American Association of Tissue Banks®

October 22, 2024

Peter Marks, MD, PhD
Director
Center for Biologics Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

**In Re: Update on Recent Tissue Bank Submissions to the Tissue Reference Group**

Dear Dr. Marks:

Two years ago, the American Association of Tissue Banks (AATB) and AATB Tissue Policy Group (TPG) wrote to share data and lessons learned from tissue bank submissions to the Tissue Reference Group (TRG) in response to various payer and other entity requests for documentation or "proof" of 361 status.[1] Over the past two years, we have seen continued requests for documentation of 361 status – even though such documentation is not necessary to market 361 HCT/Ps under FDA regulations – including from the Department of Veterans Affairs[2] and to receive a Healthcare Common Procedure Coding System code.[3] Our understanding from the Food and Drug Administration (FDA) is that the number of annual TRG requests has increased significantly in recent years – from 11 in 2020 to 145 in 2023 – with no additional resources provided to the TRG to accommodate such inquiries. We therefore conducted another review of recent tissue bank submissions to the TRG to see whether response times have similarly increased. As expected, they have.

As you know, 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." However, even when the TPG conducted an analysis of response times for the TRG (and TRG Rapid Inquiry Program or TRIP program) two years ago, we found that the average response time was 140.7 days, with a range of 26 to 344 days. Under TRIP, the average response was 47 days, with a range of 14 to 125 days. When the TPG conducted an updated analysis including only submissions from September 1, 2022, to September 1, 2024, we found that the average response times for inquiries that had received a final response is now 194.75, with a range of 73 to 268 days. There are an additional nine

[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%20VA%20letter%20regarding%20361%20HCTPs%20FINAL.pdf
[3] https://www.cms.gov/medicare/coding/medhcpcsgeninfo/downloads/2018-11-30-hcpcs-level2-coding-procedure.pdf

inquiries that have not yet received a final response from the TRG, but on average those inquiries have been pending for 119.67 days with a range of 28 to 216 days.

There are other noteworthy trends, including that in the 2022 analysis, 6 of the 39 inquiries (including both TRG and TRIP submissions) were related to birth tissue products. In the 2024 analysis, 18 of the 21 inquiries were related to birth tissue products. In the 2022 analysis, all 22 inquiries submitted to the TRG were determined to be eligible for regulation solely under section 361 of the Public Health Service Act (PHSA) and the regulations in 21 CFR part 1271, while 3 of the 12 inquiries with a final response in the 2024 analysis were determined to **not** be eligible for regulation solely under section 361 of the PHSA and the regulations in 21 CFR part 1271. The data is included in two attached charts for your further review.

In our 2022 letter, we noted that the AATB and TPG would be advising our member banks to submit fewer tissue types in each TRG application; use language consistently within the TRG process; and when submitting to the TRG, include relevant instructions for use (IFUs), 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 continue to recommend to our member banks that they include that information, and we welcome your advice as well.

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We hope that you will find this information useful as you continue to review and improve the TRG process. The AATB and TPG stand ready and willing to assist the FDA in any way that you deem appropriate.

Respectfully,

Marc Pearce
President & CEO
American Association of Tissue Banks

Doug Wilson
Chair
Tissue Policy Group

**The American Association of Tissue Banks and AATB Tissue Policy Group**
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.

The AATB Tissue Policy Group (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.

Attachments:

| **FINAL RESPONSE RECEIVED** | | | | |
|---|---|---|---|---|
| **Product Category** | **# of days between submission / final response** | **# of questions before receiving final TRG recommendation** | **Summary of questions received from TRG (if applicable)** | **If TRG decision indicated product is a 361 HCT/P?** |
| Birth tissue | 268 | 0 | N/A | Yes |
| Decellularized Nerve Segment | 190 | 1 | (1) Clarification on range of sizes | No |
| Birth tissue | 177 | 0 | N/A | Yes |
| Birth tissue | 167 | 0 | N/A | No |
| Birth tissue | 261 | 0 | N/A | Yes |
| Birth tissue | 211 | 1 | (1) Provide product labeling | Yes |
| Birth tissue | 223 | 3 | (1) Clarification on processing, packaging, and storage; (2) clarification on product labeling/IFU; and (3) clarification on how the product meets 1271.10(a) criteria | No |
| Birth tissue | 73 | 1 | (1) Request for clarification on IFU and label | Yes |
| Birth tissue | 256 | 0 | N/A | Yes |
| Birth tissue | 117 | 0 | N/A | Yes |
| Birth tissue | 183 | 2 | 1) Clarification on composition; 2) Clarification on how Tyvek backing was used based on the processing step information submitted | Yes |

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|---|---|---|---|---|
| Birth tissue | 211 | 2 | (1) Provide product labeling (2) Clarify if only one product on IFU is needing TRG recommendation, or all products listed, and if so, please describe processing of other products | Yes |
| | | | | |
| **Average:** | **194.8** | **0.8** | | |

| **PENDING SUBMISSIONS** | | | |
|---|---|---|---|
| **Product Category** | **# of days pending as of September 1, 2024** | **# of questions received thus far** | **Summary of questions received from TRG (if applicable)** |
| Birth tissue | 181 | 3 | (1) Clarification on intended use with additional product<br>(2) Additional clarification of other IFU instructions<br>(3) Clarification on brand name |
| Birth tissue | 132 | 0 | N/A |
| Birth tissue | 67 | 0 | N/A |
| Birth tissue | 132 | 0 | N/A |
| Birth tissue | 164 | 1 | (1) Clarification on brand name |
| Birth tissue | 28 | 0 | N/A |
| Birth tissue | 55 | 0 | N/A |
| Dermis | 102 | 4 | Clarification on intended use and provide additional information on sourcing, recovery, and processing |
| Dermis | 216 | 1 | (1) Clarification on intended use |
| | | | |
| **Average:** | **119.7** | **1.0** | |