March 12, 2024

**VIA UPS EXPRESS MAIL AND EMAIL**

Eusebio Coterillo
President
Amnion Florida, LLC
917 Rinehart Road
Ste 2061
Lake Mary, FL 32746
ecoterillo@amnion.us

Dear Mr. Coterillo:

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 https://amnion.us/ (last visited on March 8, 2024).

Based on your website, you and your firm sell products from amniotic membrane and amniotic fluid, referred to as "amniotic fluid (AF) therapy," "Amnion Membrane (AM) therapy," or "amnion membrane and amnion fluid based solutions" among other terms (collectively, "your products"). You market these products to treat various diseases or conditions, such as joint pain, erectile dysfunction, and urinary incontinence. Your intended uses for your products on your website indicate that your products are drugs under section 201(g)(1) of the FD&C Act [21 U.S.C. § 321(g)(1)] because they are intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease, and also because they are intended to affect the structure or function of the body. Based on your website, your products are also biological products under section 351(i) of the PHS Act [42 U.S.C. § 262(i)] because they are applicable to the prevention, treatment, or cure of a disease or condition of human beings. Your products are intended for injection.

Your website includes the following claims about your products:

> A page titled "Amnion for Joint Pain," discussing your products, states, "May Help the Following Health Issues caused by aging, chronic disease or injury:
>
> - AC Joint Separation
> - ACL Tear
> - Arthritis
> - Incontinence…

- Bursitis…
- Erectile Dysfunction…
- Plantar Fasciitis…
- Inflammation for Shoulder Dislocation
- Tarsal Tunnel Syndrome
- Tendinopathy
- Tennis Elbow"

"Amnion Membrane or Amniotic Fluid therapy for knee, feet, ankles, hips, elbows, wrist, hand, etc. is a non-surgical alternative for those who suffer from pain."

A page discussing "our amnion membrane and amnion fluid based solution" states:

- "Finally, the high concentration of growth factors, hyaluronic acid and cytokines provide the perfect mix for treating stress urinary incontinence (SUI) and erectile dysfunction (ED)…Amnion treats your incontinence at the root by naturally rejuvenating and strengthening your weakened muscles…"

- "Men with ED [erectile dysfunction] also find that the concentration of growth factors greatly assist with ED. Amnion uses Amniotic Fluid (AF), a biological therapy that is not a drug or synthetic, which means the negative side effects are limited, if not eliminated…AF cells…are able to …grow healthier blood vessels, tissues…"

Your product from amniotic membrane appears to be a human cell, tissue, or cellular or tissue-based product (HCT/P) 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].

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

Based on our 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 product from amniotic membrane fails to meet the criteria in 21 CFR 1271.10(a). Accordingly, it appears that your product from amniotic membrane would be regulated as a drug as defined in section 201(g) of the FD&C Act [21 U.S.C. 321(g)] and a biological product as defined in section 351(i) of the PHS Act [42 U.S.C. 262(i)].

Specifically, your product from amniotic membrane appears to fail to meet the criterion in 21 CFR 1271.10(a)(2) that the HCT/P be "intended for homologous use only, as reflected by the labeling, advertising, or other indications of the manufacturer's objective

intent." This product is not intended to perform the same basic function or functions of the amniotic membrane in the recipient as in the donor, such as serving as a barrier. Rather, your advertising and labeling indicates that your product is intended to treat joint pain, urinary incontinence, and erectile dysfunction, and not intended for homologous use only, as "homologous use" is defined in the applicable regulations. 21 CFR 1271.3(c).

Additionally, your amniotic fluid product intended to treat diseases or conditions in humans is regulated as a drug under the FD&C Act and a biological product under the PHS Act and requires premarket review and approval. The definition of HCT/Ps in 21 CFR 1271.3(d) excludes secreted or extracted human products. 21 CFR 1271.3(d)(3). Accordingly, secreted body fluids, such as amniotic fluid, are not considered HCT/Ps and are not regulated under section 361 of the Public Health Service Act and the regulations in 21 CFR Part 1271.

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 (IND) application in effect as specified by FDA regulations [21 U.S.C. 355(i); 42 U.S.C. 262(a)(3); 21 CFR Part 312]. Your products are not the subject of an approved biologics license application (BLA), nor is there an IND in effect for any of your products.

Further information about IND requirements for biological products may be obtained through the Division of Regulatory Project Management, Office of Therapeutic Products, at 240-402-8190 or mail to: OTPRPMS@fda.hhs.gov.

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 product 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 and PHS Acts and all applicable regulations. We advise you to comprehensively review your website, product labels, and other labeling and marketing materials to ensure that you are lawfully marketing your products in full compliance with the FD&C Act, the PHS Act, and their implementing 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.

Sincerely,

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

Cc: John R. Chewning, D.O.
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