November 10, 2020

UPS EXPRESS MAIL AND EMAIL

Crispino Santos, MD, FIPP
Founder and Medical Director
Regenerative Cell Institute LLC
2911 N Tenaya Way, Suite 200
Las Vegas, NV 89128

Dear Dr. Santos:

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 www.regenerativecellinstitute.com as well as other online sources described below.

Based on the materials reviewed, you and your firm market cellular products derived from either human adipose tissue or umbilical cord to consumers. You and your firm market these products to treat various diseases or conditions, including some that are serious or life threatening, such as fibromyalgia, multiple sclerosis (MS), Parkinson's disease, Alzheimer's disease, autism, diabetes, stroke recovery, spinal cord injury, chronic obstructive pulmonary disease (COPD), liver disease, and cardiomyopathy. Regenerative Cell Institute appears to administer these products intranasally, intravenously, intrathecally, or by inhalation. For example, your firm's website states:

- "Regenerative Cell Institute specializes in regenerative medicine making use of various stem cell therapies for people with following [*sic*] medical conditions:…Crohn's disease, Lupus, Rheumatoid arthritis, Osteoarthritis, Peripheral neuropathy, Cirrhosis…Fibromyalgia, Muscular dystrophy, Multiple sclerosis, Parkinson's disease, Alzheimer's disease, Autism, Stroke recovery, Brachial plexus injury, Radiculopathy, Spinal cord injury…COPD, Post myocardial infarction, CHF, Cardiomyopathy…Type 2 Diabetes, Osteoporosis, Liver Disease…"

A patient video testimonial on your firm's website that also appears on your firm's Facebook page, www.facebook.com/RCILasVegas/, with the header "Adipose derived stem cell IV infusion for COPD & Diabetes" states:

- "…I had the stem cell done back in January and I'm so glad that I had it done. I had trouble with COPD, my [diabetes], and my knee and my knee has improved so much. I'd cry at night that it hurt so bad and now that I've had this done it is so much better. It is improving all the time. My A1C went from 9.1 to 8.1 and my

breathing, I haven't used my inhalers for I don't know how long now."

A patient video testimonial on your firm's website entitled "Multiple Sclerosis Stem Cell Therapy" (that also appears on the "Regenerative Cell Institute" playlist on the "Crispino Santos,MD,FIPP" YouTube channel with the caption "Adipose derived stem cell intravenous infusion therapy," www.youtube.com/watch?v=TaYqKy3pDPk&list=PLSxQXjBDpwuDjUVhRanJBTMBjsY-XsHpd&index=8&t=0s) states:

- "…I was diagnosed with multiple sclerosis two years ago…I'm a 64-year-old male and I had stem cells done almost a year ago. The tremors have stopped, and my balance has vastly improved and I'm able to go back to work…"

Similarly, your firm's website includes a video entitled "Parkinson's Stem Cell Therapy," in which you and your firm were featured in a KIMT News 3 broadcast:

- You stated, "She is our first case of Parkinson's Disease."

- The news anchor stated, "Dr. Santos was happy to help. In January, he harvested stem cells from her abdomen fat. He then did an interspinal injection with the cells but not much change was seen. Round two happened last month with a similar procedure; this time using umbilical cord stem cells, that's when Shirley's life began to turn around…She began to walk again and started to feel more like her old self."

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].

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 your above-referenced products are intended for non-homologous uses. Additionally, it appears these products fail to meet other criteria in 21 CFR 1271.10(a). Accordingly, it appears that the 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)].

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 (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].

As noted above, your adipose tissue derived cellular product and umbilical cord derived cellular product are intended to treat a variety of diseases or conditions, including some that are serious or life-threatening. Such unapproved uses raise potential significant safety concerns. Moreover, because these products appear to be administered by higher risk routes of administration, including intravenously and intranasally, 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.

Your firm's website also lists exosomes as one of the regenerative medicine "services" at the Regenerative Cell Institute. Please be advised that, as a general matter, exosome products intended to treat diseases or conditions in humans are also regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act and are subject to premarket review and approval requirements described above. For more information, please see FDA's Public Safety Notification on Exosome Products, at https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products.[1]

[1] Your firm's website also refers to the "clinical applications" of amniotic fluid. 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 would be regulated as a drug and biological product under section 351 of the

This letter addresses certain issues regarding your adipose tissue derived cellular product and umbilical cord derived cellular 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 Act, 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.

Sincerely,

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

Cc: (b) (6)
Managing Member
Regenerative Cell Institute LLC
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Las Vegas, NV (b) (4)

PHS Act and the FD&C Act and would be subject to premarket review and approval requirements.

In addition, your firm's website references "[a]llogeneic stem cells… from the umbilical cord blood, …amniotic membrane… ." Please be advised that, as a general matter, allogeneic stem cell products derived from umbilical cord blood or amniotic membrane and intended to treat diseases or conditions in humans would be regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act and would be subject to premarket review and approval requirements.