



MSM Blood Donor Deferral Policy

statement of the

AMERICAN PLASMA USERS COALITION (A-PLUS)

before the

Advisory Committee on Blood Safety and Availability

Department of Health and Human Services
Thirty-eighth Meeting
June 10-11, 2010
The Universities at Shady Grove
Rockville, MD

The American Plasma Users Coalition (A-PLUS)
was formerly known as the Plasma User Coalition (PUC)

EXECUTIVE SUMMARY

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The American Plasma Users Coalition (A-PLUS) is a coalition, formerly known as the Plasma User Coalition (PUC), of national patient organizations created to address the unique needs of patients with rare diseases that use life-saving plasma protein therapies. The organizations representing these patients share a common desire to ensure that the patient voice is heard when relevant public policies, regulations, directives, guidelines and recommendations which have a major impact on their access to safe and effective therapy and treatment are considered.

Together our coalition represents more than 125,000 Americans living with chronic disorders dependent upon plasma protein therapies for their daily living. In addition, there are thousands more that remain undiagnosed.

Partners in our coalition include:

Alpha-1 Association
Alpha-1 Foundation
GBS/CIDP Foundation International
Committee of Ten Thousand
Hemophilia Federation of America
Immune Deficiency Foundation
Jeffrey Modell Foundation
National Hemophilia Foundation
Platelet Disorder Support Association
Patient Services Incorporated

A-PLUS appreciates this opportunity to present our views regarding the Advisory Committee on Blood Safety and Availability's (ACBSA) review of the current Food and Drug Administration (FDA) policy recommending that men who have sex with another man (MSM) even one time since 1977 should be deferred indefinitely from donating blood.

Both gay men and those in the plasma user community have been disproportionately impacted by the HIV epidemic. Our communities have a long history of working together on shared goals related to providing HIV support, research advocacy, treatment access, and prevention programs. We share a historical common bond. Together, we are committed to ensuring the overall safety of the nation's blood supply.

At this time, A-PLUS does not believe that the currently available knowledge and data are sufficient to support a change to the existing donor deferral policy. We acknowledge that the scientific basis for the permanent deferral requires review. However, we do not currently have enough information to determine if a one-year, five-year, ten-year, or another deferral period is more appropriate than the existing permanent lifetime deferral. Selection of another interval could also be perceived as arbitrary or lacking scientific foundation. However, this is not the end of the discussion.

We believe that there are a number of factors which should be fully evaluated before making a revision to the policy and we support research focused on high risk behaviors of both MSM and heterosexuals. Such evaluation and research could lead to a policy revision that maintains or enhances the safety of blood and blood products.

Today we are calling for a research agenda to be undertaken to address several critical areas with the following goals:

1. Achieving a better understanding of known and emerging pathogens in specific populations including MSM and heterosexual populations;
2. Developing policy that recognizes societal aspects of the blood system's safety and risk tolerance;
3. Developing alternate donor deferral strategies and the risk of blood-borne diseases;
4. Establishing a framework for accelerated approval of pathogen reduction, removal and/or inactivation technologies for fresh components; and
5. Understanding the implications of a revision on the supply and availability of treatment products globally.

If we progress in earnest with such a research strategy, and obtain reassuring answers, we foresee a time when a revision would be appropriate and donor deferrals could be made on a more individualized, behavioral-based risk review for both MSM and heterosexual donors.

We urge all stakeholders, including donors and end-users, to aggressively work together to seek answers. Equally important, is for the government to commit the necessary funding to ensure that this occurs in a timely manner. Our specific recommendations for research in the context of the research agenda mentioned above are summarized below.

SUMMARY OF RESEARCH RECOMMENDATIONS

- I. The ACBSA consideration of this issue should not supplant the rigorous scientific review of the FDA and BPAC.**
- II. We must achieve a better understanding of known and emerging pathogens in specific populations including MSM and heterosexual populations.**
- III. We must give due consideration in policy development to the societal aspects of the blood system's safety and risk tolerance.**
- IV. We must consider alternate donor deferral strategies and the resulting risk of blood-borne diseases.**
- V. We must factor into the equation the risk of multiple and cumulative exposure for those dependent upon blood and plasma therapies for their daily living.**
- VI. We must establish a framework for accelerated approval of pathogen reduction, removal and/or inactivation technologies for fresh components and where necessary, support research to develop the technology.**
- VII. We must understand the implications of a revision of the donor deferral policy on the supply and availability of treatment products globally prior to changing the deferral policy.**
- VIII. We must have a robust comprehensive hemovigilance and biovigilance program.**
- IX. We call upon the Department of Health and Human Services to encourage accelerated development and use of pathogen reduction technologies for fresh (labile) components.**
- X. We must implement a robust donor education program as part of any revised donor deferral policy.**

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The American Plasma Users Coalition (A-PLUS), formerly known as the Plasma User Coalition (PUC), appreciates this opportunity to present our views, concerns and recommendations regarding the Advisory Committee on Blood Safety and Availability's (ACBSA) review of the current Food and Drug Administration (FDA) policy recommending that men who have sex with another man (MSM) even one time since 1977 should be deferred indefinitely from donating blood.

A-PLUS is a coalition of national patient organizations created to address the unique needs of patients with rare diseases that use life-saving plasma protein therapies. The organizations representing these patients share a common desire to ensure that the patient voice is heard when relevant public policies, regulations, directives, guidelines and recommendations which have a major impact on their access to safe and effective therapy and treatment are considered. Our voices, as the users of these life-saving and enhancing therapies, must be heard and we must be consulted when measures are being considered that will have a major impact on our access to safe therapy. It is in this spirit that we appear here today.

Together our coalition represents more than 125,000 Americans living with chronic disorders dependent upon plasma protein therapies for their daily living. In addition, there are thousands more that remain undiagnosed.

Partners in our coalition include:

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The issue of MSM donors involves a mix of societal, economic and scientific issues. The ACBSA is charged to provide advice to the Secretary of Health and Human Services and to the Assistant Secretary for Health. The Committee advises on a range of policy issues that include:

1. Definition of public health parameters around safety and availability of the blood and blood products;
2. Broad public health, ethical and legal issues related to transfusion and transplantation safety; and
3. The implications for safety and availability of various economic factors affecting product cost and supply.

Holding this hearing before the ACBSA is appropriate. However, the ultimate scientific decisions are and must remain within the purview of the FDA and the advice of the Blood Products Advisory Committee (BPAC). **The ACBSA consideration of this issue should not supplant the rigorous scientific review of the FDA and BPAC.**

We see four potential outcomes of today's discussions:

1. Do nothing;
2. Define a research agenda to be completed and analyzed prior to implementation of any policy revision;
3. Recommend an immediate revision in the deferral policy coupled with an enhanced biovigilance/hemovigilance system and/or research program; or
4. Completely lift the deferral.

We anticipate the discussions will focus primarily on revision, not outright repeal of the current prohibition on MSM donors. The question then becomes what comes first – revision or additional research.

Background

We, the end-users of this nation's blood supply, stand before you today as we have since the construct of this important Department of Health and Humans Services (DHHS) advisory committee. End-users have been a part of the open public process, and we continue to insist that we be treated as equal partners in the regulatory system for the blood supply. The National Academy of Sciences, Institute of Medicine (IOM) Report, *HIV and The Blood Supply: An Analysis of Crisis Decision Making*,¹ very clearly articulated the need to ensure the participation of all the stakeholders impacted by the blood supply and its regulation.

Both gay men and those in the plasma user community have been disproportionately impacted by the HIV epidemic. Our communities have a long history of working together on shared goals

¹ HIV and the Blood Supply: An Analysis of Crisis Decisionmaking; Lauren B. Leveton, Harold C. Sox, Jr., and Michael A. Stoto, Editors; Committee to Study HIV Transmission Through Blood and Blood Products, Institute of Medicine; ISBN: 0-309-58827-8, 352 pages, (1995)

related to providing HIV support, research advocacy, treatment access, and prevention programs. We share a historical common bond. Through conversations with the Gay Men's Health Crisis (GMHC) on the issue of MSM donor deferral, we take special note that we are on opposite ends of the blood supply spectrum (donor and end-user), however, more importantly, we recognize that we are on the same side in our commitment to ensuring the overall safety of the nation's blood supply. We have pledged to move forward working together to critically examine and evaluate alternative policies for MSM donor deferrals.

The discussions within this meeting should not be simply about the donor. If there is revision in this or other deferral policies, the resulting change in risk will be borne 100% by the end-user. However, equally important, we are concerned about what happens in the middle; from the time an individual decides they would like to donate to the time that donation ultimately is administered or injected into our bodies. The regulatory framework, oversight, collection and processing systems are fundamentally important. Taking into consideration the history of pathogen transmission within the blood supply and in particular within the communities we represent, we request that the ACBSA bear in mind the continual need to examine who shoulders the risk.

Committee Questions

The ACBSA is being asked to consider five questions as stated in the Federal Register notice:

1. What are the most important societal, scientific and economic factors to consider in making a policy change?
2. Is the currently available scientific information including risk assessments sufficient to support a policy change at this time?
3. What studies, if any, are needed before implementing a policy change?
4. What monitoring tools or surveillance activities would need to be in place before implementing a policy change?
5. What additional safety measures, if any, are needed to assure blood safety under a revised deferral policy?

We, A-PLUS, would make the following comments regarding the committee questions.

<p>Committee Question 1. What are the most important societal, scientific and economic factors to consider in making a policy change?</p>
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Precautionary Principle - While we often rely upon the Precautionary Principle as a reason for putting in place a safety measure, we too often forget the corollary part of the Precautionary Principle which also calls for a review of the safety measures when new information is available.

Recommendation six of the IOM Report states: *“Where uncertainty or countervailing public health concerns preclude completely eliminating potential risks, the FDA should encourage, and*

where necessary require, the blood industry to implement partial solutions that have little risk of causing harm.“The report goes on to explain that, in all fields, decision-making under uncertainty requires an iterative process. As the knowledge base for a decision changes, the responsible agency should reexamine the facts and be prepared to change its decisions.

In other words, the Precautionary Principle calls for safety measures to be put in place in all cases, except when they can be adjusted based on scientific certainty. The measures should be proportional to the potential risk. When new science, epidemiology, or technologies are available a review of the precautionary measures is appropriate. We must act with prudence and continue to adhere to the Precautionary Principle when evaluating any change.

The Precautionary Principle, while not legally the law of the land, is based on three documents that were adopted in sworn testimony, by then DHHS Secretary Shalala, before the House of Representatives, Government Reform and Oversight Committee².

Therefore, we welcome this hearing. We see this discussion as consistent with the Precautionary Principle so long as the focus is not lost that the ultimate decision must be based on science, epidemiology, and most importantly, the potential risk impact for the end-user.

Discrimination - We recognize and empathize with the position of those advocating for a repeal or revision of the current donor deferral policy. By their very nature, blood donor screening and deferral criteria are discriminatory; however, they are justifiable when they provide increased protection to public health. Criteria for donor deferrals must put safety of the recipient first and be based on scientific and epidemiological evidence about large groups of people (populations). Epidemiology, which is the study of patterns of disease in populations and provides the strongest scientific analysis of blood donor deferral criteria, is in fact a science based on discrimination. It is important to recognize that donor deferrals are not judgments about the individual donor. Rather they are a method to reduce the risk of known, unknown, undetectable, or emerging viruses and/or other disease-causing agents being passed to recipients of blood or blood products. Testing and pathogen reduction technologies are not perfect, and it continues to be necessary to decline donations from some populations based on established epidemiological evidence.

Therefore, this discussion should not be based on whether or not the policy is discriminatory, like many other deferral measures, but rather if the discriminatory effect is still consistent with the overriding public health considerations and latest scientific information.

Blood Supply - A-PLUS and the many end-user (patient) communities dependent upon blood and plasma donations that we represent are eternally grateful for the altruism and generosity of those who donate. Without these lifesaving donations most of us would not be here today.

² 1. National Academy of Sciences, Institute of Medicine report “HIV & The Blood Supply: An Analysis of Crisis Decision Making”; 2. The House of Representatives, Government Reform and Oversight Committee report “Protecting The Nation’s Blood Supply From Infectious Agents and the Need For New Standards To Meet New Threats”; 3. The House of Representatives, Government Reform and Oversight Committee report, “Hepatitis C; The Silent Epidemic; Mute Public Health Response”

However, we do not believe that a revision in deferral policy can be justified simply on the basis of the small percentage of additional donations that would be added to the national supply if there were a revision. The estimates of how many new donations would be obtained show a one half of one percent increase³ in the roughly 15 million pints of blood collected annually if deferral standards were harmonized with the heterosexual population.

Committee Question 2. Is the currently available scientific information including risk assessments sufficient to support a policy change at this time?

At this time, A-PLUS does not believe that the currently available knowledge and data are sufficient to support a change to the existing donor deferral policy. We acknowledge that the scientific basis for the permanent deferral requires review. However, we do not currently have enough information to determine if a one-year, five-year, ten-year, or another deferral period is more appropriate than the existing permanent lifetime deferral. Selection of another interval could also be perceived as arbitrary or lacking scientific foundation. However, this is not the end of the discussion.

We believe that there are a number of factors which should be fully evaluated before making a revision to the policy and we support research focused on high risk behaviors of both MSM and heterosexuals. Such evaluation and research could lead to a policy revision that maintains or enhances the safety of blood and blood products.

Today we are calling for a research agenda to be undertaken to address several critical areas which are outlined in this statement in our response to Question 3.

Committee Question 3. What studies, if any, are needed before implementing a policy change?

Before implementing a policy revision we would urge careful consideration of the available science, what is not known about a potentially expanded donor pool and areas where additional research would be useful.

Any research agenda must be collaborative and inclusive of the donor and end-user communities, as well as the other system stakeholders. No doubt there will be differences of approach, but it is our belief that through working together we will ultimately resolve this issue.

We call for answers in five critical areas:

³ Anderson, S. et. al. Quantitative estimate of the risks and benefits of possible alternate blood donor deferral strategies for men who have had sex with men; Transfusion Vol 49, June 2009

A CALL FOR ANSWERS – THE RESEARCH AGENDA

- 1. Achieving a better understanding of known and emerging pathogens in specific populations including MSM and heterosexual populations;**
- 2. Developing policy that recognizes societal aspects of the blood system’s safety and risk tolerance;**
- 3. Developing alternate donor deferral strategies and the risk of blood-borne diseases;**
- 4. Establishing a framework for accelerated approval of pathogen reduction, removal and/or inactivation technologies for fresh components; and**
- 5. Understanding the implications of a revision on the supply and availability of treatment products globally.**

1. Known and Emerging Pathogens

We must achieve a better understanding of known and emerging pathogens in specific populations including MSM and heterosexual populations.

Good scientific evidence exists that transmission of HIV, hepatitis A, hepatitis B, hepatitis C, and parvovirus B19 occur through transfusions. Since the advent of this permanent deferral, in addition to other safety measures including screening tests, the incidence of these transfusion-associated infections has dropped from 1 in 200 units to 1 in 2 million.⁴

However, these are not the only pathogens threatening the blood supply. A May 25th report published by the Wall Street Journal indicates that some 68 emerging pathogens have been pegged as potential threats to the blood supply. Understanding the disease exposure risk from these emerging or other known pathogens is important. This includes knowing if the exposure will come from travel, risky sexual behavior, medical conditions, medication, or drug use. For many pathogens, it may take years before the route of transmission is known or a screening test is established.⁵

For some donors, the donor screening questionnaire will be the only tool to defend against pathogen transmission.

The real risk and concern is “the next HIV”, the next pathogen which follows the same route of transmission as currently known sexually transmissible viruses. There have been many examples in history which followed this route of transmission, including hepatitis and

⁴ CDC Fact Sheet. HIV and AIDS among gay and bisexual men. March 2010. Available at www.cdc.gov/nchhstp/newsroom/docs/fastfacts-msm-final508comp.pdf

⁵ Wall Street Journal, 25 May 2010, “Blood Supply Faces 68 Emerging Threats; More Screening, or Germ Zapping?”

syphilis. Types of hepatitis other than A, B, and C are just beginning to be understood. We do not fully understand the potential transmissibility or impact of other forms of hepatitis such as D, E or G.

For some pathogens, the incubation period could easily be greater than five years or take even longer to fully understand how it is transmitted. There is always the risk of new, emerging infectious agents that are not yet known, just as HIV was unknown prior to 1981.

- It took 12 years before we fully understood the transmissibility of HHV8 and that transmissibility through blood is likely to be a rare event.
- Non A Non B hepatitis was identified as distinct from other known hepatitis and as blood transmissible in the early 1970s. A test to detect the virus in blood donors was only developed in the 1990s – 17 years later. The mortality implications of acquiring HCV were not fully understood until years later.
- More recently, we have only begun to understand that variant CJD is in fact transmissible through blood transfusion and in fact has been transmitted by clotting factor concentrates.
- Another recent example is XMRV which is believed by some to be associated with chronic fatigue syndrome and prostate cancer. There are a number of things we do not know about this virus. What are the consequences of exposure? How it is transmitted? Is it transmissible sexually or via blood?

Recent data from the CDC indicate that, while HIV infection rates in the U.S. are falling in heterosexuals and intravenous drug users, they are rising in MSM. Over half (53% or 28,000) of all new HIV infections each year are in MSM. The rate of new HIV infections in MSM is 44 times the rate of new infections in other men.⁶

What other viruses known, emerging, or unknown might also be transmitted through high risk sexual behavior in the MSM or heterosexual population? Could the existing known high prevalence viruses within these populations serve as marker viruses? Is it possible to correlate high risk behavior to allow a differentiation among MSM donors? Should such a revision be applied to heterosexuals as well?

In light of the scientific evidence that HIV infections are rising in the MSM population, the possibility of other unforeseen infections, and the lack of scientific evidence that all infectious risks are eliminated by the manufacturing processes, we urge the committee to proceed cautiously. A defined research agenda such as we are proposing today is essential to clarify the risk profile of previously deferred donors, as well as existing donors who are not now, but perhaps should also be deferred.

⁶ CDC Fact Sheet. HIV and AIDS among gay and bisexual men. March 2010. Available at www.cdc.gov/nchhstp/newsroom/docs/fastfacts-msm-final508comp.pdf

2. Societal Considerations and a Behavioral-based Questionnaire

We must give due consideration in policy development to the societal aspects of the blood system's safety and risk tolerance.

How could we adapt the blood / plasma collection system so that the altruistic interests of the donor are respected in the least prejudicial way consistent with the reality that the end-user bears 100% of the risk?

The complexity and length of the existing donor screening questionnaire have grown considerably in recent years. The science of survey research is equally important when considering a revision to the questionnaire. While it may seem simple to just add or revise a questionnaire, research must be conducted to understand the completeness or veracity of the answers. Likewise it may be difficult to design a questionnaire which asks explicit questions about high risk sexual behavior but does not have a negative impact such as scaring off existing donors or possibly shaming respondents to be untruthful in their response.

The appropriate research must be conducted to assess and understand how effective revisions in questions will be and what information we may reasonably expect to obtain from a questionnaire. Will the responses be truthful and complete? Will the answers be useful in screening out individual high risk donors?

3.a. Alternate Donor Deferral Strategies – “Pre-Test and Pre-Screening”

We must consider alternate donor deferral strategies and the resulting risk of blood-borne diseases.

What will be the risk profile of previously deferred donors that show up at collection sites if the policy is revised?

Any system for donor tracking is predicated on the assumption that the underlying system for tracking donors and quarantined donations is performing optimally and is implemented uniformly across the nation's blood collection systems. The successful implementation and widespread automation throughout the blood collection industry is associated with the current low quarantine release errors rate.⁷

This becomes critically important when we consider the difficulties experienced by the American Red Cross (ARC), which collects just over forty percent of our nation's voluntary donated blood. Since 1993 the ARC has been collecting blood under a Federal District Court consent decree due to ARC's inability to meet FDA standards for the collection, processing, screening, testing and tracking of collected units of blood.

It remains troubling to our communities that the ARC has been under consent decree for 17 years. It is expected to take several more years before all segments of the blood system are

⁷ Anderson, S. et. al. Quantitative estimate of the risks and benefits of possible alternate blood donor deferral strategies for men who have had sex with men; *Transfusion* Vol 49, June 2009

fully automated. We must have assurance that the risk of quarantine release errors will not be exacerbated by this on-going situation if the deferral policy is revised.

“Pre-Test”– One option which has been discussed in the scientific literature to address such concerns is that of a “pre-test”.⁸

If revision is to occur, we need to develop a clear understanding of the risks associated with donor reentry. What will be the risk profile of an expanded donor pool, particularly within the first year of revision when one could logically expect an influx of new or previously deferred donors? If it is agreed that a revision is merited, a transitional approach to manage and understand the associated risk merits consideration as well.

We take special note that the potential for testing and recordkeeping errors are an important consideration when evaluating the risk of donor reentry. One of the major contributors of risk associated with a revision in the deferral policy would be the risk of testing or quarantine release errors when a previously deferred donor enters into the system for the first-time. To minimize this risk, a “pre-test” of first-time donors could prove beneficial.

In a “pre-test” scenario, first-time donors would only donate a small specimen, which would be screened by standard protocols. Only when previously deferred donors were determined to be suitable by screening would they be allowed to donate a unit of blood.

Segmenting Donors – “Pre-Screening” – A “pre-test” might be coupled with an enhanced donor questionnaire to allow for a more complete “pre-screening”. Such a system could prove useful to collect additional donor information on high risk behaviors. Using marker viruses such as HIV and hepatitis one might then be able to identify a subgroup of donors appropriate for continued long-term deferral or narrow the deferral to the segment of donors with high risk behaviors.

We do agree that it may not be appropriate to continue to consider MSM as a homogenous group. However, without additional research and data we cannot make an informed decision on options to segment the MSM population into high and low risk donors. Lessons learned through a “pre-screening” could be one element of a research strategy and could lead to a transitional approach to allow donor reentry with reduced risk to the end-user. However, the risk of window period infections beyond the level of nucleic acid testing (NAT) detection would remain.

3.b. Estimating the True and Total Risk

We must factor into the equation the risk of multiple and cumulative exposure for those dependent upon blood and plasma therapies for their daily living.

It is worth noting that the estimates of risk vary depending on the study, assumptions, and the donor re-entry standard ultimately adopted. The number of potentially infectious

⁸ Anderson, S. et. al. Quantitative estimate of the risks and benefits of possible alternate blood donor deferral strategies for men who have had sex with men; Transfusion Vol 49, June 2009

donations which might make their way into the blood supply is not known or agreed upon. At this time, the science is unclear on this point.

However, when considering estimates, it should also be remembered that each blood donation is typically split into three components – red cells, platelets and plasma – which could multiply the impact of an infectious donation released into the supply pipeline. These components currently cannot be virally inactivated during the preparation process. People with bleeding disorders have a higher than normal chance of needing fresh blood components such as red blood cells, platelets, and fresh frozen plasma.

We must also factor into the equation the risk of multiple and cumulative exposure for new, known, and emerging risks. The concept of cumulative lifetime risk is an important consideration. Chronic users of blood and plasma therapies depend upon essential life-saving therapies derived from blood for daily living. Over their lifetime, they will have thousands of exposures to different donors. The net impact has been overlooked in some recent discussions, particularly when looking at risks beyond those for which NAT is available today.

Additionally, plasma-derived therapies are made from plasma pools consisting of up to 60,000 donors. A single infectious unit within a pool could subsequently infect hundreds of patients.

Our concern is also for the tens of thousands of people across the nation, who need transfusions of fresh blood components including those with thalassemia, sickle cell disease, chronic anemia and cancer, along with those who have had a serious accident or who require surgery. They do not currently have access to virally inactivated therapies.

4. Pathogen Reduction

We must establish a framework for accelerated approval of pathogen reduction, removal and/or inactivation technologies for fresh components and where necessary support research to develop the technology.

Blood safety is typically built upon a tripartite approach (donor selection, donor screening, viral testing and pathogen reduction) which together provide redundancy and an overlapping margin of safety for error. It is recognized that pathogen reduction is the “Holy Grail” of blood safety.

At this time, for labile (fresh) blood components, donor selection and donor screening are the only gatekeepers to prevent infectious units from entering the system. More importantly, screening tests are only available for some pathogens. Current testing and donor questionnaires are not enough to guarantee safety. Ideally, fresh components should receive the same pathogen reduction as manufactured plasma derivatives.

This is especially true when considering the range and growing number of known and emerging threats. If there were another tragedy on the scale of HIV or Hepatitis within the blood supply, those dependent upon blood and blood derivatives would once again be at great risk.

5. Global Considerations

We must understand the implications of a revision on the supply and availability of treatment products globally prior to changing the deferral policy.

Although perhaps outside the purview of the ACBSA, this decision is not without potential global implications as well. The phrase “*blood is local, plasma is global*” is noteworthy in the context of this discussion. The implications of a revision in the MSM deferral policy include the potential to impact the global supply and availability of plasma-derived medicinal products around the world.

Presently, the European Medicines Agency (EMA) and other regulatory bodies have adopted regulatory positions similar to the U.S. donor deferral for MSM donors. If products manufactured from plasma pools containing MSM donors are no longer suitable for sale or distribution within Europe, they will often be rejected by other countries as well. Due to economic capacity and regulatory structures, many nations in the world follow the regulatory guidance of the FDA or EMA.

While it is exceedingly difficult to harmonize global regulation, given the global nature of plasma, we should not contemplate action in a U.S. vacuum.

According to estimates of the Market Research Bureau, in 2010, 32.8 million liters of plasma (recovered and source) will be collected worldwide. Of this amount, 20.4 million liters (62%) will be collected in North America;⁹ the vast majority of this amount is collected in the U.S. Plasma derivatives made from U.S. source and recovered plasma are essential if we are to meet patient needs globally. Without these products, there will be a global shortage of treatment products, and therefore thousands will be at grave risk of permanent disability or premature death.

We would ask that you explore the global implications of a U.S. policy revision so that patients around the world do not suffer due to an inability to access life-saving medicinal products derived from U.S. blood and plasma donations.

There are a range of options to be considered. None of these options would be easily implemented:

- Blood collectors could continue to differentiate plasma donations destined for fractionation between MSM and non-MSM donors;
- Plasma-derived products destined for international markets could be limited to plasma from female donors. However this potentially limits the antibody diversity which is important for the immune deficient population; or
- The MSM donor deferral could remain for source plasma collections and exclude recovered plasma from products destined for international markets.

⁹ Market Research Bureau, Estimates of Global Plasma Demand in 2015, published July 2009, updated to June 2010

Committee Question 4. What monitoring tools or surveillance activities would need to be in place before implementing a policy change?

Hemovigilance / Biovigilance

We must have a robust comprehensive hemovigilance and biovigilance program.

Although not specifically the focus of this meeting it is important to note the critical importance of having a comprehensive hemovigilance program. Regardless of whether or not a revision is made in the MSM deferral policy, encouragement and development of a robust biovigilance program is critical and will potentially enhance the overall safety of the nation's blood supply. The previous work of the ACBSA in this regard is commendable but it is not complete. Widespread implementation of a robust biovigilance program to enhance safety monitoring and development of a system to respond to emerging threats is vital. Efforts must continue to bridge this critical gap in patient safety and donor health. A robust hemovigilance system must be established to track and counter known and emerging infectious threats to the blood supply. Donor screening, donor deferral, and donor testing measures alone are an inadequate solution to a growing and complex problem.

Committee Question 5. What additional safety measures, if any, are needed to assure blood safety under a revised deferral policy?

1. Approval of Pathogen Reduction Technologies

We call upon the Department of Health and Human Services to encourage accelerated development and use of pathogen reduction technologies for fresh (labile) components

Technologies for pathogen reduction of fresh components are developing and must be encouraged. The ACBSA should address the urgent need to accelerate development and ensure that they are available within the U.S. For example, the preparation of virally inactivated, solvent-detergent-treated cryoprecipitate has advanced considerably. The technology can be used for FFP and cryo-poor plasma as well. Future innovations may allow for mini-pool preparations of PCC, FIX, FVII, FXI and FV.¹⁰ Other technologies being examined in Europe for pathogen reduction of fresh components include amotosalen plus ultraviolet light and riboflavin plus ultraviolet light. Other countries in the world have virally inactivated products which are not currently licensed or available within the U.S.

¹⁰ M. El-Ekiaby, M. A. Sayed, C. Caron, et. al. Solvent-detergent filtered (S/D-F) fresh frozen plasma and cryoprecipitate minipools prepared in a newly designed integral disposable processing bag system. *Transfusion Medicine*. 20:48-61. Doi. 10.1111/j.1365-3148.2009.00963.

2. Donor Education & Marketing

We must implement a robust donor education program as part of any revised donor deferral policy.

This has been an issue filled with misunderstanding. If a change in policy requires a differentiation among high-risk behaviors it will be essential to have clarity in the donor screening questions, as well as in the recruitment messages delivered to prospective donors and donors reentering the system.

CONCLUSION

At this time, A-PLUS does not believe that the currently available knowledge and data are sufficient to support a change to the existing donor deferral policy. We acknowledge that the scientific basis for the permanent deferral requires review. However, we do not currently have enough information to determine if a one-year, five-year, ten-year, or another deferral period is more appropriate than the existing permanent lifetime deferral. Selection of another interval could also be perceived as arbitrary or lacking scientific foundation. However, this is not the end of the discussion.

We believe that there are a number of factors which should be fully evaluated before making a revision to the policy and we support research focused on high risk behaviors of both MSM and heterosexuals. Such evaluation and research could lead to a policy revision that maintains or enhances the safety of blood and blood products.

Today we are calling for a research agenda to be undertaken to address several critical areas with the following goals:

1. Achieving a better understanding of known and emerging pathogens in specific populations including MSM and heterosexual populations;
2. Developing policy that recognizes societal aspects of the blood system's safety and risk tolerance;
3. Developing alternate donor deferral strategies and the risk of blood-borne diseases;
4. Establishing a framework for accelerated approval of pathogen reduction, removal and/or inactivation technologies for fresh components; and
5. Understanding the implications of a revision on the supply and availability of treatment products globally.

If we progress in earnest with such a research strategy, and obtain reassuring answers, we foresee a time when a revision would be appropriate and donor deferrals could be made on a more individualized, behavioral-based risk review for both MSM and heterosexual donors.

We urge the committee, the FDA, the Secretary and Congress, along with all the other stakeholders within the system, including donors and end-users, to aggressively work together to seek answers. Equally important, is for the government to commit the necessary funding to ensure that this occurs in a timely manner. Our specific recommendations for research in the context of the research agenda mentioned above are summarized below.

On behalf of the thousands of Americans whose daily living depends upon our nation's blood supply we appreciate your thoughtful consideration of our comments, concerns and recommendations. We remain committed to working with all stakeholders to advance these discussions and to reach an appropriate conclusion that recognizes our collective belief in the paramount importance of ensuring the safety of the nation's blood supply for all Americans.

Thank you for your consideration of this important matter.

SUMMARY OF RESEARCH RECOMMENDATIONS

- I. The ACBSA consideration of this issue should not supplant the rigorous scientific review of the FDA and BPAC.**
- II. We must achieve a better understanding of known and emerging pathogens in specific populations including MSM and heterosexual populations.**
- III. We must give due consideration in policy development to the societal aspects of the blood system's safety and risk tolerance.**
- IV. We must consider alternate donor deferral strategies and the resulting risk of blood-borne diseases.**
- V. We must factor into the equation the risk of multiple and cumulative exposure for those dependent upon blood and plasma therapies for their daily living.**
- VI. We must establish a framework for accelerated approval of pathogen reduction, removal and/or inactivation technologies for fresh components and where necessary support research to develop the technology.**
- VII. We must understand the implications of a revision of the donor deferral policy on the supply and availability of treatment products globally prior to changing the deferral policy.**
- VIII. We must have a robust comprehensive hemovigilance and biovigilance program.**
- IX. We call upon the Department of Health and Human Services to encourage accelerated development and use of pathogen reduction technologies for fresh (labile) components.**
- X. We must implement a robust donor education program as part of any revised donor deferral policy.**

APPENDIX

CONTEXTUAL BACKGROUND AND OTHER ISSUES

A-PLUS coalition partner, the Committee of Ten Thousand (COTT), has provided the following additional background and historical contextual information as supplementary material for the ACBSA

The Committee of Ten Thousand (COTT) represents members of the hemophilia community who contracted HIV/AIDS and/or hepatitis C from tainted blood products. We stand before you today as we have since the formation of this ACBSA to express our concerns as well as our hopes and aspirations for a truly inclusive regulatory process regarding one of our nation's most precious resources, the blood supply. Protection of the end users must always be the priority when considering changes in regulatory policy. The full participation of end-user communities is a critical part of ensuring that protection and increasing the overall safety of the blood supply.

The National Academy of Sciences, Institute of Medicine (IOM) Report, *HIV and The Blood Supply: An Analysis of Crisis Decision Making*,¹¹ very clearly articulated the need to ensure the participation of all the stakeholders impacted by the blood supply and its regulation.

The federal government and the blood community must view the end-users as equal and full participants in the regulatory process if we are to succeed at the creation of a truly representative and inclusive structure for the regulation of the nation's blood supply. The ACBSA needs to enhance its commitment to a substantive partnership that includes the end-user communities, given that it is the members of our communities who shoulder the risks associated with changes in regulatory policy.

Approximately 1 in 2 Americans will at sometime in their lives need blood, blood components or blood products. Yet it is those individuals with chronic disease conditions that require frequent and life-long treatment who depend on the safety and availability of our national blood supply to sustain life.

The regulation of the blood supply is a matter of survival for our communities. It is about the wellbeing of our families and ourselves. On a daily basis, it is about managing risk and understanding the threats and benefits associated with the lifelong usage of blood and/or blood products.

While the risk equation has improved since the days of the HIV/AIDS and hepatitis C contamination of the blood supply during the 1970s and 1980s, risk and the potential transmission of known and unknown pathogens remain constant companions for the chronic disease communities who require treatment with blood or blood products.

¹¹ HIV and the Blood Supply: An Analysis of Crisis Decisionmaking; Lauren B. Leveton, Harold C. Sox, Jr., and Michael A. Stoto, Editors; Committee to Study HIV Transmission Through Blood and Blood Products, Institute of Medicine; ISBN: 0-309-58827-8, 352 pages, (1995)

We must not forget that it was the end-users, especially the hemophilia community, who shouldered the twin, blood-borne, epidemics of HIV/AIDS and hepatitis C. Ten thousand individuals were infected with HIV/AIDS, and nearly eight thousand have already passed away, leaving roughly two thousand in varying stages of HIV disease. Many of the ten thousand were also co-infected with hepatitis C. Liver transplants have become a common reality for those who are co-infected with HIV/AIDS and hepatitis C.

In the early 1990s, hepatitis C was transmitted through Immune Globulins IV, and it was those communities who depend on IVIG who shouldered that round of blood-borne transmissions of hepatitis.

While devastated by the transmission of HIV/AIDS, in the early 1990s the hemophilia community organized to demand a formal investigation into the failure of the federal government and the blood community to effectively protect the end-users of blood and blood products. We have taken this one step further to include our brethren in the plasma user communities to remain vigilant about safety and availability.

We must never view the regulation of the blood supply in a vacuum. If we make revisions or changes in one area of regulatory policy we must always consider the impact across the entire regulatory structure and the potential unintended or underestimated consequences of that one policy revision or change.

The IOM Report stated that, "...the Committee found that decisionmakers involved with donor screening and deferral acted with good intent in some circumstances. In other instances, however, preference for the status quo under the prevailing conditions of uncertainty and danger led decision-makers to underestimate the threat of AIDS for blood recipients. The Committee concluded that when confronted with a range of options for using donor screening and deferral to reduce the probability of spreading HIV through the blood supply, blood bank officials and federal authorities consistently chose the least aggressive option that was justifiable."

It is within this context that the end-user communities are again being asked to shoulder a potential increase in risk, due to revision in the current donor deferral policy regarding MSM donors. Where are the necessary initiatives for addressing problem areas if we are going to revise a policy that will result, according to the FDA, in an increase in the number of testing or quarantine release errors that will enter the overall collection system?

The end-users continue to wait for the blood community and the federal government to share in shouldering the risk of regulatory failure. That risk continues to be borne solely by those who will potentially be harmed by regulatory failure. Without strong initiatives to address the problems and who shoulders the risk, end-users have a very difficult time viewing the risk as shared by all the stakeholders associated with the blood supply.

Why do we continue to respond to failure without considering more humane policies and structures for addressing a given failure? In the wake of the AIDS/blood epidemic, the members of our community who chose to take a stand and demand action from the federal government and the blood community were met by hostility, arrogance, and a clear unwillingness to even consider a more humane approach. It was advocated that there be a structure similar to the Vaccine Injury Act which provides restitution for those harmed by vaccines. Why do we view

failure in the regulation of the blood supply so differently from the manner in which we address failures in vaccine safety? The general consensus remains that the Vaccine Injury Act continues to serve an important societal goal for safe and available vaccines. Yet each and every time end-users raise the concept of a blood injury act, we are again met by an absolute unwillingness to act on the part of the federal government and the blood community. It cost the federal government roughly \$600-800 million to address the impact of the HIV/AIDS infection of ten thousand members of the hemophilia community. This alone should motivate us all to seek more humane and cost effective strategies for addressing regulatory failure in the blood supply.

The IOM Report also addressed the issue of the risks associated with extended usage of blood and blood products in the context of educating physicians and their patients. In recommendation 12 the IOM Report stated that, “When faced with a decision in which the options all carry risk, especially if the amount of risk is uncertain, physicians and patients should take extra care to discuss a wide range of options.”

Recommendation 12 has yet to be formally acted upon by the ACBSA, and we are troubled by that, given the importance of understanding the risk equation and how it impacts the individual users of blood and blood products and their physicians. In fact, the lack of understanding of the risk landscape by physicians treating patients dependent on blood and blood products is indicative of the inaction by the federal government and the blood community.