Nephros, Inc. 5/27/15

Department of Health and Human Services

Public Health Service
Food and Drug Administration
New Jersey District Office
Central Region
Waterview Corporate Center
10 Waterview Blvd. 3rd Floor
Parsippany, New Jersey 07054
Telephone: (973) 331-4900
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WARNING LETTER

May 27, 2015

VIA UNITED PARCEL SERVICE

Nephros Inc.
Attention: Mr. John Houghton, President & CEO
41 Grand Avenue, Suite 201
River Edge, New Jersey 07661-1947

15-NWJ-05

Dear Mr. Houghton:

During an inspection of your firm located in River Edge, New Jersey, on October 08, 2014 through October 24, 2014, an investigator from the United States Food and Drug Administration (FDA) determined that your firm manufactures medical devices

including, but not limited to: Dual Stage Ultrafilter (DSU); Single Stage Ultrafilter (SSU); OLpur H2H Hemodiafiltration System; and OLpur Mid-Dilution Series Heinodiafiltration System. 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 are intended to affect the structure or function of the body.

The inspection revealed that the 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 (cGMP) requirements of the Quality System (QS) regulation found at Title 21, Code of Federal Regulations (CFR), Part 820.

We received your written responses, dated November 13, 2014 and December 11, 2014; and responses from Mr. Greg Collins, Vice President R&D, dated January 9, 2015 and January 22, 2015, concerning our investigator's observations noted on the Form FDA 483, Inspectional Observations, issued to your firm on October 24, 2014.

We address these responses below, in relation to each of the noted violations. These violations include, but are not limited to, the following:

1. Failure to document the evaluation of potential suppliers as required by 21 CFR 820.50(a)(1).

For example, your firm evaluated potential suppliers based on a designated supplier type related to the services and/or products provided. Review of your vendor list found that not all suppliers had questionnaires completed and/or a quality agreement in order that your firm is made aware of changes to products and/or services. Quality oversight of your suppliers will ensure that your firm is made aware of changes which may affect the quality of the finished device. Examples of active suppliers who had not been adequately evaluated included a supplier used for sterilization of your finished devices and suppliers of dialyzers and dialysis equipment.

It should also be noted that deficiencies in purchasing controls had also been observed during the previous inspection of your firm.

We reviewed your firm's responses and conclude that they are not adequate. We acknowledge that your firm created CAPA 13-014, dated 09/06/2014, and CAPA 14-030, dated 10/27/2014, which included the reduction of your approved supplier list to reflect only those vendors that are actually involved in the production of your medical devices. You also revised your SOP 7.4, Purchasing and Monitoring/Supplier Monitoring Controls, dated 01/08/2015, to more clearly define your supplier types. You identified your contract manufacturer as being the responsible party for sterilization of your medical devices as they contract this service out, therefore, they

were removed from the approved supplier list. Please be advised that as the owner and 510(k) holder of medical devices, your firm is responsible for oversight of all manufacturing operations and, therefore, has regulatory responsibility for the quality and safety of the medical devices that you market and distribute.

2. Failure to include required information in your records of complaint investigations as required by 21 CFR 820.198(e).

For example, your SOP 8.2.1, Customer Feedback, Complaint Handling & Monitoring, dated 01/23/2014, Section 9.5, states that the initial investigation shall be documented on the customer complaint form and, based on the nature of the complaint, must include: evaluation of the returned product or inventory retention samples; review of in-house device history records; review of shipping records; review of complaint trends; review of risk controls; and/or review of product labeling. Your complaint investigations were observed to be inadequate in that they were lacking critical information, as evidenced by the following customer complaints including, but not limited to:

a) #2014.01.01: Complaint involved the In-Line Dual Stage Ultrafilter (DSU) which had bacterial and endotoxin counts at the machine post filter. The investigation failed to include label reviews, inventory analysis, and trend analysis.
b) #2014.03.04: Complaint involved the In-Line Single Stage Ultrafilter (SSU) which had a filter leak around the spout. The investigation failed to include label reviews, inventory analysis, and trend analysis.
c) #2014.08.04: Complaint involved the OLpur H2H Hemodiafiltration Module Substitution Filter which failed an integrity test on the module. The investigation failed to include DHR review, inventory analysis, and trend analysis.

It should also be noted that deficiencies in complaint handling had also been observed during the previous inspection of your firm.

We reviewed your firm's responses and conclude that the adequacy of your responses cannot be determined at this time. Your responses stated that you initiated CAPA 14-020, dated October 26, 2014, and CAPA 14-029, dated 10/27/2014, in order to improve the complaint handling process. Your firm also revised SOP 8.2.1, Customer Feedback, Complaint Handling & Monitoring, dated 11/11/2014, and the Customer Feedback/Complaint Form F-8.2, which requires that there shall not be any unaddressed sections or blank fields on the complaint form. Additionally, your responses stated that you conducted a retrospective review of all 2013 and 2014 complaints to ensure forms were completed. Your response includes the complaint numbers reviewed, but failed to include the actual customer complaint files, in order to provide supporting evidence that your complaint files were updated. We will review your revised procedures and ensure that they are implemented in addition to verifying that all complaint files/investigations include critical information, during the next

inspection.

FDA also noted nonconformances with section 502(t)(2) of the Act [21 U.S.C. § 352(t)(2)], which are deficiencies pertaining to the Medical Device Reporting (MDR) Regulation found at Title 21, Code of Federal Regulations (CFR), Part 803. These nonconformances include, but are not limited to, the following:

1. Failure to include the following information in your firm's reports, if known or reasonably known to your firm, as described in 21 CFR 803.50(b). This type of information corresponds generally to the format of FDA Form 3500A: "Date of event," (Form 3500A, Block 3B), as required by 21 CFR 803.52(b)(3).

Specifically, your firm submitted 33 MDRs to the FDA that did not identify the "Date of event" in Block B3 of the FDA Form 3500A. In addition, your firm did not include in Block H11- "Corrected data", of the associated 3500A forms, an explanation of why the required information was not provided and the steps taken to obtain such information.

We acknowledge that your response, dated November 13, 2014, states that you had submitted 33 supplemental MedWatch reports to CDRH's MDR Policy Branch on November 12, 2014. However, your response, dated December 11, 2014, is not adequate. Your firm submitted a revised MDR procedure titled" "US-MDR, EU-MVR, Canada-MPR, Advisory Notices & Recalls", SOP 806, Rev B, dated December 4, 2014. Although the revised procedure includes instructions for completing the FDA Form 3500A, the following additional issues need to be addressed:

(1) "US-MDR, EU-MVR, Canada-MPR, Advisory Notices & Recalls", SOP 806, does not establish internal systems that provide for timely and effective identification, communication, and evaluation of events that may be subject to MDR requirements. For example:

a. The procedure omits the definition of the term "reasonably suggests," found in 21 CFR 803.20(c)(1). The exclusion of the definition for this term from the procedure may lead your firm to make an incorrect reportability decision when evaluating a complaint that may meet the criteria for reporting under 21 CFR 803.50(a).

(2) "US-MDR, EU-MVR, Canada-MPR, Advisory Notices & Recalls", SOP 806, does not establish internal systems that provide for timely transmission of complete medical device reports.
Specifically, the following is not-addressed:

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

(3) "US-MDR, EU-MVR, Canada-MPR, Advisory Notices & Recalls", SOP 806, does not describe how your firm will address documentation and record-keeping requirements, including:

a. Documentation of adverse event related information maintained as MDR event files.

b. Information that was evaluated to determine if an event was reportable.

c. Documentation of the deliberations and decision-making processes used to determine if a device-related death, serious injury, or malfunction was or was not reportable.

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 fmal rule will take effect on August 14, 2015. If your firm is not currently submitting reports electronically, we encourage you to visit the following web link 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.

A follow up inspection will be required to assure that correction 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 reguiatory action being initiated by the FDA without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil money penalties. Also, federal agencies may be advised ofthe 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 violations are reasonably related.will not be approved until the violations have been corrected. Requests for Certificates to Foreign Government will not be granted until the violations related to the subject devices 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, as well as 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. 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 Blvd, 3rd Floor, Parsippany, New Jersey 07054 (re: CMS #449134). If you have any questions about the contents of this letter, please contact Stephanie Durso, Compliance Officer, at 1-973-331-4911 (phone) or 1-973-331-4969 (fax).

Finally, you should know that this letter is not intended to be an all-inclusive list ofthe 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/
Diana Amador-Toro
District Director
New Jersey District

More in 2015

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Contact FDA