January 22, 2025

Peter W. Marks, M.D., PhD
Director
Center for Biologics Evaluation and Research (CBER)
U.S. Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

**Re: January 6, 2025, FDA Guidance Documents Regarding Risk of Transmission of Mtb and Disease Agents Associated with Sepsis**

Dear Dr. Marks,

On behalf of The Society of Thoracic Surgeons (STS), the American Association for Thoracic Surgery (AATS), and the Congenital Heart Surgeons' Society (CHSS) we write to provide comments on the following two final guidance documents that were published by the U.S. Food and Drug Administration (FDA) on January 6, 2025, without prior public participation:

(1) Recommendations to Reduce the Risk of Transmission of Mycobacterium tuberculosis (Mtb) by Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps); and

(2) Recommendations to Reduce the Risk of Transmission of Disease Agents Associated with Sepsis by Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps).

Together, our organizations represent the physicians and healthcare professionals that provide cardiac surgery, including the implantation of heart valves and patches, to patients with severe cardiovascular disease. Our members, and their patients, depend on a consistent supply of safe implantable valves and patches and are steadfast in their commitment to using products that meet the highest standards of quality and safety.

While we are encouraged that the FDA is prioritizing patient safety, we have concerns about the final guidance documents referenced above. We believe it is essential that all guidance documents published by the FDA include stakeholder input, especially when these policies can impact patient care and the availability of products. In this instance, we are concerned that the final guidance documents were published for immediate implementation without prior public comment and could cause a steep decline in the availability of safe human tissue heart valves and patches for adult and pediatric patients – especially when the data show that current policies and procedures have not resulted in Mtb transmission from human heart valve and patch implantation in more than 45 years.

Additionally, we are very concerned with the deadline of February 3, 2025, for industry to comply with these changes and believe the timeline may adversely impact availability of heart valves and patches in the immediate future.

We believe that the FDA should consider the American Association of Tissue Bank's (AATB) newly developed Standards for Tissue Banking that are set to be effective on January 31, 2025. The AATB standards address Mtb transmission and other safety concerns with implantable human tissue. Although the risk of Mtb transmission is low, with only eight reported cases from human heart valve implantation from 1972-1979, we understand FDA's concern about the recent cases in 2021 and 2023 from bone marrow/matrix tissue allografts.[1] We also recognize that additional requirements from FDA may be necessary. However, we believe stakeholder input should be incorporated into any final guidance document, and that the agency should consider focusing specifically on tissues that present a greater risk of Mtb transmission, such as those containing viable cells.

Our organizations are dedicated to improving the health of our patients and we rely on the availability of safe human tissue for implantation in cardiac procedures. We share the FDA's goal of reducing the risk of disease transmission through implantable human tissue. However, given the concerns detailed above, we believe the requirements in the guidance documents should be rescinded or at a minimum, delayed and clarified, based on stakeholder feedback. This action is critical so that industry has adequate time and a better understanding of how to comply with the new requirements without jeopardizing the availability of tissue products for patients.

We appreciate the FDA's consideration of our feedback and welcome an opportunity to engage further on these policies to achieve the goals of implantable tissue safety and tissue availability. Please contact Molly Peltzman, Associate Director of Health Policy at STS, at mpeltzman@sts.org should you need additional information or clarification.

Respectfully,

Jennifer C. Romano, MD, MS
President, Society of Thoracic Surgeons

David R. Jones, MD
President, American Association for Thoracic Surgery

Robert D.B. Jaquiss, MD
President, Congenital Heart Surgeons' Society

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[1] Greenwald MA, Edwards N, Eastlund DT, et al. The American Association of Tissue Banks tissue donor screening for Mycobacterium tuberculosis-Recommended criteria and literature review. *Transpl Infect Dis*. 2024;26 Suppl 1(Suppl 1):e14294. doi:10.1111/tid.14294