March 01, 2023

VIA UPS EXPRESS MAIL AND EMAIL

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Dear Ms. Angeles and Dr. Bogaart:

The Office of Compliance and Biologics Quality in the Center for Biologics Evaluation and Research (CBER) of the United States Food and Drug Administration (FDA) has reviewed your firm's website available at thomasadvancedmedical.com as well as other online sources described below and other information available to FDA.

Based on the materials reviewed, you and your firm market products derived from either human umbilical cord, umbilical cord blood, or amniotic tissue, which you refer to as "regenerative therapy solutions" or "stem cell derived biological products" (collectively, "your products") to consumers. You and your firm market your products to treat various diseases or conditions, including some that are serious or life-threatening, such as cardiac diseases, Alzheimer's disease, Parkinson's disease, lung diseases, and diabetes. According to materials FDA reviewed, your products are intended for intravenous, intrathecal, intra-articular, subcutaneous, or intramuscular injection or topical use.

According to your website:

- "Through sound scientific theory coupled with clinical research, Thomas provides products that help people with regenerative therapies for treatment of cardiac diseases, vascular disorders, dementia, Alzheimer's, Parkinson's, lung diseases, diabetes, pain management, cardiovascular medicine..."

According to your firm's LinkedIn profile, (www.linkedin.com/company/thomasadvancedmedical):

- "Through sound scientific theory coupled with clinical research, our stem cell derived biological products help patients for the treatment of many diseases including cardiac diseases, vascular disorders, dementia, Alzheimer's, Parkinson's, lung diseases, orthopedic conditions, diabetes, and pain management."

Additionally, FDA has obtained information that you have offered your umbilical cord derived product, PrimePro™, to patients to treat or prevent Coronavirus Disease 2019 (COVID-19).

There is currently a global outbreak of respiratory disease caused by a novel coronavirus that has been named "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2). The disease caused by the virus has been named COVID-19. On January 31, 2020, the Department of Health and Human Services (HHS) issued a declaration of a public health emergency related to COVID-19 and mobilized the Operating Divisions of HHS.[1] In addition, on March 13, 2020, there was a Presidential declaration of national emergency in response to COVID-19 that subsequently has been renewed.[2]

Your above-referenced products appear to be human cells, tissues, or cellular or tissue-based products (HCT/Ps) as defined in 21 CFR 1271.3(d) that would be subject to regulation under 21 CFR Part 1271, issued under the authority of section 361 of the Public Health Service Act (PHS Act) [42 U.S.C. 264].[3]

HCT/Ps that do not meet all the criteria in 21 CFR 1271.10(a), and when no exception in 21 CFR 1271.15 applies, are not regulated solely under section 361 of the PHS Act [42 U.S.C. 264] and the regulations in 21 CFR Part 1271. Such products are regulated as drugs, devices, and/or biological products under the Federal Food, Drug, and

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[1] Secretary of Health and Human Services, Determination that a Public Health Emergency Exists (originally issued Jan. 31, 2020 and subsequently renewed), available at https://aspr.hhs.gov/legal/PHE/Pages/covid19-15jul2022.aspx.

[2] Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak (originally issued Mar. 13, 2020, and subsequently renewed), available at https://www.whitehouse.gov/briefing-room/presidential-actions/2022/02/18/notice-on-the-continuation-of-the-national-emergency-concerning-the-coronavirus-disease-2019-covid-19-pandemic-2/.

[3] You also market an amniotic fluid product. HCT/Ps are defined at 21 CFR 1271.3(d) as "articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient." The definition of HCT/P excludes secreted or extracted human products; accordingly, secreted body fluids, such as amniotic fluid, are generally not considered HCT/Ps subject to regulation under 21 CFR Part 1271. Although not an HCT/P, as a general matter, amniotic fluid intended to treat diseases or conditions in humans is regulated as a drug and biological product under section 351 of the PHS Act and the FD&C Act and would be subject to premarket review and approval requirements.

Cosmetic Act (FD&C Act) and/or the PHS Act, and are subject to additional regulation, including appropriate premarket review.

Based on the review of the materials described above, it appears that your firm does not qualify for any exception in 21 CFR 1271.15, and that your products are intended for non-homologous uses. Additionally, it appears that your products fail to meet other criteria in 21 CFR 1271.10(a). Accordingly, it appears that your products would be regulated as drugs as defined in section 201(g) of the FD&C Act [21 U.S.C. 321(g)] and biological products as defined in section 351(i) of the PHS Act [42 U.S.C. 262(i)].

To lawfully market a drug that is also a biological product, a valid biologics license must be in effect [42 U.S.C. 262(a)]. Such licenses are issued only after a demonstration that the product is safe, pure, and potent. While in the development stage, such products may be distributed for clinical use in humans only if the sponsor has an investigational new drug application (IND) in effect as specified by FDA regulations [21 U.S.C. 355(i); 42 U.S.C. 262(a)(3); 21 CFR Part 312]. This is true irrespective of whether you have conducted clinical trials, as you claim. None of your products are the subject of an approved biologics license application (BLA), nor is there an IND in effect for your products.

We direct your attention to FDA's comprehensive regenerative medicine policy framework for HCT/Ps, which is intended to spur innovation and efficient access to safe and effective regenerative medicine products. The policy framework is outlined in a suite of four guidance documents available on FDA's website at www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/framework-regulation-regenerative-medicine-products.

Manufacturers and health care professionals who have any uncertainty regarding the regulatory status of their products are encouraged to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P. For more information in this regard, or to obtain further information about IND requirements for biological products, please see pages 24 and 25 of the guidance entitled, "Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use" at the link to FDA's webpage provided above.

This letter addresses certain issues regarding the above-described products and is not intended to be an all-inclusive review. You and your firm are responsible for ensuring that all your products fully comply with the FD&C Act and PHS Act and all applicable regulations. We request a written response within 30 days of your receipt of this letter. If you do not believe there is a basis for the regulatory issues raised in this letter, include your reasoning and any supporting information for our consideration.

Your response should be sent to the following address: U.S. Food and Drug Administration, Center for Biologics Evaluation and Research, 10903 New Hampshire Avenue, Bldg. 71, Silver Spring, MD 20993. In addition, you may also email a copy of

your official, written response to CBERDCMRecommendations@fda.hhs.gov. If you have any questions regarding this letter, please contact the Division of Case Management, CBER at (240) 402-9156. Please be advised that only written communications are considered official.

Sincerely,

Melissa J. Mendoza
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

Cc:
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