



American Association of Tissue Banks® AATB TPG, LLC

September 7, 2021

Janet Woodcock, MD
Acting Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

In Re: Questions and Answers Regarding the End of the Compliance and Enforcement Policy for Certain Human Cells, Tissues, or Cellular or Tissue-based Products ([HCT/Ps](#))

Dear Dr. Woodcock:

In November 2017, the FDA published the final [guidance](#) titled *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use* (hereinafter “new guidance”). As a result of this final guidance, certain tissue products (HCT/Ps) not meeting the requirements of 21 CFR 1271.10 would no longer be afforded enforcement discretion after May 31, 2021. On July 9, 2021, six weeks after the end of enforcement discretion, FDA posted a document titled *Questions and Answers Regarding the End of the Compliance and Enforcement Policy for Certain Human Cells, Tissues, or Cellular or Tissue-based Products ([HCT/Ps](#))* (hereinafter “Q&As”). The American Association of Tissue Banks (AATB) and the American Association of Tissue Bank’s Tissue Policy Group, LLC (AATB TPG) submit these comments related to the internet posting of the Q&A’s. Specifically, the ***American Association of Tissue Banks (AATB) and the AATB Tissue Policy Group (TPG) are concerned that the Q&As create potential confusion with end users about HCT/Ps, which can result in patients being denied access to AATB member tissue banks tissue products.***

The American Association of Tissue Banks (AATB) is a professional, non-profit, scientific and educational organization. It is the only national tissue banking organization in the United States, and its membership totals approximately 120 accredited tissue banks and 2,000 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 U.S. The overwhelming majority of the human tissue distributed for these transplants comes from AATB-accredited tissue banks.

The AATB’s Tissue Policy Group (TPG), LLC (AATB TPG or 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 public policy in furtherance of the adoption of laws and regulations 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.

In reviewing the Q&As, there are multiple areas of concern – (1) while appropriately stating the

regulatory framework for products which were never legally marketed in the United States, the Q&As fail to address key nuances with products that were, for a time, allowed to be marketed and in interstate commerce in the United States and whose new product approval requirements relates solely to the Agency's interpretation of the HCT/P regulatory framework through the new guidance; and (2) the unintended consequences for legally marketed 361 HCT/Ps where healthcare users are potentially confused about the legal standing of all HCT/Ps, including legally marketed 361 HCT/Ps.

Nuanced Approach Similar to EUAs. Rather than treat these products, which were in interstate commerce, as if they were never allowed to be marketed, a more nuanced response to the close of the enforcement discretionary period for HCT/Ps as detailed in the Q&As should have been similar to the Agency's continued response to evolving Emergency Use Authorizations (EUAs). For instance, with respect to certain respirators and decontamination equipment, the FDA, as a Letter to Health Care Providers, provided notice to entities on [April 9, 2021](#) that they should transition away from the use of certain products, and then waited nearly three months (until [June 30, 2021](#)) to revoke the EUA. While we appreciate the enforcement discretion period, we remain concerned about the Agency's clarification regarding the status of the products already in interstate commerce, given that, despite repeated inquiries, the Agency did not provide clarification until after the enforcement discretion period closed. Therefore, ***we request that the Agency update its Q&As to clarify that, for products which have entered interstate commerce under enforcement discretion prior to June 1, 2021, clinicians can still utilize those products***, provided that there is no additional safety concern.

Unintended consequences to 361 HCT/Ps. While the Q&As focus on products that require but lack premarket approval, the Q&As are sowing confusion with clinicians related to legally marketed 361 HCT/Ps. This confusion can ultimately lead to patients being denied access to 361 HCT/Ps.

In determining product classification, the Q&As refer healthcare entities to either the new guidance or to utilize other FDA mechanisms for feedback [e.g., Tissue Reference Group (TRG) or Request for Designation]. Unfortunately, the Agency referenced guidance document only provides broad categories of 361 HCT/Ps (e.g., dermis). As such, it is not useful for healthcare personnel to confirm that a specific product is appropriately regulated as a 361 HCT/P. In addition, as acknowledged in the Q&As, healthcare personnel do not necessarily have the relevant information about the product to seek other FDA mechanisms of feedback.

Healthcare users are now being asked to contact manufacturers for letters from the FDA on obvious 361 HCT/Ps -- a requirement that was neither expressed in the new guidance nor by the FDA in the subsequent time leading up to close of the enforcement discretionary period. And, as such, manufacturers may not have the relevant documentation, which will take time to obtain as the FDA is currently backlogged in responding to such requests. As a result, the requesting hospitals may now be placing these tissues on hold from use, thus denying patients with proper care for various illness or disease states.

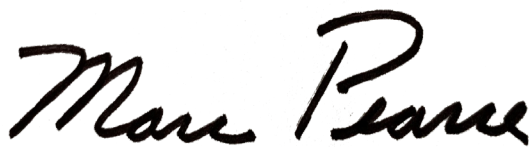
Previously, we have highlighted these issues in an e-mail communication with Dr. Marks in December 2020 when the Defense Health Agency (DHA) raised questions with respect to the 361 status of certain products. At that time, the FDA's response was to further discuss the topic during

the May 2021 liaison meeting. At that meeting, the AATB and the TPG proposed a solution in which tissue banks submitted key data to the FDA's Tissue Reference Group Rapid Inquiry Program (TRIP) with respect to broad categories of products to expedite FDA's review of those products. Unfortunately, as acknowledged by the Q&As, the TRIP is now closed, and many of those previously submitted TRIP requests have been referred to the TRG and are still awaiting a response from the Agency. Therefore, the initial proposed solution has not worked for DHA's request, and the new Q&As have only broadened the line of inquiry. ***As such, we look forward to the Agency's suggestions about how best to address this policy conundrum.***

Within tissue banking, this final guidance was the first time that the Agency had opted to utilize enforcement discretion on a wide range of products (not just a product- or class-specific determination) and with a particular date to determine its closure. As such, the AATB and the TPG requested additional information from the FDA about the particular procedures that tissue banks should follow to ensure continued compliance with the FDA's rules and regulations. Specifically, the AATB and the TPG sent three letters – one in October 2018 to Dr. Marks, one in April 2019 also to Dr. Marks, and a third letter in September 2020 to the formal docket announcing the extension of the enforcement discretion period. In addition, the AATB and the TPG had a specific meeting with Agency officials solely to discuss this topic in April 2019 and, during the liaison meeting in May 2021, the AATB and the TPG once again raised this key topic with the FDA. Despite the numerous pleas for clarity, the FDA opted not to provide much information, and some of the new information gleaned from the recently posted Q&As conflicted with prior information shared in writing with individual tissue banks. We remain disheartened that the FDA opted not to communicate its policies and procedures, as requested, before the close of the enforcement discretionary period. We are disheartened that the Agency did not reach out to the AATB or the TPG prior to publishing the Q&As.

We hope that you will find this information useful in determining next steps with respect to the regulation of HCT/Ps. The AATB and the TPG stand ready and willing to assist the FDA with its deliberations in any way that you deem appropriate.

Respectfully,



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President & CEO
American Association of Tissue Banks



Joe Yaccarino
Chair
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Cc: Dr. Peter Marks