February 17, 2021

VIA UPS EXPRESS MAIL AND EMAIL

Michael Berkowitz
Director
Pacific Stem Cells LLC
4700 Von Karman, Suite 1000
Newport Beach, CA 92660

Dear Mr. Berkowitz:

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 website available at www.pacificstemcells.com as well as other information available to FDA.

On your website, you and your firm market "stem cell therapy" products (hereinafter, "products"). You represent that the products are "derived exclusively from umbilical cord tissue and other placental materials from live healthy birthed babies." Your website homepage prominently features "stem cell therapy," followed by your representation that: "We treat a wide variety of medical conditions."

You market the products for stroke, macular degeneration, Lyme disease, Parkinson's disease, heart disease, lupus, rheumatoid arthritis, and multiple sclerosis (MS). According to the materials FDA reviewed, Pacific Stem Cells appears to administer the products by various routes, including intraorally and intravenously.

For example, your Michael Berkowitz YouTube channel features a YouTube video, www.youtube.com/watch?v=w6hZXFT-On4, accessed on February 17, 2021, entitled "Pacific Stem Cell Promotional Video," which includes the following segments showing patients before and after treatment:

- In a segment entitled "Before (Macular Degeneration Condition)," a speaker states, "…we think that the stem cells are having a hard time getting past the blood-brain barrier…we are going to go intraorally today and we pray that they stay where they are supposed to stay…and then we are going to get some eyesight." In a segment entitled "After (Macular Degeneration Condition Resolved)," a speaker asks the patient, "…can you see the ocean?" The patient states, "Oh yeah…" The speaker then states, "To be able to give someone their sight back is probably the coolest thing I could ever do in my whole…career."

- In a segment entitled "Before (Lyme & Parkinson's Disease Condition), a patient is shown requiring assistance walking. In a segment entitled "After Lyme &

Parkinson's Disease Condition (Treatment result time was 20min [*sic*])" the same patient is shown walking unassisted. A speaker states, "Were you able to walk like that before?" The patient states, "Not exactly." The speaker states, "…Now you are walking on your own?" to which the patient replies, "Yeah." The speaker then states, "After a stem cell IV."

- A segment entitled "Before (Stroke Condition)" shows a patient who states she had a stroke displaying difficulty coordinating finger movement. The segment also shows injection into the patient's mouth. In a segment entitled, "After Stroke Condition (Treatment result time was 20 minutes)," the patient demonstrates finger movement and states, "It's already working."

- In a segment entitled "After (Balance Condition Resolved)," the patient states, "When I turn my head, I lose a little balance or direction, I'm not feeling that right now." A speaker then states, "You are walking straight. It is working. You happy with these stem cells…?" The patient replies, "So far, yeah…I can feel the improvement."

The 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].[1]

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 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 the products are intended for non-homologous uses. Additionally, your products do not appear to meet all the other criteria in 21 CFR 1271.10(a) and, accordingly, they would be regulated as drugs as

[1] We also note that you market an amniotic fluid product on your website. HCT/Ps are defined as "articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient" per 21 CFR 1271.3(d). 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, amniotic fluid for clinical use is generally regulated as a biological product under section 351 of the Public Health Service Act (PHS Act), 42 U.S.C. 262, and an unapproved drug under section 505 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 355, and would be subject to the premarket review and approval requirements described in this letter.

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)].

In order 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 [21 U.S.C. 355(i); 42 U.S.C. 262(a)(3); 21 CFR Part 312].

As noted above, your above-referenced products are intended to treat a variety of serious or life-threatening diseases or conditions. Such unapproved uses raise potential significant safety concerns. Moreover, because your products appear to be administered by higher risk routes of administration, including intravenously and intraorally[2], their use, if contaminated could cause a range of adverse events. 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 https://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. 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. If you have any questions regarding this letter, please contact the Division of Case Management, CBER at (240) 402-9155. Please be advised that only written communications are considered official.

[2] Your above-referenced YouTube video explains that an intraoral route of administration was used because "the stems cells are having a hard time getting past the blood-brain barrier."

Sincerely,

Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research