DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993-0002

June 30, 2015

WARNING LETTER

VIA UPS EXPRESS

Jared Crocker
President, Nexus CMF
2825 E. Cottonwood Pkwy., Suite 330
Salt Lake City, UT 84121

Dear Mr. Crocker:

The Food and Drug Administration (FDA) approved TMJ Fossa-Eminence/Condylar Prosthesis System under P000023 on January 5, 2001 and approved TMJ Fossa-Eminence Prosthesis under P000035 on February 27, 2001. On February 4, 2011, FDA ordered TMJ Medical to conduct postmarket surveillance of the devices listed above, in accordance with section 522 of the Federal Food, Drug and Cosmetic Act (the Act) (21 U.S.C. § 360l), and Title 21 of the Code of Federal Regulations (CFR) Part 822.

This order (PS110002) was issued in response to Medical Device Reports (MDRs) submitted to FDA indicating that many of these implants were reported to be explanted after less than 3 years due to pain, which is considerably shorter than the expected minimum five-year life span of the device FDA is concerned that there is a shorter than expected time-to-failure with these devices. Additionally, it is unclear whether patients with partial implants will eventually need total implants or whether there are differences for time-to-failure between certain patient groups (such as patients with temporomandibular disease) or after revision of the initial implant.

History of Non-Compliance with Postmarket Surveillance Order

FDA has provided your firm with numerous opportunities to comply with the postmarket surveillance order and your firm has repeatedly submitted postmarket surveillance plans with serious deficiencies and has failed to keep FDA informed about the manufacturing and marketing of your devices in accordance with the terms of the conditional hold placed on your study.

In 2011, TMJ Medical submitted several study plans that were inadequate to answer the questions posed in the 522 order, as explained in FDA's responses to these proposals on April 28, 2011 and October 28, 2011. On February 10, 2012,

FDA sent TMJ Medical a letter informing it that its study plan was overdue and instructing it to submit copies of its overdue plan within 10 days.

On February 20, 2012, TMJ Medical informed FDA that it "has not sold and is not selling any devices at this time. Our manufacturing site is not as yet approved by FDA, and this is our highest priority." Based on this assertion, FDA sent TMJ Medical a letter on April 20, 2012 placing its 522 order on hold on the condition that TMJ Medical notify FDA within 10 days of initiating manufacturing and that TMJ Medical send a study plan in response to FDA's 522 order at that time. However, on January 31, 2013 TMJ indicated in its Periodic Annual Report for PMA P000023 for the reporting period of January 30, 2012 – January 31, 2013 that "Ten (10) TMJ Medical Fossa Eminence and Condylar Prosthesis Systems were sold in the reporting period." Thus, TMJ Medical violated the conditions of FDA's April 20, 2012 letter placing the 522 order on hold by failing to notify FDA within 10 days of initiating manufacturing and failing to send a study plan in response to FDA's 522 order at that time.

On June 21, 2013, FDA sent TMJ Medical a letter stating that it had come to our attention that you manufactured and distributed the devices between late October 2012 and June 2013, reminding TMJ Medical that it is obligated to complete the 522 study, and informing TMJ Medical that its study status would be marked as "Plan Overdue" on the Section 522 Postmarket Surveillance Studies webpage. On June 24, 2013, FDA received a letter from TMJ Medical explaining that it commenced manufacturing devices on June 6, 2011 and commenced distribution of devices on October 11, 2012. The letter concluded that FDA's 522 order was no longer on hold and included a 522 postmarket surveillance study plan for P000023 and P00035. Thus, even though the study hold was conditioned on TMJ Medical notifying FDA within 10 days of initiating *manufacturing*, and TMJ Medical had been manufacturing the devices since June of 2011, TMJ failed to notify FDA of this until June of 2013.

Although TMJ Medical was acquired by Nexus CMF on July 31, 2013, FDA was not informed of this until December 30, 2013 when Nexus CMF informed FDA that TMJ Medical changed its name to Nexus CMF through PMA amendments (P000023/A032 and P000035/A027). When TMJ Medical was acquired by Nexus CMF, the obligation to conduct postmarket surveillance in compliance with FDA's section 522 order (PS110002) transferred from TMJ Medical to Nexus CMF. *See* 21 CFR 822.26.

On August 23, 2013, FDA responded to TMJ Medical describing the deficiencies in the plan received on June 24, 2013, including but not limited to failure to provide the study objective or hypothesis, failure to define the study population, failure to provide detailed information on the type of study design, and failure to provide an acceptable endpoint that would answer the questions posed in the 522 order. On September 20, 2013, TMJ Medical submitted a revised study plan to FDA.

On February 7, 2014, FDA sent TMJ Medical a deficiency letter, emphasizing the need to submit two separate study plans, one for the total and one for the partial joint implants, as well as the need to include a list of study endpoints to address each of the six questions identified in FDA's 522 order and the need to justify TMJ Medical's choice of primary study endpoints, among other deficiencies. On April 7, 2014, Nexus CMF submitted a response to FDA's deficiency letter.

On June 13, 2014, FDA sent Nexus CMF another letter detailing continuing deficiencies with Nexus CMF's proposal and requesting additional information on several key aspects of the study design and how the proposed study would fulfill the original 522 order. On September 4, 2014, Nexus CMF submitted a revised study plan to FDA. This plan proposed a primary analysis for a period that the FDA determined is not sufficient given the permanent nature of this implant and the fact that failures of the device have been shown to occur at 5 years.

On November 6, 2014, FDA again issued further deficiency letters to Nexus CMF explaining, for example, the need to revise the proposal to continue the analytical phase of the study until the end of five years of follow-up and noting Nexus CMF's failure to justify a 10% non-inferiority margin. These letters gave Nexus CMF 30 days to respond. On February 20, 2015, Nexus CMF emailed FDA an update that it is "actively working on this, not just idly letting time go by," however, as of June 30, 2015, FDA has not received a substantive response regarding the deficiencies detailed in our November 6, 2014 letter. Thus, Nexus CMF continues to be out of compliance with the requirements detailed above for the study mandated under 522 order PS110002 and the study has not begun.

Appeal Options

If your firm disagrees with FDA's decision regarding your study plan submission, please note your appeal options under 21 CFR 822.22:

(a) If you disagree with us about the content of your plan or if we disapprove your plan, or if you believe there is a less burdensome approach that will answer the surveillance question, you may request review of our decision by:

(1) Requesting a meeting with the Director, Office of Surveillance and Biometrics, Center for Devices and Radiological Health (CDRH), who generally issues the order for postmarket surveillance;

(2) Seeking internal review of the order under 10.75 of this chapter;

(3) Requesting an informal hearing under part 16 of this chapter; or

(4) Requesting review by the Medical Devices Dispute Resolution Panel of the Medical Devices Advisory Committee.

Violations

Failure of a manufacturer to comply with requirements under section 522 of the Act, which includes requirements specified under 21 CFR Part 822, renders a device misbranded under section 502(t)(3) of the Act, 21 U.S.C. § 352(t)(3), and is a prohibited act under section 301(q)(1)(C) of the Act, 21 U.S.C. § 331(q)(1)(C). We have provided you ample opportunities over four years to submit adequate study plans, and you have failed to submit a plan that would address the questions in the section 522 order, failed to comply with the terms of the conditional hold, and failed to submit revised plans to FDA within the time frames specified in our deficiency letters, as required by 21 CFR 822.19. Therefore, Nexus CMF has committed a prohibited act under section 301(q)(1)(C) of the Act by failing to comply with requirements under section 522 of the Act, and your P000023 and P00035 devices are currently misbranded under section 502(t)(3) of the Act. It is also a prohibited act under section 301(a) of the Act to introduce or deliver for introduction a misbranded device into interstate commerce.

You should take prompt action to correct this violation. Failure to promptly correct this violation may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil money penalties. Please note that Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts.

Within fifteen (15) calendar days from the date you receive this letter, please submit your firm's section 522 postmarket surveillance study plan that addresses the deficiencies identified in FDA's letters dated November 6, 2014 and notify this office in writing of the specific steps you have taken to correct the noted violation. Include documentation of the corrective action you have taken. If your planned corrections will occur over time, please include a timetable for implementation of those corrections. If corrective action cannot be completed within 15 calendar days, state the reason for the delay and the time within which the corrections will be completed.

Your study plan and response to this letter should be sent to:

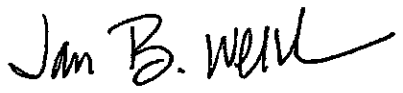
522 Postmarket Surveillance Studies Program
Food and Drug Administration
Center for Devices and Radiological Health
10903 New Hampshire Avenue
Building 66, Room 4278
Silver Spring, Maryland 20993-0002.

If you have any questions about the content of this letter please contact:

Stacey A. Priest, Consumer Safety Officer
CDRH, Office of Compliance
Division of Bioresearch Monitoring
Office: 301-796-5663
Email: Stacey.Priest@fda.hhs.gov

Finally, you should understand that there are many FDA requirements pertaining to the manufacture and marketing of devices. This letter pertains only to the issue of postmarket surveillance requirements for the devices subject to the February 4, 2011 order and does not necessarily address other obligations your firm has under the law.

Sincerely yours,



Jan B. Welch, MHS, MT (ASCP) SBB
Acting Director
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ECMS: S/M File: Nexus CMF D-A Crocker Spinal,-Salt Lake City, UT (FEI: 3010103543)

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Comments:

This warning letter is being written at the request of OSB to address non-compliance of Nexus CMF in providing an adequate response to the order for a 522 postmarket surveillance study of the TMJ Fossa-Eminence/Condylar