
4 that -- well, I am going to put everybody on the spot
5 slightly and just ask if you have any final -- what
6 your final thoughts are on the experience. So, I'll
7 start with Dr. Schreiber and we'll just go around.

8 **DR. SCHREIBER:** Based on my knowledge of what
9 we've seen today and prior knowledge, I think that this
10 is -- I think, to me, again, the most important thing
11 is patient safety. I think this proposal meets the
12 criteria for patient safety. I think there's concern
13 about continuing asking appropriate questions. I think
14 those questions should be continued to be answered. I
15 don't think that this should change that at all,
16 because I think that that process is also important. I
17 think that -- it's very nice that this is being done
18 with platelets, but I think that this technology is
19 also proof for plasma.

20 And, in the future, I'd like to see a plasma
21 involved with this. We're all saying that there's not

1 a plasma problem, but on any given day there could be a
2 plasma problem. If there's mass causalities, other
3 events could occur. So, it'd be nice to see this also
4 generalized to the use of plasma. There's essentially
5 a unit of plasma in a unit of platelets anyway. Those
6 are my comments.

7 **DR. KAUFMAN:** Thank you. Dr. Baker?

8 **DR. BAKER:** Thank you. Agreed that patient
9 safety comes first. I would love to see this also apply
10 to plasma. I just don't see that we have the data to
11 suggest that this should be an alternative to the
12 current MSM deferral policy. I think those MSM
13 questions should be asked.

14 **DR. KAUFMAN:** Thank you. Dr. Bloch?

15 **DR. BLOCH:** I agree with both. I think that
16 pathogen reduction (inaudible) is an additional layer
17 of benefits. I think the risk is so minuscule that I
18 don't think it's going to -- it makes a difference. I
19 think that's -- I would support the variance.

20 **DR. KAUFMAN:** All right. Dr. Stapleton?

21 **DR. STAPLETON:** So, I would like to mention

1 Dr. Baker's comment. I think the questions are still
2 asked; it's just they're overridden for those two.
3 Have you had sex with a man who's had sex with a man?
4 Or have you had sex with a man? So, the questions are
5 still asked.

6 I think this is an ideal way to move MSM into
7 the general donor pool, because the risk is low to
8 start with. And with the vaccine reduction, I think it
9 becomes as low as humanly possible to transmit HIV or
10 hep C from this -- hep B from these platelet units. It
11 gives us an opportunity to obtain data that we won't
12 get very easily otherwise from, potentially, a large
13 number of MSM. So, I'm very much in favor of this.

14 **DR. KAUFMAN:** Thank you. Dr. Bryant?

15 **DR. BRYANT:** I believe patient safety is at
16 most of importance. And I do believe that pathogen
17 reduction as an alternative to MSM is an acceptable
18 procedure. So, I support this variance.

19 **DR. KAUFMAN:** Thank you. Mr. Templin.

20 **MR. TEMPLIN:** I think, if the technology could
21 make the product safer, that's a good thing and it

1 should probably be used. But I also think there needs
2 to be some sort of study, and this issue needs to be
3 followed closely by the folks behind me and all the
4 other alphabet soup that goes along with making the
5 blood safe in this country. Because I want to make
6 sure it's safe for me and my children and my wife if we
7 need it.

8 **DR. KAUFMAN:** Thank you. Dr. DeVan?

9 **DR. DEVAN:** I agree. I think it's -- I think
10 the data support this is an acceptable variance. And I
11 think it expands the donor pool, which is something
12 that I think is critical. I can't transfuse the
13 platelets that haven't been collected.

14 **DR. KAUFMAN:** Dr. Shapiro?

15 **DR. SHAPIRO:** I'm a little conflicted. I'm
16 having a little trouble with this. I support the
17 pathogen inactivation. I understand the questions
18 you're still being asked in an alternative route, being
19 created for some individuals. I think that we need to
20 look at refining the questions to pick out individuals,
21 not just MSM but other individuals, who could be at

1 risk to transmit viral infections, either known or
2 unknown, to the population so that we're not using one
3 set of questions to adversely affect one group, but
4 that we get a better set of questions that affect --
5 that could put other patients at risk.

6 That being said, I'm a little concerned about
7 individuals who are on PrEP being allowed to donate.
8 They are a subpopulation of the population of MSM or
9 other individuals, even IV drug users, that could be a
10 high-risk group and could stress the technology in some
11 way or create a failure if there were some mechanical
12 failure within the system.

13 **DR. KAUFMAN:** All right. I would note that
14 the IV drug use question would still be asked.

15 **DR. SHAPIRO:** Right. But, if someone's on
16 PrEP, they've self-selected themselves as a
17 subpopulation who is probably of higher risk. Either
18 refusal to use protection, some other risk factor.

19 **DR. KAUFMAN:** Dr. Ortel?

20 **DR. ORTEL:** I feel that the variance, as
21 proposed, where the questions are still asked, the

1 baseline precautions are still in place, that there is
2 this variance on the one question that is perfectly
3 appropriate and expands the potential pool. I think
4 that continued ongoing research does need to be done to
5 try to figure out if there's ways to refine the
6 questions or improve the questions, and that can
7 replace things later down the line. But that's a
8 different question.

9 **DR. KAUFMAN:** Thank you. Dr. Lewis?

10 **DR. LEWIS:** So, first of all, I agree
11 completely with the previous comments about the value
12 of pathogen reduction in a broad sense, and that
13 anything we can do to increase the use of that or
14 similarly effective technologies to make the platelet
15 supply safer is a good thing. On slide 6 of the
16 Bloodworks presentation, I found the phrase that, I
17 think, caused some confusion. It says, "accept as
18 apheresis platelet donor; MSM, regardless of sexual
19 activity, full stop." And that's, I think, not -- in
20 retrospect -- what was intended. I think it means,
21 except for all those other questions, we're still going

1 to ask. And that's an important qualitative
2 difference.

3 The previous speakers have commented about the
4 importance of figuring out what the right other
5 questions are. The right questions may never mention
6 sexual orientation, but they should inquire about
7 practices that, based on sound epidemiologic data,
8 place people at higher risk of new acquisition of
9 transmissible agents. And anything that can be done to
10 bring nonjudgmental science to bear on the refinement
11 of those questions, I think, is a good thing. So, with
12 my renewed understanding that the slide didn't say what
13 I thought it said or it said what you didn't mean, I
14 support the variance.

15 **DR. KAUFMAN:** Thank you. Dr. Basavaraju?

16 **DR. BASAVARAJU:** So, I think that -- I
17 definitely see the advantages and benefits of PRT. I
18 also see the benefits and advantages of nucleic acid
19 testing. And I think the FDA's effort to try to
20 identify whether there's subgroups within the MSM
21 population that may be at lower risk is a good one. I

1 think, in the absence of figuring that out, I would not
2 support -- just -- no donor deferral based on that.

3 **DR. KAUFMAN:** Thank you. Dr. Chitlur?

4 **DR. CHITLUR:** Okay. So, I agree with a lot of
5 what has been said so far. I think PRT is definitely
6 going to add to the safety of the product that is being
7 infused. I definitely think this is new technology and
8 needs to be followed. Research or just data collection
9 should continue. But the questions should stay. I
10 think they still need to ask, because I'm not convinced
11 yet that we can afford to not ask the questions
12 anymore.

13 If sexual orientation has been shown to be the
14 highest risk factor for transmission of these blood
15 retroviruses, then I don't know that not asking that
16 question at this point of time is okay. I think, in
17 view of the fact that all of us agree that patient
18 safety comes first, I don't feel that not having a
19 deferral policy is okay at this point.

20 **DR. KAUFMAN:** And just for clarity, all the
21 questions that are currently asked will be asked.

1 Really, truly, the only difference -- the difference
2 with respect to the questionnaire is that, whereas
3 answering yes to the question, "Are you a man that's
4 had sex with a man?" would typically lead to a
5 deferral, it would not under this variance, given that
6 the product would be a pathogen inactivated -- sorry,
7 pathogen reduced apheresis platelet.

8 But thank you for your comments. Dr. Stramer?

9 **DR. STRAMER:** Yes. I think industry is
10 supportive of the variance and broadening the use of
11 pathogen inactivation. I think, as noted, Dr. AuBuchon
12 and Bloodworks still have some challenges ahead in
13 planning for the variance, if it's granted; and
14 pathogen inactivation towards anywhere above a 50
15 percent yield, whether they do splits or not.

16 **DR. KAUFMAN:** And finally, I support the
17 variances described. I think that some of the -- there
18 will be some logistical challenges to work out. I'm
19 optimistic that that can be done. It will -- well,
20 we'll see what happens in terms of reaction from the
21 community and from the hospitals. I think that the

1 reality is, I think the platelet products that we're
2 talking about are incredibly safe and, likely, a little
3 bit safer than a typical platelet that we would have on
4 the shelf at my hospital today which are not pathogen
5 reduced.

6 Anyway, I think it's a logical approach and I
7 support it. Dr. Schreiber?

8 **DR. SCHREIBER:** I've been sitting here, as we
9 all have, all day and I've been thinking about this
10 MSM. We talked about the social issues. It is a very
11 pointed, directed group of people that were -- you
12 know, that are being identified. As I think about
13 this, I would think -- there may be a better way to say
14 this that is more socially acceptable, such as, people
15 who practice high-risk sexual practices. It doesn't
16 fit a nice three-letter MSM, but there's other risk
17 factors involved. We talked about prostitution,
18 females who have sex with men who have HIV. These are
19 all people who are practicing high-risk sexual
20 activity.

21 I think that's a less directed way and more

1 socially acceptable way to discuss it. And I would
2 just ask the FDA to consider changing this MSM
3 terminology, which, I think, is very pointed and really
4 is kind of a social message focusing on one segment of
5 society, when really, it doesn't have to be that one
6 segment that's at risk here.

7 **DR. KAUFMAN:** I'm actually not sure of the
8 origin of that term. I don't believe it's an FDA-
9 coined expression. All right. So, anyway, I think I'd
10 like to close the meeting then. I thought it was a
11 really interesting discussion. I want to thank
12 everybody for your input. It's really great to have a
13 variety of different opinions. Anyway, I thank you all
14 for your time and for your presentations.

15 **DR. VERDUN:** And I just wanted to, on behalf
16 of the FDA, thank everyone for a very robust and
17 extremely helpful discussion over these past two days.
18 We're very appreciative of your time and thank you.

19

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MEETING ADJOURNED

21