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Public Comments for the September 13, 2018, Meeting of the Advisory Committee on Blood and Tissue Safety and Availability (ACBTSA)

Dear Committee Members:

Hemophilia Federation of America thanks ACBTSA for convening today's meeting to discuss defining a tolerable infectious disease risk in blood safety from a patient's perspective. HFA is a community-based, grassroots advocacy organization that assists, educates, and advocates for people with bleeding disorders. With our community's history always in mind, one of HFA's bedrock organizational objectives is to "promote and ensure a safe blood supply and other therapies/treatments for bleeding disorders and other related medical conditions." HFA would like to spell out some key principles, from the patients' perspective, to guide ACBTSA's discussion as it moves forward.

Background

As you know, hemophilia and other bleeding disorders are genetic conditions that impair proper blood clotting. Without treatment, people with hemophilia (often the severest of these conditions) experience internal bleeding that can lead to severe joint damage and permanent disability or even death.

For most of history, affected individuals had no effective way to control their bleeding episodes. That changed in the mid-20th century, first with the derivation of plasma extracts and, later, the development of blood-based clotting factor concentrates. But these advances came at a devastating price. Contamination of the blood supply in the 1970s and 1980s meant that people with severe hemophilia who used commercial clotting factors (derived from tens of thousands of pooled blood donations) were almost universally infected with HIV, hepatitis C, or both. The bleeding disorders community served, involuntarily, as the "canaries in the coal mine" who proved, in many cases with their lives, the transmissibility of HIV through blood.

Recombinant therapies became available for people with hemophilia in the 1990s, but only in 2015 did individuals with von Willebrand disease gain access to recombinant products. Today, many people with bleeding disorders use non-plasma-based therapies to treat or avoid painful bleeding episodes. But other individuals, including some with inhibitors or rare bleeding disorders, still rely on plasma-based products. Blood safety – which is a national priority, essential to the lives of all Americans – has very particular importance for the bleeding disorders community, and for all others who depend on regular and ongoing use of blood and plasma products for their daily living. In our comments, HFA will draw on our community's history to spell out some key principles from the patients' perspective to guide ACBTSA's examination of infectious disease risk in blood safety.

Key Principles of Blood Safety from the Patient Perspective

1. **Patient safety must take the highest priority.**

HFA understands that blood safety is a complex issue, with numerous interests at stake: availability, sustainability, and affordability, among others. But highest priority has to be given to patient safety. In the final analysis, it is the end user of blood products who shoulders the risk. Policy makers have to give due recognition to this fact, and to the magnitude of possible harm to patients.

For many years, the blood industry told regulators and patients that measures to improve blood safety were too costly or too constrictive. We urge policy makers to question these automatic assertions and to adopt, instead, the foundational principle that cost does not take precedence over patient safety. We call on all involved to redouble their efforts to put patients first: to articulate and implement policies that have as their goal the promotion of quality and safety, and the highest possible standards in all aspects of blood transfusion and fractionation.

2. **Blood safety policy must be based on rigorous science.**

The past four decades have seen a significant advance in knowledge, and a corresponding decrease in risk, with respect to blood-borne infections. And yet real gaps and areas of unmet need still persist. Known pathogens continue to present risk, albeit at a reduced level, as do previously non-prevalent or unknown pathogens. Policy makers need to address these remaining and emerging threats on the basis of good science and rigorous evidence-based standards.

We are pleased that the Food and Drug Administration in recent years has created and launched the Transfusion-Transmission Infections Monitoring System (TTIMS). This safety monitoring system provides a mechanism for gathering evidence to evaluate the effectiveness of current and new risk-reduction policies. We believe that TTIMS will play an important role in blood surveillance efforts. But regulatory efforts should not stop with TTIMS. Regulators and industry need to continue investing in and accelerating new safety innovations (e.g. pathogen reduction technologies and further infectious disease/emerging infectious disease testing). Policy makers also need to recognize that it will be important to maintain overlapping risk reduction methodologies for some period of time, until the innovative technologies prove their effectiveness in reducing pathogen transmission.

3. **The federal government bears responsibility for maintaining a strong regulatory framework, investing resources in blood safety, and enforcing safety standards**.

In 1993, the US Secretary of Health and Human Services asked the Institute of Medicine (IOM) to study how HIV came to contaminate the blood supply and infect thousands of patients in the 1970s and 1980s. The IOM Report, published in 1995 following a year-long study, did not "seek to determine liability or affix blame for any individual or collective decisions regarding HIV transmission through blood or blood products." Nonetheless, the report's authors deemed it important to "make a critical assessment of the difficult decisions that were made," and to conduct "an organizational analysis of the major players involved in the blood supply system," including the Food and Drug Administration.[1]

Among other things, the IOM Report found that FDA's policies during the period under review were "very much influenced, if not wholly determined," by the advice it received from its industry-dominated advisory committee. At a critical time, FDA reliance on industry self-regulation fell sadly short. One lesson drawn from this experience: it is

[1] Institute of Medicine. (1995). *HIV and the Blood Supply: An Analysis of Crisis Decisionmaking.* (L. B. Leveton, H. C. Sox Jr., & M. A. Stoto, Eds.) National Academies Press, at iv.

essential for agencies to remain independent from the industry that they regulate. Further, agencies need to have – and also, crucially, to *exercise* – appropriate regulatory authority. The tragic failures of the 1980s showed that the FDA "**did not adequately use its regulatory authority and therefore missed opportunities to protect the public health**." Instead, agency decisionmakers were "complacent," lacked a sense of urgency, and were overly cautious about exposing themselves to industry and political criticism.[2]

How can government avoid the pitfalls outlined in the IOM Report? First and foremost, regulators need to avoid conflicts of interest and regulatory capture. Relatedly, regulators must continually question the assumptions that underpin their decisions.[3] As stated above, US health agencies need to commit to supporting a robust system of hemovigilance, and to acting promptly and proactively with respect to emerging or suspected threats. They need to support safety technology development and implementation (e.g., pathogen reduction technology and infectious disease/emerging infectious disease testing). And they should implement reimbursement methodologies that provide for adequate reimbursement to providers for the costs of safety measures.

4. **The policy-making process must be transparent and inclusive, involving meaningful patient/end-user input.**

Patients need to be included, at all stages and in meaningful capacities, in developing blood safety policy and making decisions about risk. Since patients, as end users, bear the ultimate risk of blood-borne infections, they must have the opportunity to bring their experiences to bear, and to express the concerns most important to them. Patients must have a voice in setting priorities; determining questions for research; weighing evidence; defining standards; communicating policies; and more. Patient representation in the policymaking process will add needed perspective and, in the end, will ensure better community acceptance of the policies developed via an inclusive process.

5. **Users of blood and blood products are entitled to clear disclosures that allow them to understand the risks they face and truly give informed consent.**

"One powerful lesson of the AIDS crisis is the importance of telling patients about the potential harms of the treatments that they are about to receive."[4] In the 1980s, hemophilia patients did not have the basis for informed choice about their treatment. The IOM Report noted that, "in instances of great uncertainty, it is crucial for patients to be fully apprised of the full range of options available to them and to become active participants in the evaluation of the relative risks and benefits of alternative treatments. . . . The failure to communicate adequately about these options prevented many hemophiliacs from making choices in which they accepted responsibility for balancing the risk of AIDS and the risks of bleeding. Ultimately the failure to communicate led to a powerful sense of betrayal that exacerbated the tragedy of the epidemic for many patients and their families."[5]

Circumstances today, thankfully, are very different from those in the 1980s, but the use of blood and blood products still entails risk. Patients still need timely access to clear information about the risks involved in the products they use, allowing them to make informed decisions about their treatment options.

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[2] IOM at 6-7, 10, 94.
[3] For example, it was for many decades considered "medically acceptable" to subject blood product users to a high risk of infection with hepatitis. But acceptance of those "prevailing assumptions about medically acceptable risks, especially regarding hepatitis," led to "complacency and a failure to act with sufficient concern upon reports of a new infections risk." Id. at 8, 203.
[4] Id. at 231.
[5] Id. at 231-2.

6. **The federal government should consider establishing a no-fault compensation system for individuals who suffer adverse consequences from the use of blood or blood products.**

Twenty years have passed since publication of the IOM Report, and yet its third recommendation – establishing a no-fault compensation system for those harmed through the use of blood or blood products – remains unrealized.

Individuals who got sick or died from blood-borne infections in the 1970s and 1980s (and their family members) had to fight hard and wait a long time for compensation – if indeed they received any compensation at all. (Individuals who contracted HCV and transfusion recipients who contracted blood-borne disease were not included among those eligible for "compassionate relief payments" under the 1998 Ricky Ray Act). While blood safety has improved, and while regulators and stakeholders work to make the blood supply still yet safer, it is still important to have a system in place to prevent injustice and relieve hardship in the event of future transfusion errors.

Conclusion

Most patients understand that a blood supply with zero risk may not be an attainable goal. But nor is it enough to say, our existing system does a good enough job at protecting against risks of transmission of known pathogens. Our nation needs a blood safety system that is attuned to the risk of unknown pathogens. We need to foster investment in hemovigilance and in the scientific research necessary to develop rigorous, evidence-based standards. We need to have strong commitment from government to exercise appropriate regulatory oversight and enforcement. We need to put in place a system of no-fault compensation to relieve anyone who falls victim to a hoped-against failure of the blood safety system. Most of all, our system has to put patient safety and patient interests at the center – including robust patient involvement in the articulation of standards – recognizing that patients bear the ultimate risk in the event of blood-borne infection.

HFA appreciates ACBTSA's attention to these crucially important issues, and thanks the Committee for considering our views. If you have any questions or need further information, please contact Kim Isenberg, VP for Policy, Advocacy, Government Relations and Education (k.isenberg@hemophiliafed.org) or Miriam Goldstein, Associate Director, Policy (m.goldstein@hemophiliafed.org).

Sincerely,

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President & CEO
Hemophilia Federation of America