DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
19701 Fairchild Irvine, CA 92612-2445 (949)608-2900 Fax:(949)608-4417	7/17/2017-7/26/2017* FEI NUMBER 3009436720

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Elliot B. Lander, MD, FACS , Owner

FIRM NAME	STREET ADDRESS
California Stem Cell Treatment	72780 Country Club Dr Ste 301
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Rancho Mirage, CA 92270-4150	Manufacturer

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

The observations noted in this Form FDA-483 are not an exhaustive listing of objectionable conditions. Under the law, your firm is responsible for conducting internal self-audits to identify and correct any and all violations of the quality system requirements.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established and followed.

Specifically,

Since April 01, 2015, your firm has recovered and deployed approximately (b) (4) batches of autologous stromal vascular fraction (SVF), recovered approximately (b) (4) adipose tissue kits, and deployed approximately (b) (4) (b) (4) SVF product intravenously or through a combination of IV injections, intra-articular, intrathecal spinal injections, intravitreal injection, intramuscular injections, spinal taps, nasal nebulization.

A. Your firm has failed to validate and document your aseptic manufacturing process through media fill and establish written procedure to prevent microbial contamination of the autologous SVF product. For example,

   i. The recovered fat in the (b) (4) syringe is opened to the environment several times during processing
   ii. (b) (4) is added to adipose fat tissue in a (b) (4) syringe. Scrub technicians are trained to add (b) (4) to help

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make mixing of (b) (4) go smoothly; prior to (b) (4) (b) (4) (b) (4).

B. Your firm failed to validate the (b) (4) sterilization process used to sterilize various reusable stainless steel instruments, syringes, (b) (4) (b) (4) and other (b) (4) instruments.

C. Manufacturing supplies sterilized in the (b) (4) are opened up to the uncontrolled environment throughout the manufacturing process prior to subsequent deployment.

D. The processing containers (syringes) used in the manufacture of SVF are opened multiple times, exposing the product to the uncontrolled environment prior to reintroduction into the patient's body, through various methods such as injection via hypodermic needle, intravenous infusion, intra-cerebrovascular infusion, intra-articular injection, and nebulizer.

OBSERVATION 2

Each batch of drug product required to be free of objectionable microorganisms is not tested through appropriate laboratory testing.

Specifically,

A. Your firm has failed to perform sterility testing on approximately (b) (4) batches of autologous SVF product, manufactured from April 01, 2015 to July 17, 2017.

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B. Your firm failed to follow procedures that required "SVF will only be released for injection after confirmation of (b) (4) (b) (4) (b) (4) (b) (4) and (b) (4) results", for SVF to be mixed with (b) (4) (b) (4) There is no documentation that the (b) (4) was tested for either (b) (4) or (b) (4) .

OBSERVATION 3

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically,

no environmental monitoring is performed during manufacture of SVF, SVF with (b) (4) (b) (4)

A. There is no nonviable particulate monitoring
B. There is no active or passive air monitoring
C. There is no personnel monitoring

OBSERVATION 4

The identity of each component of a drug product is not verified by conducting at least one test to verify the identity, using specific identity tests if they exist.

Specifically,

Since April 01, 2015, your firm has manufactured approximately (b) (4) batches of autologous SVF product, yet your firm failed to perform identity testing for the following components, which were used in the manufacturing of the autologous SVF product:

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A. (b) (4)
B.
C.
D.

OBSERVATION 5

Laboratory controls do not include the establishment of scientifically sound and appropriate specifications, sampling plans and test procedures designed to assure that components and in-process materials conform to appropriate standards of identity, strength, quality and purity.

Specifically,

A. Your firm has not established written acceptance criteria for components or written procedures for sampling, testing or examining each lot of components received and released for use in the manufacture of approximately (b) (4) batches of autologous SVF product manufactured since April 01, 2015. Components received and used to manufacture autologous SVF product include, but are not limited to:

I. (b) (4)
II.
III.
IV.

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B. Your firm failed to assure that (b) (4) s free of extraneous matter, not discolored, and failed to document that the (b) (4) was used within expiry.

C. Your firm has not established a written procedure which describes the in-process and release criteria for the autologous SVF product. A(b) (4) (b) (4) is used to calculate (b) (4) for autologous SVF product. However, your firm has failed to establish specifications for (b) (4) (b) (4) for the release of autologous SVF product.

OBSERVATION 6

The batch production and control records are deficient in that they do not include documentation of the accomplishment of each significant step in manufacturing, processing, packing and holding.

Specifically,

Your firm has not prepared and maintained batch records for the approximately (b) (4) batches of autologous SVF product. For example:

A. Your firm failed to identify the specific component lot identifiers used in the manufacture of each batch of autologous SVF product. Components used in the autologous SVF manufacturing include, but are not limited to: (b) (4) (b) (4) (b) (4) .

B. Your firm failed to identify the equipment used in the manufacture of each batch of autologous SVF product, including, but not limited to, (b) (4) Syringes,

the (b) (4) (b) (4) the (b) (4) (b) (4) and the (b) (4) (b) (4) (b) (4)

C. Your firm has failed to document the preparation of (b) (4) including (b) (4) date of preparation, quantity of preparation and expiration date.

D. Your firm failed to record the start and stop times for the (b) (4) in the manufacturing of each batch of autologous SVF product. For example, (b) (4) of (b) (4) and the mixing and (b) (4) time for SVF mixed with (b) (4) were not documented. Your firm (b) (4) of SVF with (b) (4) for (b) (4), but procedures required (b) (4) for (b) (4) (b) (4) prior to administration to patients.

E. Your firm failed to identify the personnel performing each significant step in the manufacture of each batch of autologous SVF product, including, but not limited to, the personnel preparing the (b) (4) and the personnel obtaining the (b) (4) (b) (4)

OBSERVATION 7

Written procedures are lacking which describe in sufficient detail the receipt, identification, storage, handling, sampling, testing, approval and rejection of components.

Specifically,

A. Your firm failed to determine the safety and stability of (b) (4) SVF prior to administration to patients. (b) (4) SVF products shipped from (b) (4) through ambient conditions and through refrigerated conditions were both administered to patients.

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B. Your firm lacked written stability procedures and stability test data to support the expiration dating of (b) (4) and/or stored frozen by your firm.

C. Your firm lacked written procedures for the storage and temperature monitoring of (b) (4) in your firm's freezer and during transport to your firm's additional sites located hours away.

D. Your firm lacked storage and temperature monitoring of (b) (4) and (b) (4)

OBSERVATION 8

There is no quality control unit.

Specifically,

Your firm does not have an established quality control unit which has the responsibility and authority to approve or reject all components, in-process materials, labeling, or procedures or specifications which could impact the identity, strength, quality, and purity of the autologous SVF product.

OBSERVATION 9

Employees are not given training in current good manufacturing practices.

Specifically,

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A. On 07/20/2017 Investigator Lagud observed the SVF manufacturing process in its entirety for patient (b)(6) Employees who performed the autologous SVF product manufacturing did not appear to be adequately trained in aseptic technique and the proper handling of all components in order to prevent the microbial contamination of the autologous SVF product. During the observation of multiple autologous SVF product manufacturing, I observed deficiencies, including, but not limited to:

I. During the above manufacturing process, the employee's gloves were not regularly sanitized or changed as appropriate throughout the autologous SVF product manufacturing process which lasted approximately (b) (4)

II. During the above manufacturing process, the procedure room door to the hallway remained open throughout the procedure, and a floor fan was placed just outside the doorway, in the hall, blowing air into the procedure room. During the recovery manufacturing process, the fan was pointed toward the patient and during processing, it was pointed toward the Technologist performing the processing over the processing table.

III. On 07/20/2017 Investigator Lagud observed the non-sterile Technologist exit and enter the room repeatedly to obtain supplies for the manufacturing process from the hallway storage area.

B. Improper documentation was observed on manufacturing records in which information was not legible, error correction did not reveal the original entry, and incomplete documentation.

OBSERVATION 10

Equipment used in the manufacture, processing, packing or holding of drug products is not of appropriate design to facilitate operations for its intended use.

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Specifically,

A. Your firm has not performed equipment qualification, which includes Installation Qualification (IQ), Operational Qualification (OQ), and Performance Qualification (PQ) for the following equipment used in the manufacture of SVF product: (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) sterilizer, and (b) (4) (b) (4) (b) (4)

OBSERVATION 11

Written procedures describing the handling of all written and oral complaints do not include provisions for review to determine whether the complaint represents a serious and unexpected adverse drug experience which is required to be reported to the Food and Drug Administration.

Specifically,

A. Your firm has failed to establish written procedures for handling reports of adverse drug experiences. There is no assurance that adverse drug experiences are evaluated: For example:

i. Serious Adverse Event Report submitted on 11/08/2016 to your firm reporting that SVF manufactured using the (b) (4), (b) (4), and (b) (4) manufacturing procedure was administered to a patient's eyes and this patient subsequently experienced retinal detachment in the left eye. This event was not investigated and not reported to FDA.

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ii. Serious Adverse Event Report submitted on 05/19/17 to your firm reported that SVF manufactured using the (b) (4), (b) (4), and (b) (4) manufacturing procedure was administered to (b) (4) (b) (4) and subsequently the patient was hospitalized for confusion and headache. During his hospital course, the patient mobility, gait, and balance declined. This event was not investigated and not reported to FDA.

iii. Serious Adverse Event Report with event date 08/10/2015 submitted to your firm reported that SVF manufactured using the (b) (4), (b) (4), and (b) (4) manufacturing procedure was deployed to a patient which subsequently reported cartilage deterioration and "severe infection". This event was not investigated and not reported to FDA.

iv. Serious Adverse Event Report with event date 07/25/2016 submitted to your firm reported that SVF (b) (4) manufactured using the (b) (4), (b) (4) (b) (4), and (b) (4) manufacturing procedure was administered to a patient, bilateral hip injections. A week later, the patient complained of left hip pain and an infection of the hip was found. This event was not investigated and not reported to FDA.

B. Your firm has failed to establish written procedures for handling complaints in order to determine whether an investigation is needed. There is no system in place to document complaints from affiliates that have purchased equipment and supplies from (b) (4).

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***DATES OF INSPECTION**

7/17/2017(Mon),7/18/2017(Tue),7/19/2017(Wed),7/20/2017(Thu),7/21/2017(Fri),7/24/2017(Mon),7/25/2017(Tue),7/26/2017(Wed)

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FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS

Date: September 14, 2017

Elliot B. Lander, MD, FACS
California Stem Cell Treatment
72780 Country Club Dr Ste 301
Rancho Mirage, CA 92270-4150

Subject: System Notification

Dear Elliot B. Lander, MD, FACS,

We are notifying you that due to a technical error related to a software update, the FDA Form 483 you received recently inadvertently included a sentence meant only for medical device firms. That statement says, "Under the law, your firm is responsible for conducting internal self-audits to identify and correct any and all violations of the quality system requirements."

This statement refers to quality system requirements applicable only to medical device establishments, but was inadvertently included on certain Form 483's issued to non-device establishments for a brief period of time. Please note that the statement has no bearing on the inspection observations themselves, which remain applicable as of the date that you were issued the Form FDA 483.

Should you have any questions, please send to AskORAIT@fda.hhs.gov.

Sincerely,

Lisa Creason
Director, Office of Information Systems Management
Office of Regulatory Affairs
Food and Drug Administration