



American Association of Tissue Banks® AATB TPG, LLC

March 22, 2022

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244

RE: Recent MAC Coverage Policies Related to Certain Injectable Birth Tissue Products

Sent electronically to Chiquita.Brooks-LaSure@cms.hhs.gov

Dear Administrator Brooks-LaSure:

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) requests that you take action and provide clarification to all of your Medicare Administrative Contractors (MACs) regarding appropriate coverage of certain injectable birth tissue products. ***Specifically, we ask that you ensure all MACs:***

- (1) are aware that not all birth tissue products contain exosomes; and***
- (2) rescind their policies to retroactively deny claims for injectable birth tissue products and instead only apply their claims denial policies on a prospective basis. To the extent that retroactive policies are applied, they should not be tied to the date that the Food and Drug Administration (FDA or Agency) provided safety information regarding exosomes (i.e., December 6, 2019) but would be best tied to the day following the close of the enforcement discretion period (as noted [here](#) and [here](#))(i.e., June 1, 2021).***

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.

MAC information. The AATB and the TPG are aware of at least seven MACs who, in late February 2022, issued notices specifying that injectable amniotic or placental products are considered in experimental exosomal biologic products that are not covered under the Medicare program.¹ As a result of this determination, the MACs have specified that claims for such products will be denied retroactively back to December 6, 2019. Unfortunately, these notices inappropriately conflate exosomes with certain birth tissue products (e.g., amnion, placenta, umbilical cord, amniotic fluid, etc.). Exosomes are naturally present in all human tissues. However, for an exosome to be in a final tissue product, the processing steps must deliberately maintain those structures, and not all manufacturers manipulate such products in a way to retain exosomes. Thus, it is not appropriate to state that all birth tissue products contain exosomes.

Exosomes and birth tissue products.² As noted [here](#), [here](#), and [here](#), an exosome (in layman's terms) is a small membrane-enclosed sac outside of a cell that contains certain portions of the cell (e.g., protein, DNA, and RNA). They may be involved with cellular communication, given that other cells can incorporate these sacs and then use the newly acquired materials to change cellular function. While some exosomes may be extracted from amnion (see references at end of document), the process for exosome extraction is very specialized, and not all injectable birth tissue products will contain exosomes. **Thus, to simply claim that all injectable birth tissue products are exosome products is simply scientifically inaccurate.**

Enforcement discretion period. As you may be aware, the FDA has issued final guidance ([here](#)), providing key examples and clarifications regarding products which may be regulated as 361 human cells, tissues, and cellular and tissue-based products (HCT/Ps) and, as such, do not need

¹ Please see the following links for the Medicare A/B MAC announcements:

J5 – WPS: https://www.wpsgha.com/wps/portal/mac/site/policies/news-and-updates/claim-denials-manipulated-amniotic-placental-tissue-injections!/ut/p/z0/fY5BCsIwEEVPNEytULpVUYo06ErabGRIYh1Np8Eken3jBVx-3uPxUeOAWujNEyVehHzZo26u565rulVb9adaVdVGHS7rfdtvq32NR9T_hVKoX2qnJtSB0h1YbgsO4j4RSCzkYcm5iIPxxDNYJ0w-wkySQ_YFWaBZeElsIHgyThJ5SBxjdqX1cOb3NGJ46vELijt4sQ!!/

JF – Noridian: <https://med.noridianmedicare.com/web/jfb/article-detail/-/view/10534/manipulated-reconstituted-and-or-injectable-amniotic-and-placental-derived-products>

J6 – NGS: <https://www.ngsmedicare.com/web/ngs/news-article-details?selectedArticleId=3966444&lob=96664&state=97178®ion=93623>

JM – Palmetto: <https://www.palmettogba.com/palmetto/jma.nsf/DID/CWI3P9545A>

JL – Novitas: <https://www.novitas-solutions.com/webcenter/portal/MedicareJL/pagebyid?contentId=00259906>

JN – FSCO: https://medicare.fcso.com/Billing_news/0493589.asp

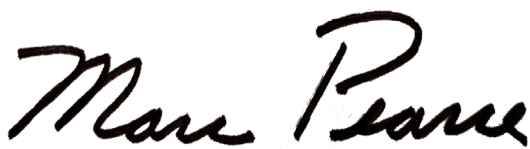
J15 – CGS: <https://www.cgsmedicare.com/partb/pubs/news/2022/02/cope25182.html>

² Note: The MAC announcements generally do not use the term “birth tissue products” but rather “manipulated amniotic and/or placental tissue biologics for injections” (WPS, Palmetto, Novitas, and FSCO), “amniotic and/or placental derived products used for indications other than as a membranous covering for burns, wounds, or ophthalmic condition” (Noridian), “manipulated and/or reconstituted membranous grafts or products used in liquid or other forms” (NGS), or “manipulated amniotic and/or placental tissue biologics” (CGS). Per the AATB *Standards* “birth tissue” is “gestational tissue donated at the time of delivery of a living newborn. This includes placenta, Wharton’s jelly, amniotic fluid, chorionic membrane, amniotic membrane, placental/chorionic disc, umbilical veins, and umbilical cord tissue.”

official FDA review or approval before marketing. In issuing the final guidance, the Agency recognized that it may take some time for certain entities to come into compliance. As such, the guidance specifically states: "To give manufacturers time to determine if they need to submit an IND or marketing application in light of this guidance and, if such an application is needed, to prepare the IND or marketing application, FDA generally intends to exercise enforcement discretion through May 31, 2021." **Therefore, while the AATB and the TPG strongly urge CMS to clarify to MACs that any retroactive period for payment decisions is inappropriate and potentially unlawful, if the MACs still insist on such retroactivity, then it should only be retroactive to June 1, 2021 - after the close of the enforcement discretion period.**

We hope that you will find this information useful in your deliberations, and we look forward to your response. If it would be helpful to further discuss this topic, we would make ourselves available. The AATB and the TPG stand ready and willing to assist CMS in any way that you deem appropriate.

Respectfully,



Marc Pearce, MBA
President & CEO
American Association of Tissue Banks



Joe Yaccarino
Chair
Tissue Policy Group

cc: Peter Marks, M.D., Ph.D., Director, Center for Biologics Evaluation and Research (CBER), FDA (Peter.Marks@fda.hhs.gov)

Lee Fleisher, M.D., CMS Chief Medical Officer and Director, Center for Clinical Standards and Quality (Lee.Fleisher@cms.hhs.gov)

Tamera Syrek-Jensen, Director, Coverage and Analysis Group (CAG) (tamera.syrekjensen@cms.hhs.gov)

References related to extracting exosomes from amnion:

- Mao Y, Jacob V, Singal A, Lei S, Park MS, Lima MRN, Li C, Dhall S, Sathyamoorthy M, Kohn J. Exosomes Secreted from Amniotic Membrane Contribute to Its Anti-Fibrotic Activity. *Int J Mol Sci.* 2021 Feb 19;22(4):2055. doi: 10.3390/ijms22042055. PMID: 33669673; PMCID: PMC7922650.
- Tan JL, Lau SN, Leaw B, Nguyen HPT, Salamonsen LA, Saad MI, Chan ST, Zhu D, Krause M, Kim C, Sievert W, Wallace EM, Lim R. Amnion Epithelial Cell-Derived Exosomes Restrict Lung Injury and Enhance Endogenous Lung Repair. *Stem Cells Transl Med.* 2018 Feb;7(2):180-196. doi: 10.1002/sctm.17-0185. Epub 2018 Jan 3. PMID: 29297621; PMCID: PMC5788876.

- Sheller S et al. 2016. Amnion-Epithelial-Cell-Derived Exosomes Demonstrate Physiologic State of Cell under Oxidative Stress. PLoS ONE 11(6):e0157614
- Farhadhosseinabadi B et al. 2018. Amniotic membrane and its epithelial and mesenchymal stem cells as an appropriate source for skin tissue engineering and regenerative medicine, Artificial Cells, Nanomedicine, and Biotechnology, 46:sup2, 431-440.