



Advancing Transfusion and
Cellular Therapies Worldwide



American
Red Cross

Department of Health and Human Services
Advisory Committee on Blood and Tissue Safety and Availability
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A Joint Perspective on Tolerable Risk in Blood Safety

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I am presenting the following perspective on behalf of AABB, America's Blood Centers and the American Red Cross. Collectively, our organizations represent the nation's blood collection establishments, transfusion services, and transfusion medicine professionals. We commend the Advisory Committee on Blood and Tissue Safety and Availability (ACBTSA) for convening this meeting to explore the definition of a tolerable risk for infectious diseases from a patient's perspective. We are pleased to present our joint perspective on a tolerable level of risk in blood safety, with an emphasis on infectious diseases.

Our joint perspective focuses on the following six principles related to risk tolerability in blood safety:

1. Validated risk-based models enable decisionmakers to evaluate blood safety in the context of a range of emerging risks and other societal priorities that must compete for limited resources; balance demands for safe blood with the need to ensure that blood is available for patients; and are useful tools to drive policymaking and evaluate blood safety;
2. A comprehensive approach to "blood safety" that is inclusive of donor safety, the safety of blood products, the safety of transfusion medicine and the safety of the patient;
3. Support for research related to new threats to the safety of the blood supply;
4. Recognition that biovigilance and hemovigilance are critical to advancing the safety of the blood supply;
5. Voluntary standards and guidance contribute to blood safety; and
6. Risk tolerability may vary significantly between different constituencies, as well as between organizations and individuals within a single constituency.

Background on the United States Blood System

As most ACBTSA members are aware, the United States blood system is comprised of a complex web of private and public stakeholders. Blood and blood components originate from altruistic, volunteer donors. Blood collection establishments collect, test, process and distribute blood components to hospitals and other settings of care where blood is transfused to patients. Other key private stakeholders include device manufacturers, testing laboratories, clinicians, private standard setting and accreditation organizations, and payors. Public stakeholders central to the U.S. blood system include the Food and Drug Administration, the Centers for Disease

Control and Prevention, the National Institutes of Health, the Office of the Assistant Secretary for Health and the Office of the Assistant Secretary for Preparedness and Response, as well as other federal, state and local governmental agencies.

The committee is considering risk tolerability for infectious diseases in the context of this diverse system at a critical time for the blood community. The blood sector faces mounting economic pressures from existing and emerging voluntary and mandatory safety measures, which are intended to protect the health of patients and donors but are costly to implement. Current reimbursement mechanisms are not aligned with the blood community's role in protecting the public's health. Additional challenges include changing medical practices, reduced blood utilization, a limited donor pool and consolidation throughout the health care system. Together, these challenges limit the ability of the blood system to invest in research and development and adopt innovative technologies.

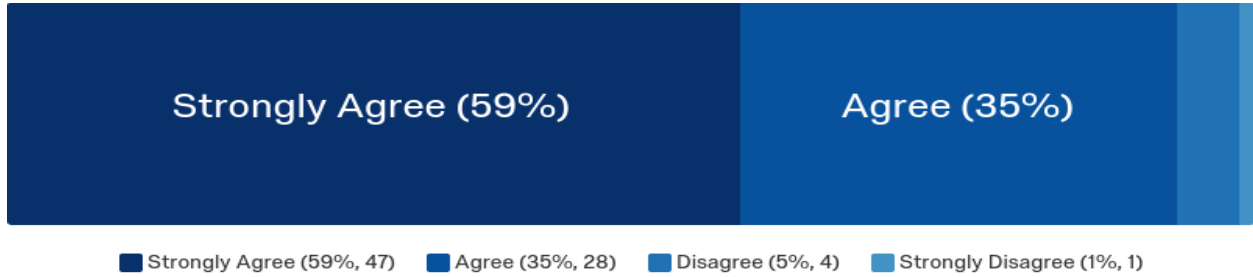
Process Used to Develop Perspective on Risk Tolerability

The following perspective on risk tolerability reflects feedback received through a process that AABB piloted to assess the viewpoints of its diverse membership, which includes both institutions and individuals involved in transfusion medicine and cellular therapy. AABB surveyed subsets of its volunteer leadership and members, including members of certain committees, blood center Chief Executive Officers, medical directors of transfusion services and hospital-based blood banks and the AABB board of directors to gauge whether there is consensus among its diverse membership on the positions being presented today. The survey was delivered to 313 participants and 81 (26 percent) responses were completed.

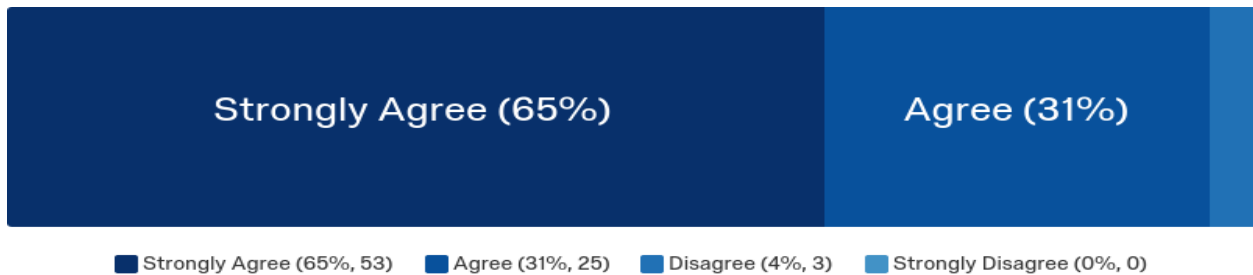
The results of this survey illustrate that there is widespread agreement on general principles related to risk tolerability. Some alternative viewpoints were shared with AABB, and we have included those responses in an addendum we will provide to the committee. As the ACBTSA continues to explore tolerable levels of risk in blood safety, we urge the committee to work with stakeholders to explicitly and clearly define all terms. All stakeholder in the U.S. blood system must have a common understanding of key terms, such as "safe," "blood safety," "risk," and "risk-based model" prior to defining a tolerable level of infectious disease risk in blood safety.

Perspective

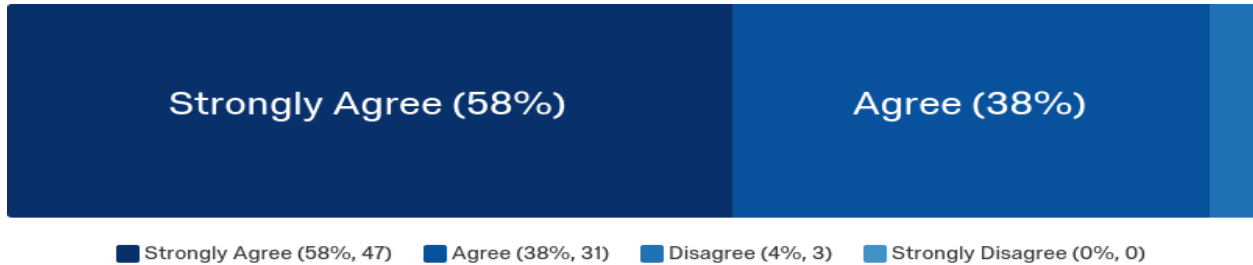
1. **AABB, America’s Blood Centers and the American Red Cross support the use of validated risk-based models to drive policymaking and arrive at decisions related to blood safety interventions and new technologies.** Importantly, risk-based models do not consider a particular risk, such as a specific infectious disease, in a vacuum. Rather, models enable decisionmakers to evaluate blood safety in the context of a range of emerging risks and other societal priorities that must compete for limited resources. They also balance demands for safe blood with the need to ensure that blood is available for patients.



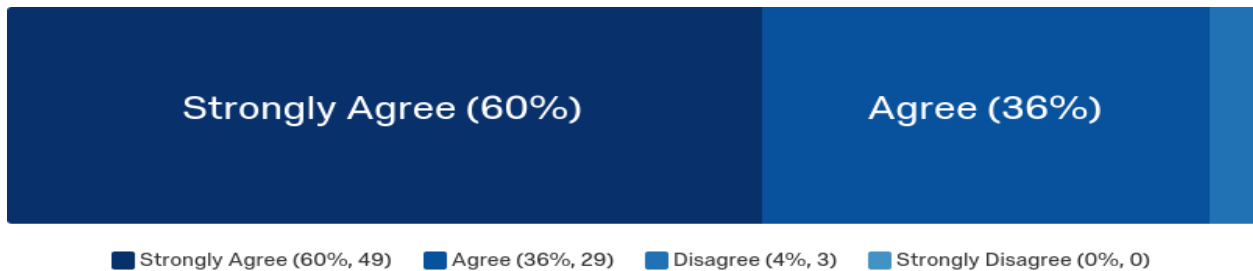
Risk-based models are useful tools to evaluate blood safety since the terms “safe” and “safety” are continuously evolving and are not uniformly defined for the U.S. blood supply. The blood community has revolutionized blood safety over the past 30 years, implementing new processes and tests that have substantially reduced the risk of transmitting infection via transfusion. Despite these tremendous strides and similar to all biologics, blood will always have inherent risk.



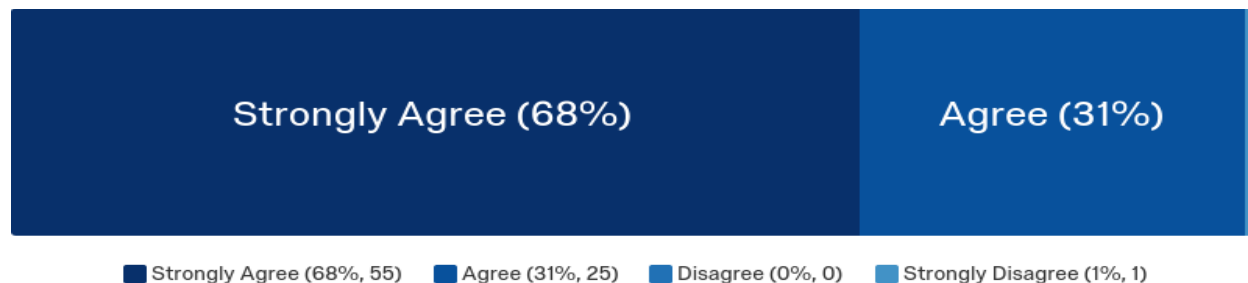
2. **AABB, America’s Blood Centers and the American Red Cross take a vein-to-vein approach to blood safety and believe that “blood safety” includes donor safety, the safety of blood products, the safety of transfusion medicine and the safety of the patient.** Critically, “blood safety” is inextricably intertwined with the availability of blood and blood products. Patient safety is jeopardized when a new safety requirement or the implementation of new technology limits the availability of blood.



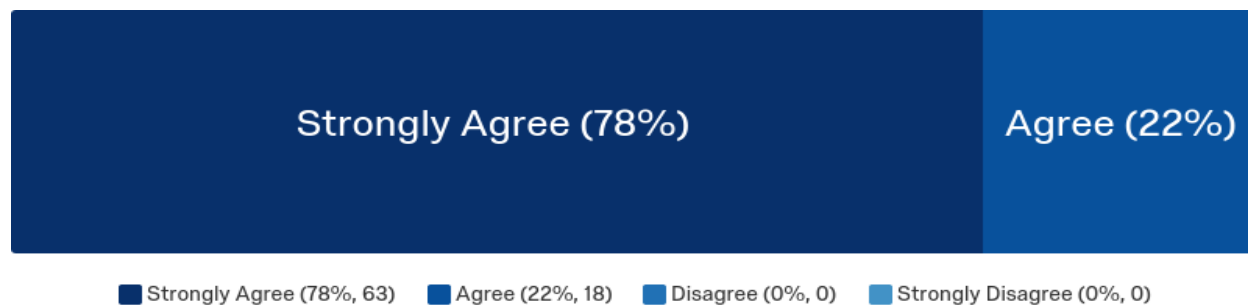
As we consider tolerable levels of transfusion-transmitted risks, we must remember that patient safety is much more vulnerable to non-infectious complications, including transfusion-associated circulatory overload (TACO), the transfusion of an incompatible unit of blood and transfusion-related acute lung injury (TRALI).



3. Emerging infectious diseases will continue to pose new threats to the safety of the blood supply. Therefore, the nation must continue to support research related to these potential threats. Ongoing public and private investment in research is critical to identifying new threats as well as developing and evaluating new safety processes and technologies.



In addition to investments in research, we encourage the ACBTSA and policymakers to consider (i) programs and reimbursement mechanisms related to blood safety mandates and FDA recommendations in guidance, as well as (ii) ways to support the implementation of safety measures and innovation when market incentives do not otherwise exist. Novel blood safety technologies and interventions cannot be effective and will not contribute to improved safety unless they are accessible, affordable and implemented by the blood community.



Although the Biomedical Advanced Research and Development Authority (BARDA) has provided critical financial support for developing new technologies to protect the blood supply, there have not been similar investments to support the implementation of these safety technologies. For instance, in 2016 the Food and Drug Administration required all U.S. blood collection establishments to implement additional safety measures within 4 to 12 weeks, using either testing for Zika with an investigational nucleic acid test or pathogen reduction technology. HHS estimated in a June 2017 study that this requirement for universal adoption of individual donor testing for Zika virus would cost the blood system approximately \$137 million annually. A recent study published in the *New England Journal of Medicine* concluded that testing individual blood donations for Zika not only had a high cost, but also had a low yield; out of 4 million blood donations screened, only nine were confirmed positive for Zika.¹ Current reimbursement mechanisms are not aligned with the blood community’s role in protecting the public’s health.

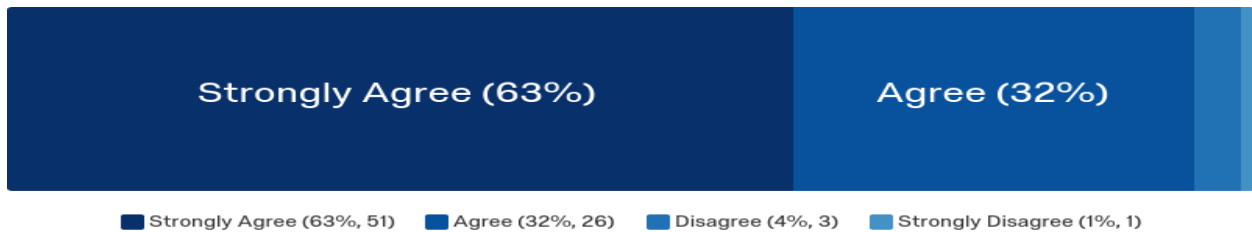
¹ Saa, P, Proctor M, Foster G, Krysztof D, Winton C, Linnen J, Gao K, Brodsky J, Limberger R, Dodd R, Stramer S. Investigational Testing for Zika Virus among U.S. Blood Donors, *N Engl J Med* 2018;378:1778-88.

We believe that public policies need to support and finance the implementation of new technologies that are required for blood safety initiatives.

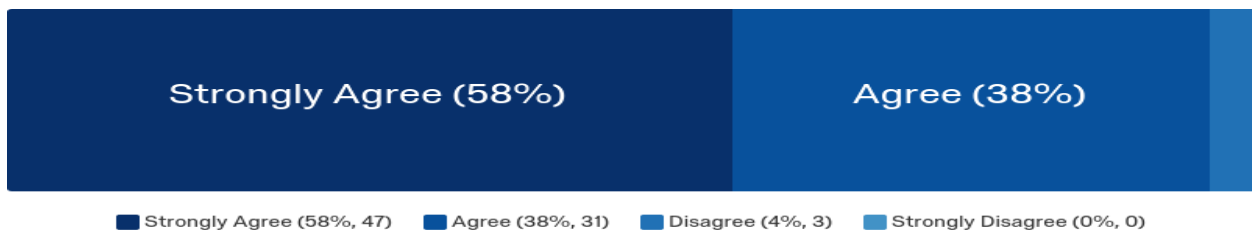


■ Strongly Agree (84%, 67) ■ Agree (15%, 12) ■ Disagree (1%, 1) ■ Strongly Disagree (0%, 0)

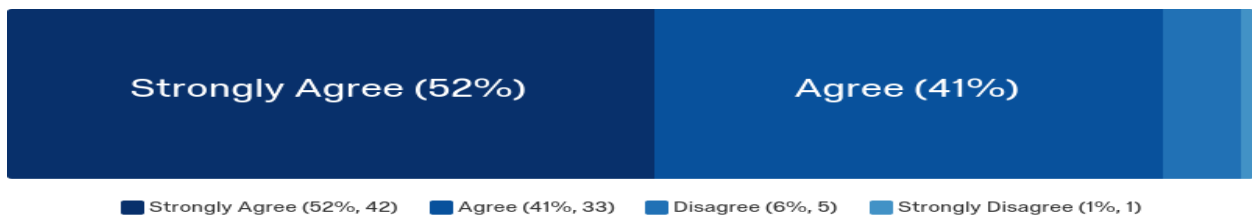
4. **We believe that real-time data, including biovigilance and hemovigilance, are important to advancing the safety of the blood supply.** AABB specifically surveyed its members on the need for a robust, well-funded biovigilance program in the United States to track the risks and benefits of transfusion, as well as the effectiveness of safety interventions, both proposed and existing, to reduce risk. As this committee has discussed in the past, comprehensive surveillance data will enable the entire blood community to engage in more thorough risk assessments and make more informed decisions regarding strategies to protect patient and donor safety that will not adversely impact the availability of blood products.



At present, biovigilance efforts are limited and inconsistent throughout the United States. For example, in 2011, babesiosis was classified as a nationally notifiable condition and the Centers for Disease Control and Prevention (CDC) began conducting surveillance for the disease.² Despite this classification, as of 2015, babesiosis was only reportable in 33 states. Cases are reported by state and county of residence, which may differ from where exposure occurred. Thus, it is difficult to fully understand the incidence and prevalence of babesiosis.

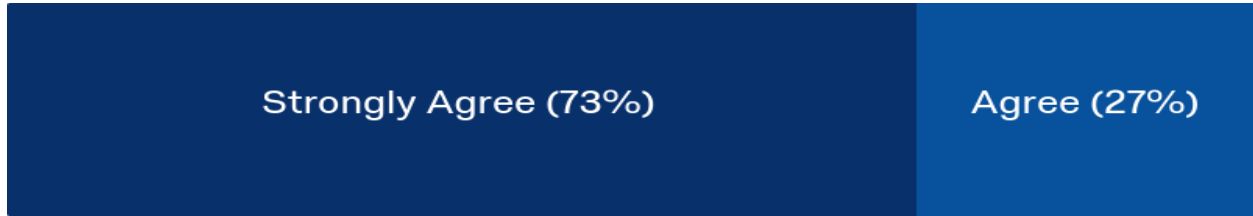


Similarly, hemovigilance is necessary to monitor donor safety, transfusion safety and patient safety. Since 2006, AABB has worked with the federal government to establish a U.S. national hemovigilance program. We believe that increasing the resources available for national hemovigilance efforts will contribute to improved assessments of risk, stronger evidence-based policymaking and continued quality and safety improvements in transfusion medicine.



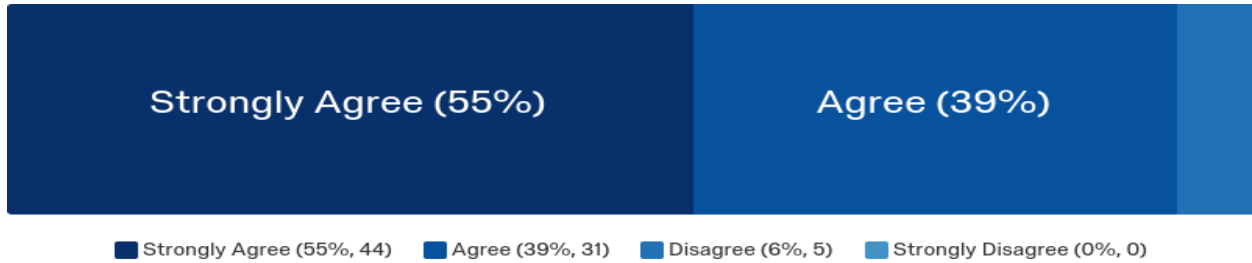
² Centers for Disease Control and Prevention. *Surveillance for Babesiosis – United States, 2014 Annual Summary [monograph on the internet]*. 2016. Available from: https://www.cdc.gov/parasites/babesiosis/resources/babesiosis_surveillance_summary_2016.pdf

We believe that the public and private sectors should work together to ensure that new biovigilance and hemovigilance efforts do not create burdensome, unfunded mandates for blood centers, transfusion services or other private stakeholders.

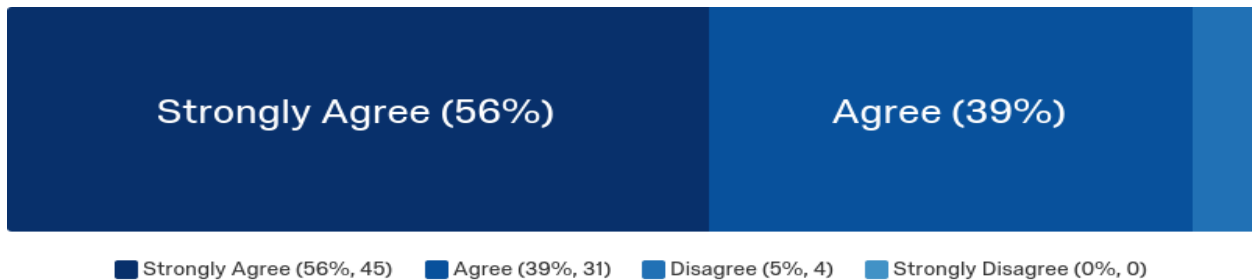


■ Strongly Agree (73%, 59) ■ Agree (27%, 22) ■ Disagree (0%, 0) ■ Strongly Disagree (0%, 0)

5. Voluntary standards and guidance will continue to play an important role in blood safety. AABB examines the current science and aims to assist its members – blood collection establishments as well as hospital transfusion services – in improving patient care. AABB’s quality-based standards and systems assessment help mitigate risk for AABB accredited organizations. These organizations set quality goals and use processes within their individual frameworks to reduce specific risks.

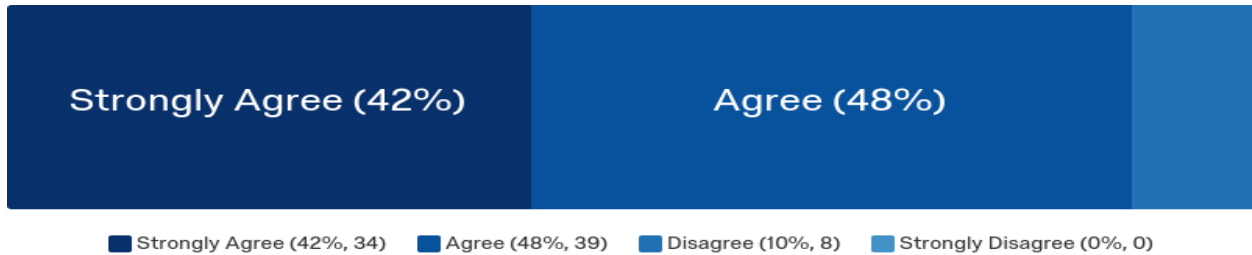


As an example, AABB adopted standards and issued guidance aimed at reducing the incidence of bacterial contamination as well as TRALI. Following AABB’s November 2006 recommendation that blood collection and transfusion facilities begin to implement TRALI risk reduction measures for high plasma-volume components, FDA fatality reports indicated that deaths due to TRALI fell significantly from 34 in FY2007 to 16 by FY2008, with 8 fatalities reported for 2016.³

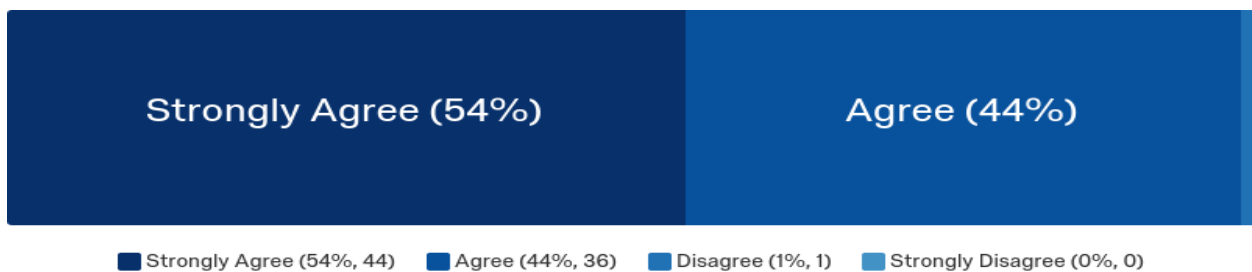


³ Food and Drug Administration, Fatalities Reported to FDA Following Blood Collection and Transfusion Annual Summary for Fiscal Year 2016, *available at* <https://www.fda.gov/downloads/biologicsbloodvaccines/safetyavailability/reportaproblem/transfusiondonationfatalities/ucm598243.pdf> (last visited August 17, 2018).

6. We appreciate that different constituencies, and organizations and individuals within a single constituency, may have different risk tolerances. Risk tolerability may vary significantly from one patient to another and that risk tolerability from a societal perspective will be quite different from an individual patient’s perspective. We commend the ACBTSA for its initial focus on the patient’s perspective. We believe the Advisory Committee should continue engaging with a wide variety of patients, prospective patients, and the public through activities that promote widespread discussions on risk tolerability and the prioritization of healthcare resources, such as in-person and virtual town hall meetings.



We believe that a multi-disciplinary approach is needed to understand risk tolerability related to blood safety. Today’s agenda scratches the surface of this complex topic, and representatives of physicians, blood centers and hospitals must continue to be included in these discussions. In addition, representatives from federal departments, offices and agencies, including the Department of Health and Human Services, the Office of the Assistant Secretary for Health, the Office of the Secretary for Preparedness and Response, the Office of the Assistant Secretary for Planning and Evaluation, the Food and Drug Administration, Centers for Disease Control and Prevention, National Institutes of Health, Armed Services Blood Program and Centers for Medicare and Medicaid Services, must continue to be at the table. We also recommend including representatives of state and local governments in future discussions, since regional, state and local factors may impact decisions related to blood safety. Finally, we believe industry provides an important perspective on risk tolerability, since these companies bring forth innovative technology that continually advance blood safety.



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Thank you for providing AABB, America’s Blood Centers and the American Red Cross with the opportunity to share our joint perspective on risk tolerability related to blood safety. We look forward to working with the ACBTSA as well as with other private and public stakeholders, on this important topic.

AABB is an international, not-for-profit association representing individuals and institutions involved in the fields of transfusion medicine and cellular therapies. The association is committed to improving health through the development and delivery of standards, accreditation and educational programs that focus on optimizing patient and donor care and safety. AABB membership includes physicians, nurses, scientists, researchers, administrators, medical technologists and other health care providers. AABB members are located in more than 80 countries and AABB accredits institutions in over 50 countries.

Founded in 1962, America's Blood Centers is North America's largest network of community-based, independent blood programs. Recognized by the U.S. Congress for its critical work in patient care and disaster preparedness and response, the federation operates more than 600 blood collection sites providing half of the U.S., and a quarter of the Canadian blood supply. These blood centers serve more than 150 million people and provide blood products and services to more than 3,500 hospitals and healthcare facilities across North America.

The American Red Cross shelters, feeds and provides emotional support to victims of disasters; supplies about 40 percent of the nation's blood; teaches skills that save lives; provides international humanitarian aid; and supports military members and their families. The Red Cross is a not-for-profit organization that depends on volunteers and the generosity of the American public to perform its mission. About 5.6 million units of whole blood are collected from roughly 3.3 million Red Cross volunteer donors, separated into 8 million transfusable blood products and supplied to approximately 2,700 hospitals and transfusion centers across the country for patients in need.

Addendum: Alternative Viewpoints

The perspective on risk tolerability in blood safety presented on behalf of AABB, America's Blood Centers and the American Red Cross consists of principles approved by AABB's Board of Directors and agreed to by a substantial majority of AABB members who responded to the survey on the perspective. AABB's membership is quite diverse, and some of the respondents who disagreed or strongly disagreed with a principle provided AABB with an alternative opinion. AABB committed to noting areas of consensus as well as alternative viewpoints. This addendum provides information on the alternative viewpoints shared with AABB. The feedback included in this addendum does not represent AABB's position on risk tolerability.

Risk-Based Models: In response to the principle related to using risk-based models evaluate blood safety, AABB received several alternative viewpoints highlighting the need to establish explicit common definitions. For example, one respondent highlighted that "risk" is broad, and suggested that certain risks, such as bacterial contamination, must be fully mitigated over time, while other risks, such as those of reactions and efficacy due to donor differences, cannot be managed. A different respondent was uncertain about the meaning of "risk-based model" and questioned whether existing evidence illustrates that using a risk-based model results in better decision-making.

One person highlighted that decisions related to the adoption of new safety interventions and technologies are not insulated from financial considerations; while safer products, such as platelets, are available, hospitals may be reluctant or unable to pay for these new technologies. One respondent was concerned that a risk-based approach is too relativistic and may result in contradictory policies that could reflect prevailing political opinion.

Blood Safety: One alternative viewpoint highlighted that new safety requirements may prevent adverse events occurring in transfusion recipients, while a different opinion questioned the levels of risk associated with blood transfusions due to a passive hemovigilance system. One person emphasized that blood safety is held to a different standard than other activities with higher levels of risk. One respondent did not believe that patient care is currently impacted by blood availability, while a different respondent highlighted that collaboration among blood centers helps safeguard the availability of blood for patients.

Research Related to New Threats: One respondent opined that public policies should not be equated with government policies and requested that policies support private market innovation.

Biovigilance and Hemovigilance: One respondent cautioned against hemovigilance and biovigilance efforts that create unnecessary new burdens, increase costs or slow down innovation and research. There were four alternative opinions shared related to a national hemovigilance program: one respondent supported a national hemovigilance program, two alternative viewpoints questioned whether hemovigilance should be a priority, and one respondent opined that hemovigilance can be accomplished without a federal mandate.

Role of Voluntary Standards and Guidance in Blood Safety: One person opined that the blood community should agree that safety is important, implement the agreed upon level of safety and suggested that those who use blood components underwrite the costs. Two respondents suggested that previous AABB decisions did not undergo risk-based assessments.

Risk Tolerability Varies Among Constituencies: Several respondents highlighted that decisions related to blood safety and risks to the blood supply should be based on evidence rather than opinion. There was support for engaging with and educating all stakeholders involved in the blood system.