August 26, 2026

Karim Mikhail, B. Pharm, MSc
Acting Director
Center for Biologics Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Dear Acting Director Mikhail:

In 2022 and again in 2024, the American Association of Tissue Banks – now the Association for Advancing Tissue and Biologics (AATB) – wrote to share data and lessons learned from tissue bank submissions to the Tissue Reference Group (TRG).[1,2] We recently repeated this survey of our members in order to gain a better understanding of TRG submission turnaround time from September 2024 to July 2026. Our findings are described in greater detail below, but to summarize the key information: since our first survey in 2022, the average TRG response time reported by our members has nearly doubled, from 140.7 days to 276.2 days (nearly **five times** FDA's stated goal of 60 days in SOPP 8004). Not one of the thirteen inquiries with a final response in our survey this year received that response within 120 days (twice FDA's stated goal of 60 days), and only one received a response within 180 days (three times FDA's stated goal), although a few others were close. We recognize there are numerous, legitimate reasons for these delays, but we also believe there are several steps the FDA could take to help provide clarity to sponsors and potentially decrease the review and response times for inquiries. We have described them below and would welcome the opportunity for a meet-and-greet to discuss them in further detail, as well as other issues facing the industry.

Our members are especially interested in improving the TRG process because they have been increasingly asked by payers and other entities for documentation or "proof" that their products are eligible for regulation solely under section 361 of the Public Health Service Act (PHSA) and the regulations in 21 CFR part 1271 (361 status), even though, as you know, such documentation is not necessary to legally market human cells, tissues, and cellular and tissue-based products (HCT/Ps) with 361 status under FDA regulations. These requests have come from the Department of Veterans Affairs,[3] among others, and have also become necessary to receive a Healthcare Common Procedure Coding System code. AATB recognizes that the number of TRG inquiries has increased significantly as a result of these requests, and that the TRG has not been provided with additional resources to accommodate such inquiries. Nevertheless, we believe our 2026 review of recent tissue bank submissions to the TRG is informative, and we hope you find this information useful.

[1] https://www.aatb.org/sites/default/files/2023/Federal%20Advocacy%20Letters/TRGLessonsFINAL20220906withattachments.pdf
[2] https://www.aatb.org/sites/default/files/2023/Federal%20Advocacy%20Letters/AATB%20TPG%20TRG%20lessons%20learned%20update%20October%202024%20FINAL.pdf
[3] https://www.aatb.org/sites/default/files/2023/Federal%20Advocacy%20Letters/AATB%20TPG%20Allograft%20Tissue%20Historically%20Regulated%20as%20361%20HCTPs%20FINAL.pdf

As noted in our previous correspondence to the agency, SOPP 8004 pertains to the TRG and states that "the TRG generally responds in writing to the inquirer within 60 days of receipt by the Executive Secretary of an inquiry that contains sufficient detail for evaluation."[4] However, AATB's 2022 survey found that this was not the case at that time, and the average response time has continued to increase since then. In 2022, the average TRG response time was 140.7 days, with a range of 26 to 344 days. In 2024, the average TRG response time had increased to 194.8 days, with a range of 73 to 268 days. For this year's survey, which covers September 1, 2024, through July 17, 2026, the average response time is 276.2 days, with a range of 177 to 428 days. In 2024, there were an additional nine inquiries that had not yet received a final response from the TRG, but on average those inquiries had been pending for 119.7 days with a range of 28 to 216 days. This year, there are eight inquiries that are still pending a final response, but on average those inquiries have been pending for 135.5 days with a range of 12 to 263 days.

Most of the inquiries included in this year's survey were related to birth tissue products, as they were in 2024. This year, all 13 inquiries with a final response were related to birth tissue products, while 18 of the 21 inquiries in 2024 were related to birth tissue products. Interestingly, in 2022, all 22 inquiries submitted to the TRG were determined to be eligible for 361 status, while three of the 12 inquiries in the 2024 analysis and four of the 13 inquiries in this year's analysis were determined to **not** be eligible for 361 status. The data is included in three attached tables for your review.

AATB has also summarized the questions received from the TRG in the charts below, and in an effort to streamline such inquiries for your review, we continue to advise our members to submit fewer tissue types in each TRG application; use language consistently within the TRG process; and include relevant instructions for use, as well as a table that provides information related to (1) common names, (2) proprietary names included as part of the Human Cell and Tissue Establishment Registration, and (3) relevant sizing. We welcome further advice from you on recommendations for our members that would make it easier for the TRG to respond on a timely basis.

Our members have also shared several process-related frustrations that we ask the FDA to consider addressing:

1. **Point of Contact:** Our members have shared that all correspondence from the TRG is signed "The TRG Executive Secretary," and the sole named individuals that they encounter appear as signatories on a final decision letter, not as reviewers who could be reached while the review is underway. We recommend an assigned point of contact for inquirers to submit questions to.

2. **Status Visibility:** Similarly, our members have shared that there is no online portal for the TRG; status can only be learned by emailing to ask, and replies are consistently a variation of "remains under review" or "no additional information is needed at this time." We recommend establishing a tracking mechanism, such as a portal, for sponsors to check on the status of their submission.

3. **Estimated Timelines:** Target review timelines, even if non-binding and not required by statute, would support sponsors' regulatory and commercial decisions around a realistic horizon; for purposes of strategic planning, it is therefore helpful for sponsors to have a realistic expectation of when they can expect to receive a final decision from the TRG. This is especially important

[4] https://www.fda.gov/files/vaccines%2C%20blood%20%26%20biologics/published/SOPP-8004-Tissue-Reference-Group-V6.pdf

now that the average TRG response time based on our surveys is significantly higher than the 60-day timeline described in SOPP 8004 and has nearly doubled since 2022 based on data reported by our members. These delays significantly impact our members' decisions around introduction of new products to the market.

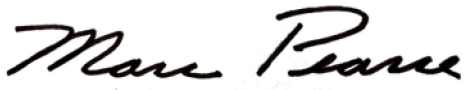
4. **Additional Information:** There are two instances in which our members would appreciate additional information from the TRG:
    a. Insufficient submissions: When the TRG finds a submission insufficient, it would be helpful to understand what information would cure that insufficiency or offer a brief clarifying discussion.
    b. "Not a 361" determinations: When the TRG determines that a product does not qualify for regulation solely under Section 361 of the PHSA and 21 CFR Part 1271, we recommend providing the sponsor with information on why the TRG came to that decision. Even if the TRG makes that determination based on only one of the four criteria in 21 CFR 1271.10(a), our members would appreciate having a brief explanation regarding why the product fails to meet that criterion.

5. **Public Statement:** As noted above, payers continue to request "proof" of 361 status, which we believe has led to a significant increase in TRG inquiries over the past five years and contributed to the delays described in this letter. We urge the FDA to issue a public statement or other communication confirming that a TRG response indicating that an HCT/P is a "361 HCT/P is not necessary to legally market a 361 HCT/P.

Thank you for taking these recommendations into consideration. We understand the challenges the FDA, and more specifically the TRG, are facing, but the delayed response times are becoming increasingly challenging for our members. We believe our recommendations will help provide greater clarity for sponsors, and we are eager to hear any advice you have for our members that may help facilitate faster response times.

We hope that you will find the information in this letter useful as you review and improve the TRG process. To schedule a meet-and-greet, please contact Andrew Vogt, AATB's Director of Governmental Relations, at vogta@aatb.org. AATB stands ready and willing to assist the FDA in any way that you deem appropriate.

Respectfully,



Marc Pearce
President & CEO
Association for Advancing Tissue and Biologics

About AATB
AATB is a non-profit organization dedicated to advancing the safety, quality, availability, and benefits of donated human tissue for transplantation worldwide. AATB achieves this through standards development, accreditation, education, and collaboration with regulatory partners to ensure donated tissue has the greatest impact on patient care.

Survey Results In Detail

Tissue Reference Group Inquiries: Final Response Received Between September 1, 2024 and July 17, 2026			
Product Category	**Days Between Submission / Final Response**	**Summary of Questions Received from TRG (If Applicable)**	**TRG Decision - 361 HCT/P?**
Birth Tissue	177	N/A	Yes
Birth Tissue	392	N/A	Yes
Birth Tissue	376	Clarification of brand name and further questions on processing steps	Yes
Birth Tissue	257	Additional details on processing steps, product size, storage conditions, and package inserts	No
Birth Tissue	289	N/A	Yes
Birth Tissue	192	N/A	Yes
Birth Tissue	193	Clarification of brand name	No
Birth Tissue	188	Clarification of brand name	Yes
Birth Tissue	337	Clarification on intended use and language potentially implying an active biological effect	No
Birth Tissue	254	N/A	Yes
Birth Tissue	254	N/A	Yes
Birth Tissue	254	N/A	Yes
Birth Tissue	428	Questions regarding processing	No
Average:	276.2		

Tissue Reference Group Inquiries: Pending Inquiries as of July 17, 2026		
Product Category	**Days Pending (As of July 17, 2026)**	**Summary of Questions Received from TRG (If Applicable)**
Birth Tissue	168	N/A
Bone	78	Clarification of brand name
Tendon	263	Clarification of processing steps, labeling information, and package insert
Birth Tissue	140	N/A
Birth Tissue	241	N/A
Birth Tissue	80	Request for information on manufacturer's proprietary cleaning process and any reagents used
Birth Tissue	102	N/A
Birth Tissue	12	N/A
Average:	135.5	

	2022	**2024**	**2026**
Average Final Response (days)	140.7	194.75	276.2
Fastest Final Response (days)	26	73	177
Slowest Final Response (days)	344	268	428
Average Pending (days)	N/A	119.67	135.5
Longest Pending (days)	N/A	216	263