American Association of Tissue Banks®

Testimony for the Record
House Committee on Energy and Commerce Health Subcommittee
"Legislative Proposals to Support Patients with Rare Diseases"
Thursday, February 29, 2024

Chairs Rodgers and Guthrie, Ranking Members Pallone and Eshoo, and members of the Subcommittee, thank you for holding this important hearing today, which includes H.R. 6705, the Effective Screening and Testing for Tuberculosis Act, and H.R. 7188, the Shandra Eisenga Human Cell and Tissue Product Safety Act. The American Association of Tissue Banks (AATB) and AATB Tissue Policy Group (TPG) are pleased to submit this statement for the record and hope the committee will consider AATB as a resource for future activities related to human tissues.

As you may know, in May 2021, a tuberculosis (TB) outbreak was linked to a contaminated viable allograft bone matrix product used in spinal surgery. While the investigation of the 2021 transmission events was ongoing, the AATB Physicians Council worked with an independent contractor to review the literature and the information available at the time. This culminated in an advisory Bulletin (AATB Bulletin 22- 2, published March 22, 2022) along with a companion document with more medical and scientific details.

In August 2022, a paper was published by Schwartz, et al with details of the investigation and findings. In September 2022, after review of details provided in the Schwartz et al manuscript, the Physicians Council formed a Working Group. This group has been meeting on an ongoing basis, at least twice a month, to carefully consider the Mycobacterium tuberculosis (MTB) science and medical literature and

develop more specific and binding requirements for AATB members regarding screening potential donors for MTB.

In July 2023, the same tissue processor announced another investigation of post-surgical MTB infections in two patients treated with viable allograft bone matrix products from a different single donor lot.

Due to the urgency of putting into place donor screening requirements regarding MTB for AATB members, in August 2023 the Physicians Council MTB Working Group deemed it necessary to publish current consensus donor screening requirements that represent the highest risks for tissue transplantation, particularly among products containing viable cells.

The new requirements, published in AATB Bulletin 23-6, will help improve donor screening processes and improve patient safety, but will only apply to AATB-accredited banks. Congress can take additional steps to improve the safety of human cell and tissue transplants.

H.R. 7188, the Shandra Eisenga Human Cell and Tissue Product Safety Act

The Shandra Eisenga Human Cell and Tissue Product Safety Act would provide the Department of Health and Human Services (HHS) with important authorities related to tissue products. First, the legislation would authorize a national, evidence-based public awareness campaign regarding the potential risks and benefits of human cell and tissue transplants. HHS would be required to consult with stakeholder experts regarding the campaign, and HHS may award grants to nonprofit organizations to carry out the initiative.

The legislation would also authorize civil penalties for violations of section 361 of the Public Health Services Act. This authority would help FDA bring rogue stem cell clinics and other "bad actors" into compliance with FDA regulations for human cell and tissue product manufacturers.

Finally, the bill would require HHS to initiate a review of existing regulations and guidance documents related to human cell and tissue products; and inspection rates of human cell and tissue product manufacturing facilities compared to blood and Source Plasma establishments. HHS would be required to issue updated guidance related to determining eligibility of donors of human cell and tissue products within 3 years of enactment of the legislation.

H.R. 6705, the Effective Screening and Testing for Tuberculosis Act

In general, the AATB and TPG are concerned that the Effective Screening and Testing for Tuberculosis Act emphasizes donor testing over donor screening. Donor screening is the review of the potential donor's relevant medical records, including lab results other than communicable disease testing, coroner/autopsy reports, and the donor history medical interview, for risk factors and clinical evidence of communicable diseases. Donor testing is the actual testing of a potential donor's serum or plasma for evidence of infection. It is ideal to have overlapping layers of safety to include both donor screening and testing, but there are significant limitations to any testing that can currently be performed, as will be discussed below. Therefore, donor screening is the most important component of donor-eligibility determinations to reduce the potential risk of TB transmission through transplanted human cells, tissues, and cellular and tissue-based products (HCT/Ps), as opposed to donor or product testing.

Regarding section 2, which would require HHS to establish an expedited development and priority review pathway for a new and innovative donor screening test with heightened sensitivity to effectively screen HCT/P product donors for evidence of active or latent tuberculosis infection, AATB is not aware of any entity currently developing a deceased tissue donor test for TB. The development of such a test could take years, and there may not be a test that can be developed that provides dependable results. However, AATB has no concerns with establishing an expedited review process for potentially new and innovative donor screening tests in this space.

It appears that Section 3 would require regulations be promulgated to require donor screening to include screening for active and latent TB, and to require "an establishment that performs donor testing to test for active and latent tuberculosis." AATB recommends either striking section 3 or revising it to focus solely on donor screening. It is also noted that rulemaking may not be necessary for FDA to achieve the goal of requiring donor screening for tuberculosis.

AATB Bulletin 23-6 was published with a frequently asked questions (FAQs) document that includes a section on testing. From that section:

> "There are no FDA licensed/cleared/approved tests for tuberculosis for deceased tissue donors. The 2 approved tests for clinical/diagnostic purposes are QuantiFERON-TB Gold Plus and T-SPOT TB test. These interferon gamma release assays (IGRA) rely on the ability of white blood cells to release interferon gamma in response to TB antigen, and therefore require living cells. As a result, testing must be completed in a very short timeframe that is not possible with deceased tissue donors. Furthermore, poor immune function will negatively impact the ability to obtain

positive test results. More information about IGRA testing can be found at https://www.cdc.gov/tb/publications/factsheets/testing/igra.htm.

For the 2023 tuberculosis transmission event, the viable bone matrix tissue was tested for MTB using polymerase chain reaction (PCR) methodology."

Furthermore, those blood tests do not differentiate between latent or active TB, and a negative result cannot rule out that the presence of latent or active TB.

There are many limitations that come with testing the HCT/P for MTB, which can be accomplished either by performing culturing, or performing nucleic acid amplification testing (NAT) + culturing. Limitations include but are not limited to challenges in determining an appropriate sampling plan given TB is not evenly distributed within the body, the possibility of having to use so much of a tissue sample for testing that there is significantly diminished volume left to distribute for transplant, and the time that it takes for culture results to be available—up to 8 weeks. While NAT testing provides faster results, it is less sensitive than culture, and would need to be performed in addition to, not instead of, culture—which in turn, would require additional sample for testing. It is notable that the second transmission case happened in the context of product testing by NAT methodology. Both culture and NAT testing for *Mycobacterium tuberculosis* are challenging to perform, and require specialized expertise to do correctly. It is common to obtain a negative test result in the presence of MTB (or a "false negative") if the testing is not performed correctly, which would lead to a false sense of safety.

For these reasons, AATB believes that the focus should be on enhanced donor screening specific for TB, and not on donor testing.

Finally, the guidance referenced in section 4 is related to complying with requirements under 21 CFR Part 1271, subparts D and E, which has to do with manufacturing of HCT/Ps. The AATB and TPG think it would be more appropriate to instead direct the FDA to finish updating the Eligibility Determination for Donors of HCT/Ps Guidance for Industry, which hasn't been fully updated since 2007.

Thank you for taking these comments into consideration. The AATB and TPG stand ready and willing to assist in any way that you deem appropriate.

The American Association of Tissue Banks

The American Association of Tissue Banks (AATB) is a professional, non-profit, scientific, and educational organization. AATB is the only national tissue banking organization in the United States, and its membership totals more than 120 accredited tissue banks and over 7,000 individual members. These banks recover tissue from more than 70,000 donors and distribute in excess of 3.3 million allografts for more than 2.5 million tissue transplants performed annually in the US. The overwhelming majority of the human tissue distributed for these transplants comes from AATB-accredited tissue banks.

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