DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10 Waterview Blvd., 3rd Floor Parsippany, NJ 07054 (973) 331-4900 Fax:(973) 331-4969 Industry Information: www.fda.gov/oc/industry	03/17/2014 - 05/19/2014* FEI NUMBER 3001236616

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Bruce William Stroever, President/CEO

FIRM NAME	STREET ADDRESS
Musculoskeletal Transplant Foundation	125 May St Ste 300
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Edison, NJ 08837-3264	HCT/P Processer and Medical Device 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.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

HCT/Ps were not processed in a way that does not cause contamination or cross contamination during processing and that does not increase the risk of introduction, transmission, or spread of communicable disease.

Specifically, there is no assurance that the processing of tissue products, Osteochondral Grafts (OC) and Osteoarticular Grafts (OA) does not cause contamination or increase the risk of the transmission of communicable disease. The process for OC and OA Grafts were not validated.

A. The validation protocol for OC Grafts, PV-028, Sterility Validation of the Production of Storage Bags of Nutrient Media for Osteochondral (OC) Grafts from Raw Materials, was not followed. The protocol states the acceptance criteria will be based on the (b) (4) consisting of (b) (4) each and a (b) (4) The protocol also states all (b) (4) bags from the (b) (4) batch and the (b) (4) samples would be tested for sterility. However, in Validation 112, PV-028-Sterility Validation of the Production of Storage Bags of Nutrient Media for Fresh Osteochondral (OC) Grafts from Raw Materials, memo dated 8/29/2000, batches # (b) (4) through # (b) (4) consisted of only (b) (4) bags, and batch # (b) (4) consisted only of (b) (4) bags. In addition, only 4 samples were tested for sterility from batch # (b) (4) and the syringes were not tested for batches # (b) (4) through # (b) (4) This validation was approved on 7/19/2004.

B. The acceptance criteria in the validation protocol for OA Grafts, was not met. The acceptance criteria in Protocol No. 200515801-01, Advanced Tissue Processing (ATP) Soft Tissue (ST) Microorganism Reduction (b) (4) Hours Study, states (b) (4) (b) (4) '. However, Final Report for Protocol No. 200515801-01, completed 11/29/2005, shows all treated tissue had growth of test organisms after the (b) (4) hour (b) (4) Validation 675, Summary of ATP Soft Tissue Microbial Reduction Study Results (b) (4) Hours, (b) (4) Hours, and (b) (4) Hours, only shows a log reduction of the test organisms on the treated tissue; this validation was approved on 10/4/2006.

OBSERVATION 2

Labeling procedures were not designed to ensure proper HCT/P identification and to prevent mix-ups.

Specifically:
The labeling system does not ensure tissue is correctly identified. For example:
- There is no verification performed to assure that the donor number linked to a work order is the donor number provided on

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the Planning Worksheet. The labels printed for the work order are verified against the donor number on the work order which may contain an incorrect donor number.

- In process labels listed an incorrect donor number but were verified as correct at donor planning and at processing and were used to identify the tissue (medical device Work Order 746051 created for donor [redacted] had labels printed with the donor number [redacted] HCT/P Work Order 758419 created for donor number [redacted] had labels printed with donor number [redacted]
- During in process bioburden sampling for frozen donors two pieces of tissue were incorrectly identified with labels identifying the tissue as being from donor [redacted] when the tissue was sampled from donor [redacted]
- Tissue from donor [redacted] nd tissue from donor [redacted] were used to make one lot of medical device DBX putty.

OBSERVATION 3

The quality program has not ensured that appropriate corrective actions relating to core CGTP requirements are taken and documented.

Specifically:

1. There is no process in place to ensure deficiencies identified relating to core CGTP requirements are monitored and appropriate corrective actions are taken when the deficiency is identified via the complaint handling system. For example:
A. As *a result of* complaints of cracked blister packs for Trinity Evolution a new tray was developed and tested by the Business Unit. The deficiency was not entered into the CAPA system, Nonconformance system or other quality system to assure monitoring of the corrective actions and review of documentation.
B. Complaint CMP201310016 reported Cort/Canc Granules, 30cc with granules outside of bone jar, inside the packaging. The Base Business Unit was requested to open a nonconformance report for the verified complaint or to respond. The complaint was closed without a root cause analysis being performed or a nonconformance report generated.

2. ITCCD-880 was generated to link the work order and the donor number so labels would not print with an incorrect donor number due to multiple incidents of labels being used with the incorrect donor number. Processing/Planning creates a work order and manually enters the donor number identified on the Planning Worksheet. The work order and donor number are then linked in the computer system. Labels are then printed and verified against the work order to assure the correct donor number is printed. However there is no verification that the donor number entered into the work order is the donor number identified on the Planning Worksheet. If the incorrect donor number is entered on the work order all labels generated from that work order will have the incorrect donor number and incorrect donor tissue could be used.

3. Nonconformance Report NCR201304042 regarding incorrect expiration dates on packaging for Allograft Bone Plugs has corrective actions to relabel the product. An investigation determined that the incorrect expiration date was assigned through QAD which was corrected but packaging and labeling was not notified to relabel the units. The investigation did not identify that Quality Assurance 2nd Review for labels should have identified the incorrect expiration date since the expiration date

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had been corrected on Form-380 which is the form documenting the 2nd Review. Also the investigation did not identify that the incorrect expiration date was not identified during Quality Assurance Final Release which is performed to assure the batch complies with MTF Processed Tissue Release Specifications, which includes the approved expiration time. The QA personnel involved were not retrained.

OBSERVATION 4

Procedures appropriate to meet core CGTP requirements for all steps that you perform in the manufacture of HCT/Ps were not followed.

Specifically, procedures regarding donor processing pathway were not followed in that the incorrect donor pathway was selected. For example:
- WI-335, Quality Assurance First and Second Review for Whole Donor Musculoskeletal Tissue and IPBB Review was not followed. Donor [redacted] (b) (6) should have been a pretreat donor but the aseptic pathway was circled on Template-150 and the donor was processed as aseptic.
- FLOW-105, QA Review of Sterility Path Criteria was not followed. Donor [redacted] (b) (6) should have been a pretreat donor but was assigned the aseptic pathway and the donor was processed as aseptic.
- WI-338, First and Second Review for DBX Putty, Paste, and Mix, was not followed. Medical device donor [redacted] (b) (6) should have been an interim pathway donor but was assigned as an aseptic pathway donor and the donor was processed as aseptic.

OBSERVATION 5

HCT/P deviations relating to core CGTP requirements that occurred in your establishment were not reported to FDA.

Specifically, no HCT/P deviations have been reported to FDA from January 2013 through April 2014. For example,
- CMP201310016 reports Cort/Canc Granules, 30cc with granules outside of the bone jar, inside the packaging. The complaint was received 10/4/13 but the HCT/P deviation was not reported to FDA.
- CMP201304055 reports Allograft Bone Plug, 6mm x 40mm labeled with the expiration date 16 AUG 2015 when the correct expiration date is 16 AUG 2014. The complaint was received 4/23/13 but the HCT/P deviation was not reported to FDA.
- CMP201401031 regarding Cancellous Chips, 30cc reports the outer carton and shipping container were undamaged but the inner plastic packaging was broken. The complaint was received 1/20/14 but the HCT/P deviation was not reported to FDA.
- CMP201310049 regarding Cancellous Chips, 90cc reports the shipping box and tissue carton were undamaged but the inner packaging had a crack. The complaint was received 10/22/13 but the HCT/P deviation was not reported to FDA.
- CMP201309014 regarding Cort/Canc Granules, 90cc reports the seal on the container holding the granules was loose. The complaint was received 9/10/13 but the HCT/P deviation was not reported to FDA.

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OBSERVATION 6

Complaints were not reviewed and evaluated to determine if the complaint is related to an HCT/P deviation or adverse reaction and whether a report to FDA is required.

Specifically, complaints were not reviewed and evaluated to determine whether they were HCT/P deviations and if they were deviations if they were reportable deviations.

A. Complaints were not reviewed and evaluated to identify reportable deviations (for example, CMP201310016, CMP201304055, CMP201401031).

B. Complaint CMP201312009 was received 11/20/13 regarding a surgeon finding a foreign object that looked like a (b) (4) (b) (4) on a FlexHD Structural, 6cm x 16cm. It was confirmed by the photo to be a piece of (b) (4) used during processing. No health hazard analysis was conducted to determine if the (b) (4) may lead to HCT/P contamination or potential transmission of a communicable disease, and therefore would be a reportable to FDA.

OBSERVATION 7

The complaint file did not contain sufficient information about each complaint for proper review and evaluation and did not contain sufficient information for determining whether the complaint is an isolated event or represents a trend.

Specifically:

A. When complaints are received via email the email is not always part of the complaint file (for example, CMP201310019, CMP201310016, CMP201304055).

B. The complaint file contains trending information only for the specific complaint lot and/or other complaints received for this donor and/or other complaints received from the complainant. There is insufficient information to determine if the complaint is an isolated event or represents a trend (for example CMP201401031, CMP201310049, CMP201309014).

C. CMP201307058 was received 7/29/13 via email. It was voided 8/19/13 due to lack of complaint details. The complaint file does not contain the complaint email or evidence of attempts to obtain additional information from the complainant.

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OBSERVATION 8

The quality program has not established and maintained appropriate monitoring systems.

Specifically, there is no procedure for trending complaints to identify areas needing corrective or preventive actions.

OBSERVATION 9

Environmental controls do not provide for adequate cleaning and disinfecting of rooms and equipment to ensure aseptic processing.

Specifically, there is no documentation of the preparation of the cleanser and sanitizer solutions used in cleaning and disinfecting equipment and processing rooms to assure the solution was prepared correctly.

OBSERVATION 10

Adverse reactions which involved a communicable disease related to an HCT/P made available for distribution and were fatal or life threatening, resulted in permanent impairment or damage to the body, or necessitated medical or surgical intervention, were not reported to FDA.

Specifically, a determination of reportability was not made within 15 days and the following reports of adverse reactions were not reported to FDA:
- CMP201312007 reports patient with fever, high leukocytes, surgical site erythema, edema and was placed on antibiotics. The aware date is 12/3/13 and the determination that the event is not reportable was made 3/8/14.
- CMP201301051 reports two patients with infections (positive cultures) and were placed on antibiotics. The aware date is 1/30/13 and the determination that the event was not reportable was made 3/27/13.

OBSERVATION 11

Adverse reactions involving a communicable disease related to HCT/Ps were not investigated.

Specifically, investigations into reports of adverse reactions were incomplete. For example:
- CMP201301051 reported two patients with infections (positive cultures) that were placed on antibiotics. The date of the

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complaint is 1/30/13. The distributor was requested to obtain the serial numbers of the product utilized in the surgeries on (b) (6) 3, (b) (6) 13 (b) (6) /13 and (b) (6) 13. On 3/14/13 the representative at the distributor responded that he did not receive the serial numbers from the surgeon. At no time did Musculoskeletal Transplant Foundation contact the surgeon directly to request this information or obtain patient names to determine if tracking documents had been received that would indicate the serial numbers used.
- CMP201304052 reported a patient with redness and discharge at the surgical site, with the patient being placed on oral antibiotics. The date of the complaint is 4/22/13. The distributor indicated belief that the cultures were negative. The distributor was requested to obtain the Event Report and lab/culture reports from the surgeon. No Event Report or lab/culture report(s) were provided. Musculoskeletal Transplant Foundation did not pursue requesting the Event Report and lab/culture report(s) and no further information regarding the event was obtained until the Medical Director spoke with the surgeon on 5/21/13 and determined that the patient was started on Keflex (antibiotic) two days before the cultures were obtained.

OBSERVATION 12

Adverse reactions were not reported to FDA using form FDA 3500A within 15 calendar days of initial receipt of information.

For example:
- CMP201303002 reports fever, chills, pain, redness, swelling at surgery site of a patient. The aware date is 2/11/13 (3/1/13 on complaint form) but the adverse reaction report was not reported to FDA until 3/29/13.
- CMP201303051 reports three patients with adverse reactions (one with skin necrosis and positive culture; one with fever, mild erythema and positive culture; and one with erythema and positive culture). The aware date is 3/22/13 but the adverse reaction report was not reported to FDA until 4/29/13.
- CMP201402014 reports patient infection. The aware date is 2/10/14 but the adverse reaction report was not reported to FDA until 3/7/14.
- CMP201312003 reports a patient with bilateral infection. The aware date is 11/25/13 (12/2/13 on complaint form) but the adverse reaction report was not reported to FDA until 12/17/13.
- CMP201304048 reports a patient with infection. The aware date is 4/19/13 but the adverse reaction report was not reported to FDA until 5/13/13.

OBSERVATION 13

Procedures for the cleaning of equipment were not established.

Specifically, the procedures for the cleaning of the (b) (4) saw was established on inadequate validation. Validation-1205, Process Equipment Cleaning Validation (b) (4) Saw, MTF Edison & Jessup protocol states the MTF process technician and sterilization technician will clean the (b) (4) saws before and after soiling using a (b) (4) solution. There is no documentation of the preparation of the (b) (4) solution to assure the cleaning solution was prepared correctly.

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*** DATES OF INSPECTION:**
03/17/2014(Mon), 03/19/2014(Wed), 03/20/2014(Thu), 03/24/2014(Mon), 03/25/2014(Tue), 03/26/2014(Wed), 03/27/2014(Thu), 04/02/2014(Wed), 04/03/2014(Thu), 04/07/2014(Mon), 04/08/2014(Tue), 04/10/2014(Thu), 04/14/2014(Mon), 04/16/2014(Wed), 04/17/2014(Thu), 04/22/2014(Tue), 04/23/2014(Wed), 04/25/2014(Fri), 04/28/2014(Mon), 04/29/2014(Tue), 04/30/2014(Wed), 05/01/2014(Thu), 05/05/2014(Mon), 05/06/2014(Tue), 05/07/2014(Wed), 05/08/2014(Thu), 05/13/2014(Tue), 05/19/2014(Mon)

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