Stanmore Implants Worldwide Ltd. 11/26/14

Department of Health and Human Services

Public Health Service
Food and Drug Administration
10903 New Hampshire Avenue
White Oak Building 66
Silver Spring, MD 20993

WARNING LETTER

November 26, 2014

VIA UNITED PARCEL SERVICE

Michael Mainelli
Chief Executive Officer
Stanmore Implants Worldwide Ltd.
210 Centennial Avenue
Centennial Park
Elstree WD6 3SJ
United Kingdom

Dear Mr. Mainelli:

During an inspection of your firm located at 210 Centennial Avenue, Centennial Park, Elstree, United Kingdom, on July 28, 2014, through July 31, 2014, an investigator from the United States Food and Drug Administration (FDA) determined that your firm manufactures implantable extendable femoral and total knee replacement devices. Under section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 321(h), these products are devices because they are intended for

use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or to affect the structure or function of the body.

This inspection revealed that these devices are adulterated within the meaning of section 501(h) of the Act, 21 U.S.C. § 351(h), in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformity with the current good manufacturing practice requirements of the Quality System regulation found at Title 21, Code of Federal Regulations (CFR), Part 820.

We received a response from Samantha Shelley, Head of Compliance, dated August 21, 2014, concerning our investigator's observations noted on the Form FDA 483 (FDA 483), List of Inspectional Observations, which was issued to your firm. Your firm's responses dated September 26 and October 15, 2014, to FDA 483 were not reviewed because they were not received within fifteen business days of issuance of the FDA 483. These responses will be evaluated along with any other written material provided in response to the violations cited in this Warning Letter. These violations include, but are not limited to, the following:

1. Failure to establish and maintain procedures for implementing corrective and preventive action, as required by 21 CFR 820.100. For example:

a. Your firm's Corrective and Preventive Action (CAPA) procedure, SOP **(b)(4)**, is deficient. Specifically:

i. The procedure does not require the use of appropriate statistical methodology, where necessary, to detect recurring quality problems.

ii. The procedure does not ensure that information related to quality problems and nonconforming product is disseminated to those directly responsible for assuring the quality of such product or the prevention of such problems.

iii. The procedure does not include requirements for the documentation of all CAPA activities.

b. Your firm failed to implement and record corrective actions needed to correct and prevent identified quality problems. Specifically:

i. CAPA file 14009 did not contain records of the implementation of all of the corrective actions or contain records confirming that the corrective actions had been completed. However, the CAPA was closed as effective.

ii. CAPA file 140022 did not contain records of the implementation date of the corrections to the Instructions for Use. The CAPA was closed, but the

verification of effectiveness had not yet been completed, as per SOP **(b)(4)**.

iii. CAPA file 140033 did not contain adequate post irradiation validation of the corrective action to change the material for certain plastic components in the ITAP impactor. For example, the validation did not ensure that a statistically valid number of post irradiated samples were tested prior to release.

We reviewed your firm's response and conclude that it is not adequate. Your firm's response did not address whether your firm retrospectively reviewed closed CAPAs, to ensure that the CAPA activities were conducted in accordance with your firm's revised procedure. Your firm's response did not indicate that personnel were trained on the revised CAPA procedure.

2. Failure to establish and maintain procedures for receiving, reviewing, and evaluation complaints by a formally designated unit, as required by 21 CFR 820.198. For example, your firm's complaint handling procedure is deficient. Specifically:

a. Your firm's procedure does not include requirements to ensure that:

i. Complaints are processed in a uniform and timely manner.

ii. Oral complaints are documented upon receipt.

iii. Complaints are evaluated for MDR reportability.

b. Your firm's procedure do not include requirements that records of investigation include:

i. The name of the device.

ii. Any device identification and control number.

iii. The name, address, and phone number of the complainant.

iv. The nature and details of the complaint.

v. The dates and results of the investigation.

vi. Any reply to the complainant.

We reviewed your firm's response and conclude that it is not adequate. Your firm's response did not address whether personnel have been trained on your firm's revised complaint handling and MDR reporting procedures. Your firm's response did not address whether a retrospective review of complaints was conducted to ensure

compliance with the revised procedure.

3. Failure to establish and maintain a design history file (DHF) for each type of device to demonstrate that the design was developed in accordance with the approved design plan, as required by 21 CFR 820.30(j). For example, your firm does not have a Design History File (DHF) for the original METS Modular Distal Femur, design Project **(b)(4)**, developed from 2000 to 2002.

The adequacy of the firm's response cannot be determined at this time. Your firm's response indicated that your firm will compile the DHF for the METS Modular Distal Femur, Project **(b)(4)**, and retrospectively review DHFs for METS and JTS product lines to ensure compliance with your firm's current design control procedure. However, your firm's response did not include evidence of implementation of these corrective actions.

4. Failure to establish and maintain procedures to ensure that design history records (DHRs) for each batch, lot, or unit are maintained to demonstrate that the device is manufactured in accordance with the Device Master Record, as required by 21 CFR 820.184. For example, your firm's DHRs do not include the primary identification label and labeling used for each production unit.

Your firm's response appears to be adequate.

5. Failure to establish and maintain procedures for quality audits and conduct such audits to assure that the quality system is in compliance with the established quality system requirements and to determine the effectiveness of the quality system, as required by 21 CFR 820.22. For example, your firm's Quality Audit Procedure includes requirements which ensure auditors do not have responsibility for the areas they audit. However, during the 2012 and 2013 Internal Audit Programs, an individual who conducted quality audits had direct responsibility for matters being audited.

We reviewed your firm's responses and conclude that it is not adequate. Your firm's response did not address whether a retrospective review of audit files was conducted to ensure compliance with your firm's revised procedure.

Our inspection also revealed that your firm's devices are misbranded under Section 502(t)(2) of the Act, 21 U.S.C. § 352(t)(2), in that your firm failed or refused to furnish material or information regarding the devices that is required by or under Section 519 of the Act, 21 U.S.C. § 360i, and 21 CFR Part 803 - Medical Device Reporting. Significant violations include, but are not limited to, the following:

6. Failure to report to FDA no later than 30 calendar days after the day that your firm received or otherwise became aware of information, from any source, that reasonably suggests that a device that your firm markets has malfunctioned and this device or a

similar device that your firm markets would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur, as required by 21 CFR 803.50(a)(2). For example, complaints **(b)(4)**, **(b)(4)**, and **(b)(4)** describe malfunctions occurring with your firm's long-term implanted device. There is no information in your firm's complaint files justifying why the referenced malfunctions would not be likely to cause or contribute to a reportable death or serious injury, if the malfunctions were to recur. These complaints should have been reported as Medical Device Report (MDR) to the FDA within 30 calendar days.

Your firm's response did not address this violation.

7. Failure to develop, maintain and implement written MDR procedures, as required by 21 CFR 803.17. For example, your firm's MDR procedure, Vigilance Procedure, is deficient. Specifically:

a. There is no evidence that the procedure was adequately implemented. For example, the procedure states that your firm will report adverse events occurring outside the United States, if it markets the same or a similar device in the United States. The MDR reportable events described in complaints **(b)(4)**, **(b)(4)**, and **(b)(4)** occurred in the United Kingdom and involved same or similar devices marketed in the United States. However, the events were not reported to FDA per the procedure.

b. The procedure does not establish internal systems that provide for timely transmission of complete medical device reports. Specifically:

i. The procedure does not refer to or include instructions for how to obtain and complete the FDA 3500A form.

ii. The procedure does not include the address for where to submit MDR reports: FDA, CDRH, Medical Device Reporting, P.O. Box 3002, Rockville, MD 20847-3002.

We reviewed your firm's response and conclude that it is not adequate. Your firm's revised MDR procedure does not refer to or include instructions for how to obtain and complete the FDA 3500A form.

The eMDR Final Rule requiring manufacturers and importers to submit electronic Medical Device Reports (eMDRs) to FDA was published on February 13, 2014. The requirements of this final rule will take effect on August 14, 2015. If your firm is not currently submitting reports electronically, we encourage you to visit the following weblink for additional information about the electronic reporting requirements:

http://www.fda.gov/ForIndustry/FDAeSubmitter/ucm107903.htm
If your firm wishes to discuss MDR reportability criteria or to schedule further

communications, it may contact the Reportability Review Team by email at ReportabilityReviewTeam@fda.hhs.gov.

Given the serious nature of the violations of the Act, devices, including Implantable extendable femoral and total knee replacement devices,manufactured by your firm are subject to refusal of admission under section 801(a) of the Act, 21 U.S.C. § 381(a), in that they appear to be adulterated. As a result, FDA is taking steps to refuse entry of these devices into the United States, known as "detention without physical examination," until these violations are corrected. In order to remove the devices from detention, your firm should provide a written response to this Warning Letter as described below and correct the violations described in this letter. We will notify you regarding the adequacy of your firm's response and the need to re-inspect your firm's facility to verify that the appropriate corrections and/or corrective actions have been made.

Also, U.S. federal agencies may be advised of the issuance of Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, premarket approval applications for Class III devices to which the Quality System regulation deviations are reasonably related will not be approved until the violations have been corrected.

Please notify this office, in writing within fifteen business days, from the date you receive this letter of the specific steps your firm has taken to correct the noted violations, including an explanation of how your firm plans to prevent these violations, or similar violations, from occurring again. Include documentation of the corrections and/or corrective actions (which must address systemic problems) that your firm has taken. If your firm's planned corrections and/or corrective actions will occur over time, please include a timetable for implementation of those activities. If corrections and/or corrective actions cannot be completed within fifteen business days, state the reason for the delay and the time within which these activities will be completed. Please provide a translation of documentation not in English to facilitate our review.

Your firm's response should be sent to: Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Field Inspections Support Branch, White Oak Building 66, Rm 2622, 10903 New Hampshire Ave., Silver Spring, MD 20993.Refer to CMS case #444402 when replying**.** If you have any questions about the contents of this letter, please contact: Daniel Walter, Chief, Foreign Enforcement Branch at telephone +1 301-796-5587, or fax +1 301-847-8139.

Finally, you should know that this letter is not intended to be an all-inclusive list of the violations at your firm's facility. It is your firm's responsibility to ensure compliance with applicable laws and regulations administered by FDA. The specific violations noted in this letter and in the Inspectional Observations, FDA 483, issued at the close of the inspection may be symptomatic of serious problems in your firm's

manufacturing and quality management systems.

Your firm should investigate and determine the causes of the violations, and take prompt actions to correct the violations and bring the products into compliance.

Sincerely yours,
/S/
Steven D. Silverman
Director
Office of Compliance
Center for Devices and
Radiological Health

More in Compliance Actions and Activities
Warning Letters
2015
2014
2013
2012
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Tobacco Retailer Warning Letters

Page Last Updated: 04/10/2015
Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
1-888-INFO-FDA (1-888-463-6332)

Contact FDA