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	7/21/2017-7/27/2017*
	FEI NUMBER 3013670025

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Judi E. Meglio , Office Manager

FIRM NAME	STREET ADDRESS
California Stem Cell Treatment Center/Cell Surgical Network	120 S Spalding Dr, Suite 300
CITY, STATE, ZIP CODE, COUNTRY Beverly Hills, CA 90212-1800	TYPE ESTABLISHMENT INSPECTED 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

There are no written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess.

Specifically,

Your firm has failed to validate your manufacturing process for the autologous SVF product and the (b) (4) product at your Beverly Hills facility.

OBSERVATION 2

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

Specifically,

Since July 2, 2015, your firm has manufactured approximately (b) (4) batches of autologous Stromal Vascular Fraction (SVF) product. The autologous SVF product is to be administered by intravenous

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infusion, intra-articular injection, injection into soft tissue, intra-cerebroventricular injection, or nebulization.

Since December 3, 2015, (b) (4) batches of product that is a mixture of autologous SVF and (b) (4) (b) (4) were manufactured at your firm. The (b) (4) was prepared, mixed with SVF, and (b) (4) at your firm by an outside affiliate under their procedures. Your firm prepared the autologous SVF product from recovered adipose tissue using your SVF preparation procedure and deployed the mixed (b) (4) product. The (b) (4) product is to be administered by intravenous or intra-tumoral injection. As an example, one batch of the (b) (4) product was manufactured in this manner and deployed at your firm on 7/19/17.

(A) An aseptic process for manufacturing the autologous SVF product and (b) (4) product has not been established and validated to assure that these products can be consistently manufactured in a manner that prevents microbiological contamination.

i. No evidence was provided to show that the manufacturing of autologous SVF product and (b) (4) product is performed in a controlled environment. For example, no evidence was provided to demonstrate that clean area control parameters, such as pressure differentials, air flow, temperature, humidity and air particulate count, have been established for the suite used for production of these products.

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iii. The written procedure for gowning in the suite where the autologous SVF product is prepared is deficient. According to "Standard Operating Procedures of (b) (4) " used by your firm for preparation of the autologous SVF product, personnel are only required to wear a cap, mask, and sterile gloves. There is no requirement for personnel who prepare the SVF product to wear an appropriate gown as a barrier to protect exposed containers and materials from microbiological contamination.

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(B) Your firm has failed to validate the (b) (4) sterilization process used to sterilize various reusable stainless steel instruments and (b) (4) used for production of the autologous SVF product.

OBSERVATION 3

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

Specifically,

Your firm has failed to perform sterility testing on approximately (b) (4) batches of SVF product manufactured from July 2, 2015 to July 20, 2017 and (b) (4) batches of (b) (4) product manufactured from December 3, 2015 to July 19, 2017. Autologous SVF batches manufactured by your firm are administered by intravenous infusion, intra-articular injection, injection into soft tissue, intra-cerebroventricular injection, or nebulization. The (b) (4) batches manufactured by your firm are administered by intravenous or intra-tumoral injection.

OBSERVATION 4

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

Specifically,

No environmental monitoring is performed during the manufacture of the autologous SVF product and the (b) (4)

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(A) There is no personnel monitoring.

(B) There is no non-viable particulate monitoring.

(C) There is no active or passive air monitoring.

OBSERVATION 5

Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the room and equipment to produce aseptic conditions.

Specifically,

(A)Your firm utilizes a checklist for cleaning of the suite where the autologous SVF product and (b) (4) product is prepared and deployed, but there is no written procedure established for cleaning the suite that includes assignment of responsibility and a description in sufficient detail of the methods, equipment, and materials used to perform the cleaning.

(B) Your written procedure for cleaning reusable stainless steel instruments used for the production of the autologous SVF product and (b) (4) product does not include sufficient detail of the methods, equipment, and materials used to perform cleaning operations.

OBSERVATION 6

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.

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Your firm failed to perform an identity test for the following components used for the autologous SVF product manufacturing: (b) (4) (b) (4) Since July 2, 2015, your firm has manufactured approximately (b) (4) batches of autologous SVF product. Since December 3, 2015, your firm has manufactured (b) (4) batches of the (b) (4) product.

OBSERVATION 7

Laboratory controls do not 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 and drug products conform to appropriate standards of identity, strength, quality and purity.

Specifically,

(A) Your firm failed to perform an identity test for the following components used for the autologous SVF product manufacturing: (b) (4) in (b) (4) Since July 2, 2015, your firm has manufactured approximately (b) (4) batches of autologous SVF product.

(B) Your firm did not establish a written procedure that describes the in-process and release criteria for the autologous SVF product. An (b) (4) is used to calculate the (b) (4) for autologous SVF product. Your firm has failed to establish written specifications for (b) (4) for the release of autologous SVF product. Since July 2, 2015, approximately (b) (4) batches of autologous SVF product were manufactured and deployed to

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patients by your firm without these specifications in place. Since December 3, 2015, (b) (4) batches of the (b) (4) product were manufactured and deployed to patients by your firm.

OBSERVATION 8

Batch production and control records are not prepared for each batch of drug product produced and do not include complete information relating to the production and control of each batch.

Specifically,

(A) Your firm has not prepared and maintained batch records for approximately (b) (4) batches of autologous SVF product since July 2, 2015 and (b) (4) batches of the (b) (4) product manufactured since December 3, 2015.

(B) Your firm failed to identify the specific component lots used in the manufacturing of each batch of autologous SVF product and (b) (4) product. These components include, but are not limited to: (b) (4) (b) (4).

(C) Your firm failed to identify the equipment used in the manufacture of each batch of autologous SVF product and (b) (4) 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).

(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 and (b) (4) product.

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

OBSERVATION 9
Written procedures are lacking which describe in sufficient detail the receipt, identification, storage, handling, sampling, testing, approval and rejection of components.

Specifically,

Written procedures are limited in regards to the manufacturing process for autologous SVF product in that:

(A) Your firm lacks written stability procedures and stability test data to support the expiration date of one year for (b) (4) and frozen form.

(B) Your firm lacks written procedures for monitoring the storage and temperatures of frozen (b) (4) in your freezer.

OBSERVATION 10
The responsibilities and procedures applicable to the quality control unit are not in writing.

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(a) No written procedures have been established for the approval or rejection of all components, in process materials, and drug products.

(b) No written procedures have been established for approving or rejecting all procedures impacting on the identity, strength, quality, and purity of the autologous SVF product and (b) (4) (b) (4) product. Your firm uses written procedures that have not been reviewed and approved by the quality control unit.

OBSERVATION 11
Employees are not given training in current good manufacturing practices.

Specifically,

No training in current good manufacturing practices is provided to employees engaged in the manufacture of the autologous SVF product and (b) (4) product.

OBSERVATION 12
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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Your firm has not performed equipment qualification at your Beverly Hills facility, including Installation Qualification (IQ), Operational Qualification (OQ), and/or Performance Qualification (PQ) for the following equipment used in the manufacture of autologous SVF product and (b) (4) (b) (4) product: (b) (4) (b) (4) and (b) (4)

OBSERVATION 13

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,

Your written procedure for handling adverse events does not assure that events are adequately evaluated and reported to the FDA. The following events were not investigated or reported to the FDA:

i. Patient (b) (6) was treated for astrocytoma with the (b) (4) product manufactured by your firm and deployed by your firm by IV drip on 12/17/15. The patient died on 4/21/16.

ii. A patient treated for COPD with the SVF product manufactured by your firm experienced hyperventilation during the deployment procedure on 2/6/17. He passed out at the end of the procedure and was subsequently resuscitated and hospitalized. The SVF product was administered by IV and nebulization.

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*DATES OF INSPECTION

7/21/2017(Fri),7/24/2017(Mon),7/25/2017(Tue),7/27/2017(Thu)

X Michele L Forster
Investigator - Team Biologics
Signed By: Michele L. Forster -S
Date Signed: 7/27/2017

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

Date: September 14, 2017

Judi E. Meglio
California Stem Cell Treatment Center, Inc
120 S Spalding Dr Suite 300
Beverly Hills, CA 90212-1800

Subject: System Notification

Dear Judi E. Meglio,

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