U.S. Department of Health & Human Services

U.S. Food & Drug Administration

Inspections, Compliance, Enforcement, and Criminal Investigations

IntelliCell Biosciences, Inc. 3/13/12

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research
1401 Rockville Pike
Rockville, MD 20852-1448

WARNING LETTER

March 13, 2012

CBER-12-01

VIA FACSIMILE AND UPS

Dr. Steven Victor
Chief Executive Officer
IntelliCell Biosciences, Inc.
30 East 76th Street
New York, NY 10012

Dear Dr. Victor:

During an inspection of your firm, IntelliCell Biosciences, Inc., located at 30 East 76th Street, New York, NY 10012, conducted between November 8 and December 12, 2011, the Food and Drug Administration (FDA) determined that your firm recovers and processes adipose tissue (aka lipoaspirate) from donors for autologous use. Using ultrasonic cavitation, your firm processes the lipoaspirate into stromal vascular fraction known as IntelliCell™, adipose-derived stem cells. The IntelliCell product is administered to patients intravenously, **(b)(4)**, or is injected into specific areas of the body, such as the lips, cheeks, knees, scalp, and/or buttocks.

Your internet promotion through YouTube video explains that the IntelliCell product can be used "off-label to treat various patient ailments." It further explains that the IntelliCell product can be used to treat wrinkles, osteoarthritis, and gum recessions; and for breast augmentation. http://www.youtube.com/watch?v=sK0G4GE9UZs.

IntelliCell's adipose derived stem cells are human cells, tissues, or cellular and tissue-based products (HCT/Ps) as defined in 21 CFR 1271.3 (d). However, this cellular product does not meet all of the criteria in 21 CFR 1271.10(a) and therefore is not regulated solely under section 361 of the Public Health Service Act (PHS Act) [42 U.S.C. 264] and the regulations in 21 CFR Part 1271. Specifically, your processing alters the relevant characteristics of the adipose tissue relating to the tissue's utility for reconstruction, repair, or replacement. Therefore the processing would not meet the definition of minimal manipulation for structural tissue such as adipose tissue. As a result, the IntelliCell product does not meet the criterion in 21 CFR 1271.10(a)(1).

In addition, some of the treatments you offer do not meet the definition of homologous use in 21 CFR 1271.3(c) (e.g., use of the IntelliCell product to treat osteoarthritis, gum recession). Also, records collected during the inspection indicate clinical uses of the IntelliCell product involving IV administration or administration **(b)(4)** of adipose-derived stem cells. These uses would not likely be considered homologous use. As a result, the IntelliCell product is a drug under section 201(g) of the Federal Food, Drug, and Cosmetic Act (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)] that cannot qualify for regulation solely under section 361 of the PHS Act and 21 CFR Part 1271.

Please be advised that in order to lawfully market such a biological drug product, a valid biologics license must be in effect [21 U.S.C. 355(a); 42 U.S.C. 262(a)]. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products may be used 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); 21 CFR Part 312). The IntelliCell product is not the subject of an approved biologics license application (BLA) nor is there an IND in effect. Based on this information, we have determined that your product violates the FD&C Act and the PHS Act.

Additionally, during the inspection, FDA investigators documented evidence of significant deviations from current good manufacturing practice (CGMP) and current good tissue practice (CGTP) from August 2010 through November 2011 in the manufacture of the IntelliCell product. These deviations from CGMP and CGTP include the applicable requirements of Section 501(a)(2)(B) of the FD&C Act, Section 361 of the PHS Act, and Title 21, Code of Federal Regulations, (21 CFR) Parts 210, 211, and 1271.

At the close of the inspection, our investigators issued a Form FDA 483, Inspectional Observations, which described a number of significant objectionable conditions relating to your facility's compliance with CGMP and CGTP. These include, but are not limited to the following:

1. Failure to have written procedures designed to prevent microbiological contamination of drug products purporting to be sterile. Such procedures include validation of all aseptic and sterilization processes [21 CFR 211.113(b)]. For example:

a. You failed to validate your aseptic manufacturing process and establish written procedures to prevent microbiological contamination of your IntelliCell product.

b. **(b)(4)**

c. There are no written procedures to ensure your manufacturing environment is adequately maintained to prevent the contamination of the IntelliCell product.

2. Failure to ensure appropriate laboratory testing of each batch of drug product required to be free of objectionable microorganisms [21 CFR 211.165(b)]. Specifically, from August 2010, to November 2011, you failed to perform sterility testing on more than **(b)(4)** batches of IntelliCell product manufactured that were later administered to patients.

3. Failure to reject drug products failing to meet established standards or specifications and any other relevant quality control criteria [21 CFR 211.165(f)]. Specifically, you explained to the investigator that the viability of the cells in the IntelliCell product should be **(b)(4)** in order for the product to be used for patients. However, products with cell viabilities ranging from **(b)(4)** were released and administered to more than **(b)(4)** patients.

4. Failure to maintain laboratory controls that include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity, including a determination of conformance to written descriptions of sampling procedures and appropriate specifications for acceptance of each lot of drug products [21 CFR 211.160(b)].

5. Failure to establish and follow written production and process control procedures designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess [21 CFR 211.100(a)]. For example:

a. **(b)(4)**

b. **(b)(4)**

6. Failure to establish a written record of major equipment cleaning, maintenance, and use, and to include in that record the date, time, product and lot number of each batch processed [21 CFR 211.182]. For example:

a. **(b)(4)**

b. **(b)(4)**

c. **(b)(4)**

7. Failure to ensure batch production and control records are prepared for each batch of drug product produced [21 CFR 211.188]. For example, during the IntelliCell manufacturing process you failed to record, for more than **(b)(4)** IntelliCell batches manufactured, the adipose lipoaspirate **(b)(4)**

8. Failure to record and justify any deviations from written procedures [21 CFR 211.100(b)]. Deviations from the established procedure entitled "Ultrasonic Cavitation of Processing Stem Cells from Adipose Tissue" were not recorded and justified. For example:

a. **(b)(4)**

b. **(b)(4)**

9. Failure to establish and follow written procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, testing, and approval or rejection of components and drug product containers and closures [21 CFR 211.80(a)]. **(b)(4)**

10. Failure to establish and follow written procedures describing the handling of all written and oral complaints regarding a drug product [21 CFR 211.198(a)]. Your firm does not have any procedures that describe a process for documenting and investigating complaints relating to your IntelliCell product.

11. Failure to establish a quality control unit that shall have the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging material, labeling, and drug products, and the authority to review production records to assure that no errors have occurred or, if errors have occurred, that they have been fully investigated [21 CFR 211.22(a)].

12. Failure to establish and follow written procedures for cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing, or holding of a drug product including a description in sufficient detail of the methods, equipment, and materials used in cleaning and maintenance operations [21 CFR 211.67(b)]. For example:

a. **(b)(4)**

b. Your firm did not establish any cleaning procedures for utensils used in manufacture of the IntelliCell products.

c. **(b)(4)**

13. Failure to maintain your building, used in the manufacture, processing, packing, or holding of a drug product in a good state of repair [21 CFR 211.58]. Specifically, your processing area ceiling had missing tiles exposing the building's ventilation system.

14. Failure to ensure that each container or grouping of containers for components or drug product containers, or closures is identified with a distinctive code for each lot in each shipment received [21 CFR 211.80(d)]. For example, you failed to record the lot numbers of the following components and supplies utilized in manufacturing of the IntelliCell product: **(b)(4)**

15. Failure to establish and maintain procedures to control the labeling of HCT/Ps. The procedures must be designed to ensure proper HCT/P identification and to prevent mix-ups [21 CFR 1271.250(a)]. Specifically, during the inspection, the FDA investigator observed products in tubes and syringes that were either labeled with only a first name, or not labeled at all.

16. Failure to label each HCT/P in accordance with the requirements in 21 CFR 1271.370. For example:

a. The following information did not appear on the IntelliCell product label: a distinct identification number in accordance with 21 CFR 1271.290(c); a description of the type of HCT/P; an expiration date, if any.

b. The IntelliCell product, which is for autologous use, was not prominently labeled as being "For autologous use only" and "Not evaluated for infectious substances." These warnings are required under 21 CFR 1271.90(b).

We acknowledge receipt of your written response dated January 3, 2012 requesting an extension until January 30, 2012 to respond to the observations in the FDA Form 483 issued at the close of the inspection. On January 13, 2012, we agreed to this extension. We then received two additional letters from you on January 30, 2012, and March 9, 2012, both requesting additional time to submit a written update to FDA regarding

the progress of your corrective actions. The minimal response you have submitted to date is not adequate to address the serious violations described above. Your updated response may be included with your response to this Warning Letter, as described below.

Neither this letter nor the observations noted on the form FDA 483, which were discussed with you at the conclusion of the inspection, are intended to be an all-inclusive list of deficiencies that may exist at your facility. It is your responsibility as management to assure that your establishment is in compliance with the provisions of the FD&C Act, PHS Act, and all applicable federal laws and regulations. Federal agencies are advised of the issuance of all Warning Letters about biological products so that they may take this information into account when considering the award of contracts.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. Such actions include seizure and/or injunction.

For further information about IND requirements, contact Dr. Patrick Riggins, Director of Regulatory Management Staff, Office of Cellular, Tissue, and Gene Therapies, at (301) 827-5366. Please include a copy of this letter with your initial submission to CBER.

Please notify this office in writing, within 15 working days of receipt of this letter, of any additional steps you have taken or will take to correct the noted violations and to prevent their recurrence. Include any documentation necessary to show that correction has been achieved. If corrective actions cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your response should be sent to the U.S. Food and Drug Administration, Center for Biologics Evaluation and Research, HFM-600, 1401 Rockville Pike, Rockville, Maryland 20852-1448. If you have any questions regarding this letter, please contact Robert A. Sausville, Director, Division of Case Management, CBER at 301-827-6201.

Sincerely,
/S/
Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

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