American Association of Tissue Banks® AATB TPG, LLC

September 14, 2022

Division of Dockets Management (HFA–305)
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

In Re: Docket No. FDA-2022-D-0745 for "Voluntary Consensus Standards Recognition Program for Regenerative Medicine Therapies; Draft Guidance for Industry"

Submitted electronically at www.regulations.gov

Dear Madams and Sirs:

The American Association of Tissue Banks (AATB or Association) and the American Association of Tissue Bank's Tissue Policy Group, LLC (AATB TPG or TPG) submit these comments related to draft guidance by the Food and Drug Administration (FDA or Agency) titled *Voluntary Consensus Standards Recognition Program for Regenerative Medicine Therapies*. In particular, our comments focus on (1) requesting that the Agency consider providing this framework for all human cells, tissues, and cellular and tissue-based products (HCT/Ps) requiring a Biologics License Application (BLA), not just regenerative medicine therapies (RMTs); (2) providing a list of important standards utilized by tissue banks which should be subject to this program, including standards related to sterility; and (3) ensuring that the Agency is aware of ongoing activities supported by tissue banks to help identify and coordinate the development of regenerative medicine standards.

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 6,000 individual members. These banks recover tissue from more than 58,000 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.

The AATB TPG includes Chief Executive Officers and senior regulatory personnel from U.S. tissue banks that process donated human tissue. The purpose of the TPG is to drive policy in furtherance of the adoption of laws, regulations, and standards that foster the safety, quality, and availability of donated tissue. The TPG's membership is responsible for the vast majority of tissue available for transplantation within the U.S.

Broader application. While we appreciate that the FDA is setting forth this draft guidance in accordance with section 3036 of the *21st Century Cures Act* (P.L. 114-255), the Agency has the authority to go beyond the strict statutory requirement and can opt to include additional regulated products within the voluntary consensus program. As such, **we request that you explicitly include all HCT/Ps requiring a BLA, not just RMTs**, given that the FDA has the authority to do so and given that all HCT/Ps requiring a BLA is a better delineation of covered products and, as such, provides greater regulatory clarity.

List of appropriate standards. Previously, the AATB and the TPG have sent information to the Centers for Biologics Evaluation and Research (CBER) related to specific standards related to sterility. Specifically, those standards include:

- International Organization for Standardization (ISO) 11137-1 *Sterilization of health care products – Radiation – Part 1: Requirements for development, validation, and routine control of a sterilization process for medical devices*;
- ISO 11137-2 *Sterilization of health care products – Radiation – Part 2: Establishing the sterilization dose*;
- AAMI TIR 37 *Sterilization Of Health Care Products-Radiation-Guidance On Sterilization Of Biologics And Tissue-Based Products*; and
- ANSI/AAMI ST67: 2019 *Sterilization Of Health Care Products - Requirements And Guidance For Selecting A Sterility Assurance Level (SAL) For Products Labeled "Sterile."*

As the Agency considers developing a list of standards as part of the standards recognition program for regenerative medicine therapies (SRP-RMT), the AATB and the TPG note that **the Centers for Devices and Radiological Health (CDRH) has a series of Recognized Consensus Standards which may be applicable.** For instance,

- ASTM has a series of standards related to tissue engineering, biocompatibility, and sterility;
- USP-NF has monographs on biocompatibility, sterility, and general plastic surgery;
- ISTA has transportation standards focused on maintenance of temperature in transit;
- ICH is focused on developing harmonized international standards for drug quality and safety;
- ISO provides quality management, biocompatibility, environmental management, sterilization, risk management, performance testing, labeling, and IT security standards;
- AAMI has safety and performance criteria, conformance measures, sterilization, performance testing, and design specifications; and
- ANSI supports conformance assessment activities.

While these include a whole host of relevant standards, we have highlighted a few standards below which are of critical importance to tissue banking and HCT/Ps.

Standards Related to Manufacturing & Sterilization

- ANSI/AAMI/ISO TIR13004, *Sterilization of Health Care Products – Radiation – Substantiation of a Selected Sterilization Dose: Method VDmaxSD*;
- ISO 14644-1:2015, *Cleanrooms and Associated Controlled Environments* (the series); and
- ISO 10993 (the series).

Standards Related to Analytical Procedures

- ANSI/AAMI ST72, *Bacterial Endotoxins - Test Methods, Routine Monitoring, and Alternatives to Batch Testing*;
- ANSI/ASQ, *Sampling Procedures and Tables for Inspection by Attributes*;
- ICH Q2(R1), *Validation of Analytical Procedures: Text and Methodology*;
- ICH Q3D(R1), *Elemental impurities*;
- ISO 11737-1, *Sterilization of health care products – Microbiological methods – Part 1: Determination of a population of microorganisms on products*;
- ISO 11737-2, *Sterilization of health care products – Microbiological methods – Part 2: Tests of sterility performed in the definition, validation, and maintenance of a sterilization process*;
- ISO 13319, *Determination of Particle Size Distributions – Electrical sensing zone methods*;
- USP <61>, *Microbiological Examination of Nonsterile Products: Microbial Enumeration Tests;*
- USP <71>, *Sterility Tests*;
- USP <85>, *Bacterial Endotoxins Test*;
- USP <232>, *Elemental Impurities – Limits*;
- USP <233>, *Elemental Impurities – Procedures*;
- USP <730>, *Plasma Spectrochemistry*;
- USP <921>, *Water Determination*;
- USP <1033>, *Biological Assay Validation*;
- USP <1223>, *Validation of Alternative Microbiological Methods*;
- USP <1224>, *Transfer of Analytical Procedures*; and
- USP <1225>, *Validation of Compendial Procedures*.

Standards Related to Container Closure Systems, Packaging, and Transportation

- ASTM D4169, *Standard Practice for Performance Testing of Shipping Containers and Systems*;
- ASTM F88/F88M, *Standard Test Method for Seal Strength of Flexible Barrier Materials*;
- ASTM F1980, *Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices*;
- ASTM F2096, *Standard Test Method for Detecting Gross Leaks in Packaging by Internal Pressurization (Bubble Test)*;
- ISO 15223-1, *Medical devices - Symbols to be used with medical device labels labelling and information to be supplied - Part 1: General requirements*;
- ISTA 3A, *Packaged-Products for Parcel Delivery System Shipment 70 kg (150 lbs) or less*;
- ISTA 3B, *Packaged-Products for Less-Than-Truckload (LTL) Shipment*;
- ISTA 3E, *Similar Packaged-Products in Unitized Loads of Truckload Shipment*;
- USP <87>, *Biological Reactivity Tests, In Vitro*;
- USP <381>, *Elastomeric Closures for Injection*;
- USP <660>, *Pharmaceutical Glass Testing*; and
- USP <788>, *Particulate Matter in Injections*.

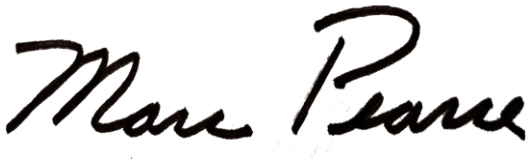
In addition, the AATB and the TPG urge the Agency to take a broad view of the CDRH Recognized Consensus Standards. While the title of the Recognized Consensus Standard may indicate that it applies

to medical devices, it may still have full applicability to BLA products. And, to the extent that it is not fully applicable, the CDRH Recognized Consensus Standards may serve as a good starting point for a standard suitable for the BLA products or, alternatively, certain sections may be generally appropriate.

Other activities. Finally, given that many tissue banks participate in the project working groups of the Standards Coordinating Body for Regenerative Medicine, we wanted to ensure you were aware of those activities and note that you may find their work useful to your efforts.

We hope that you will find this information useful in your deliberations. The AATB and the TPG stand ready and willing to assist the FDA in any way that you deem appropriate.

Respectfully,



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