



PLUS

AMERICAN PLASMA
USERS COALITION

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

of the statement on behalf of the
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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

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:

Alpha-1 Association
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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.

Committee Question 1. What are the most important societal, scientific and economic factors to consider in making a policy change?

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*

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

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

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

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

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.



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)

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.