Collagen Matrix Inc 9/20/16

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Department of Health and Human Services

Public Health Service
Food and Drug Administration
New Jersey District Office
Central Region
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Parsippany, New Jersey 07054
Telephone: (973) 331- 4900
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WARNING LETTER

September 20, 2016

16-NWJ-15

VIA UNITED PARCEL SERVICE

Mr. Bareld J. Doedens
CEO
Collagen Matrix, Inc.
15 Thornton Road
Oakland, NJ 07436

Dear Mr.Doedens:

During an inspection of your firm, located in Oakland and Franklin Lakes, New Jersey, on November 9, 2015 through November 25, 2015, an investigator from the United States Food and Drug Administration (FDA) determined that your firm manufactures collagen-based finished devices for use in oral/maxillofacial surgery, neurosurgery and orthopedic-spine surgery. These devices include, but are not limited to, Porcine Anorganic Bone Mineral granules in plastic jars and syringes; Kontour Sustain Resorbable Collagen Membrane; OssiMend Bone Graft Matrix; NuOssXc Umbrella; and ZCORE Porcine Xenograft Particulate in Syringe. Under section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 32l(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 are intended to affect the structure or function of the body.

This inspection revealed that your firm's ZCORE Porcine Xenograft Particulate in Syringe device is 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 (QS) regulation found at Title 21, Code of Federal Regulations (CFR), Part 820.

We received a written response from Mr. Stuart A. Heit, Director, Quality Assurance, dated December 15, 2015, concerning our investigator's observations noted on the Form FDA 483 (FDA 483), List of Inspectional Observations, issued to your firm on November 25, 2015. We address this response below, inrelation to each of the noted violations. These violations include, but are not limited to, the following:

1. Failure to adequately conduct design validation to ensure that the device conforms to defined user need and intended uses, as required by 21 CFR 820.30(g). For example:

> A. The Instruction for Use for ZCORE Porcine Xenograft Particulate in Syringe indicates that the porcine material in the syringe is hydrated with osseous coagulum, patient blood or sterile normal saline by pulling and pushing the syringe plunger to draw and expel the blood or saline mixture. The firm conducted a functional assessment of the product by assessing the hydration using a saline solution and ease of deployment of the hydrated porcine material through the syringe tube using a **(b)(4)**. However, the design verification or validation study was not conducted to ensure that the product conforms to defined user needs and intended uses. Complaint No. CC-347, received on

9/4/15, indicates that Porcine Mineral in Syringe, Lot No. PMCSU15A1 and Lot No. PMCSUA2, were not ejecting smoothly from the syringes. MRB No. 0915-454, dated 9/16/15, and ICAR No. 1156, dated 11/14/15, indicate that Porcine Mineral in Syringe, Lot No. PMCSU15A1, was rejected because it was difficult to eject the porcine material from the syringe. The firm's memo to Correction and Removals File, dated 11/17/15, indicates that Porcine Mineral in Syringe, Lot No. PMCSU15A1 and PMCSU15A2, were removed from your firm's distributor before or on 11/17/15 due to the afore-mentioned syringe issue.

We reviewed your firm's response and determined that the response is inadequate at this time. We acknowledge that your response states that your firm will update QS.200b to more clearly define the requirements for design validation activities and conduct design validation on updated syringe-based products when production samples are available. Your Corrective/Preventive Action Request (ECAR #1168) report has proposed a completion date for 3/31/2016; however, your response does not provide any supporting documentation todemonstrate that the corrections have been completed.

Our inspection also revealed that the ZCORE Porcine Xenograft Particulate in Syringe is adulterated under section 501(f)(1)(B) of the Act, 21 U.S.C. § 351(f)(1)(B), because your firm does not have an approved application for premarket approval (PMA) in effect pursuant to section 515(a) of the Act, 21 U.S.C. § 360e(a), or an approved application for an investigational device exemption under section 520(g) of the Act, 21 U.S.C. § 360j(g) for the device as described and marketed. The ZCORE Porcine Xenograft Particulate in Syringe is also misbranded under section 502(o) of the Act, 21 U.S.C. § 352(o), because your firm did not notify the agency of your intent to introduce the device into commercial distribution in that a notice or other information respecting the modification to the device was not provided to the FDA as required by section 510(k) of the Act, 21 U.S.C. § 360(k), and 21 CFR 807.81(a)(3)(i).

Specifically, your firm made significant design changes to the MatrixOss Granules (ZCORE Porcine Xenograft Particulate) since its initial 510(k) clearance on July 16, 2014, and such changes could significantly affect the safety and effectiveness of this device. For example, FDA cleared the ZCORE Porcine Xenograft Particulate (K140714) for the delivery/packaging of the device in a plastic jar surrounded by outer blister package. However, your firm made a significant change to this device by including the delivery/packaging of the ZCORE Porcine Xenograft Particulate in a syringe and then markets the device as ZCORE Porcine Xenograft Particulate in Syringe. This change in packaging and delivery via the manufacturing process of the device presents biocompatibility and sterilization validation concerns and, thus, could significantly affect the safety and effectiveness of this device. For such a change, a 510(k) submission is required to demonstrate that the polymers used in the syringe applicator/packaging do not give off leachables or extractables that could contaminate the biocompatibility of the materials in the subject device.

Furthermore, sterilization validation via a 510(k) submission is required to demonstrate an acceptable sterility assurance level (i.e., SAL of 10-6) for the subject device in new syringe packaging, to be conducted for largest product model and packaging specifications under worst case considerations.

As another example, the ZCORE Porcine Xenograft Particulate in Syringe was released with the following modifications that would affect the syringe assembly: (1) teal color syringe plunger and (2) through-hole size of the perforated cap from **(b)(4)** in diameter. These design changes were not verified and/or validated to ensure that the device conforms to the defined user needs or intended use. Your firm has not notified the Agency of these significant changes, and a new 510(k) or supplement has not been submitted to date.

For a device requiring premarket approval, the notification required by section 510(k) is deemed satisfied when a PMA is pending before the agency. 21 CFR 807.81(b).The kind of information that your firm needs to submit in order to obtain approval or clearance for the device is described on the Internet at http://www.fda.gov/MedicalDevices/DeviceRegulationsandGuidance/HowtoMarketYourDevice/defa FDA will evaluate the information that your firm submits and decide whether the product may be legally marketed.

A follow up inspection will be required to assure that corrections and/or corrective actions are adequate.

Your firm should take prompt action to correct the violations addressed in this letter. Failure to promptly correct these violations may result in regulatory action being initiated by the FDA without further notice. These actions include, but are not limited to, seizure, injunction, and civil money penalties. Also, 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. Failure to adequately conduct design validation to ensure that the device conforms to defined user need and intended uses, as required by 21 CFR 820.30(g). Additionally, premarket approval applications for Class III devices to which the Quality System regulation violations are reasonably related will not be approved until the violations have been corrected. Request for Certificates to Foreign Governments will not be granted until the violations related to the subject device have been corrected.

Please notify this office in writing within fifteen (15) business days from the date you receive this letter of the specific steps your firm has taken to correct the noted violations, as well as an explanation of how your firm plans to prevent these violations, or similar violations, from recurring. Include documentation of these corrections and/or corrective actions (which must address systemic problems) that your firm has taken. If your firm's planned corrections and/or correction 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. Your firm's response should be comprehensive and address all violations included in this Warning Letter.

Your firm's response to this letter should be sent to: U.S. Food and Drug Administration, 10 Waterview Boulevard, 3rd Floor, Parsippany, New Jersey 07054. Refer to the Unique Identification Number **CMS #496451 when replying**. If you have any questions about the contents of this letter, please contact Charles J. Chacko, Compliance Officer, at 1-973-331-4946 (telephone) or 1-973-331-4969 (fax).

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 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 correctthe violations and bring the products into compliance.

Sincerely yours,
/S/
Craig W. Swanson
Acting District Director
New Jersey District

More in 2016

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http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2016/ucm522402.htm[10/6/2016 12:34:22 PM]