Cook Inc. 9/16/14

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Detroit District
300 River Place
Suite 5900
Detroit, MI 48207
Telephone: 313-393-81 00
FAX: 313-393-8139

WARNING LETTER
2014-DET-16

September 16, 2014

VIA UPS

Mr. Kem Hawkins, President
Cook, Inc.
750 North Daniels Way
Bloomington, Indiana 47404-9120

Dear Mr. Hawkins:

During an inspection of your firm located in Bloomington, Indiana, from June 17 through July 16, 2014, Investigators from the United States Food and Drug Administration (FDA) determined that your firm manufactures vascular implants, intravascular catheters and related systems. 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 any function of the body.

This inspection revealed that your firm's 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 your firm's responses, dated August 7, 2014 and September 12, 2014, concerning our Investigator's observations noted on the Form FDA 483 (FDA 483), Inspectional Observations, which was issued to your firm. We address this response below, following the noted violations.

These violations include, but are not limited to, the following:

1. Failure to validate, with a high degree of assurance and approve according to established procedures, a manufacturing process that cannot be fully verified by subsequent inspection and testing, to ensure the process will continue to meet specifications, as required by 21 CFR 820.75(a). For example, your firm's process validations are inadequate in that:

A. Your firm's officials were unable to provide a justification for the Performance Qualifications (PQ) sample size for your Radio Frequency Company (RFC) B Machine WW, Cook ID #3064 (Q 1688 R2) and RFC Machine XX, Cook ID #3062 (Q 1688 R31), and the sample size utilized does
not demonstrate that the Catheter Tip Bonding process is repeatable and reproducible with a high degree of assurance. For example:

a. Your firm collected 2 samples from 30 lots for the Cp calculation however, the lot sizes ranged from 18 to 99 devices. A sample selection of 2 per lot could not be traced back to valid statistical rationale and your firm's protocol for collecting samples for analysis did not indicate how validation samples were selected. Therefore, it cannot be determined if the samples were collected in a manner that would make them representative of the lot.

B. Your firm did not maintain documentation of the settings that were used in the Performance Qualifications (PQ) for RFC Bonding Machines XX, Cook ID #3062 and WW, Cook ID #3064.

C. Your firm's Sets/Bonder Settings Specification for Bonding Machine X, Cook ID# 1237, lists settings for twenty-six different materials, but your firm has performed a validation for only 1 of them, HNB-5.0-GBT. For example, validation has not been complete for the following materials that are utilized regularly to manufacture your

firm's devices:

a. Material 30316-A-1: Heat (%) - 16±3; Time (seconds) - 6.0±3; Dwell (seconds) - 6 REF; and Cylinder Pressure (psi) - 5 REF.
b. Material 50094-10.2: Heat (%) - 16-17.5 REF; Time (seconds) - 3.8-4.1 REF; Dwell (seconds) - 15 REF; and Cylinder Pressure (psi) - 6 REF.
c. Material WCLT16.5D-GJS: Heat (%) - 14-15; Time (seconds) - 15.1±0.5; Dwell (seconds) - 16 REF; and Cylinder Pressure (psi) - 17.5 REF.

2. Failure to establish and maintain procedures for monitoring and control of process parameters for validated processes to ensure the specified requirements continue to be met, as required by 21 CFR 820.75(b). For example, your firm's process monitoring for validated processes is inadequate in that:

A. From July 01, 2012 to June 18, 2014, 186,468 devices were identified as being "built incorrectly" and scrapped by the quality control department for catheter tip bonding, but these failures are not currently traced back to determine the actual failure rates for your firm's 52 bonding machines. This does not allow for an accurate assessment of whether the bonding process continues to be repeatable and reproducible. Additionally, your firm does not perform revalidation testing or any other form of process monitoring for any of your bonding machines.

B. Your firm performs process monitoring on forty-four validated processes that are considered critical however; this monitoring is required to be performed once every 5 years and evaluations for revalidation have not occurred since the initial validations of these processes. This frequency does not provide for sufficient detection and mitigation of process drifts.

3. Failure to establish and maintain procedures for implementing Corrective and Preventive Action (CAPA,) as required by 21CFR 820.100. For example:

A. Your firm failed to adequately analyze all sources of quality data to identify existing and potential causes or nonconforming product as required by 21 CFR 820.100(a)(1). For example:

a. Your firm scrapped 545,914 in-process medical devices across all device families from the third quarter of 2012 through the second quarter of 2014 however; this information was not included as an input into your analysis of quality data sources under the CAPA system.
b. A review of your firm's scrap data across all in-process devices revealed three spikes in July 2012, November 2012, and April 2013 where each spike consisted of over 20,000 devices being scrapped for "Built Incorrectly", but your firm decided not to open a CAPA based on your assessment of this data. From July 2012 to June 2014, all other months averaged approximately 2,000

scrapped devices.

c. Despite the on-going occurrence of foreign matter across all of your firm's in-process and distributed devices, your firm decided not to open a CAPA based on your assessment of the following quality data:

i. 236,706 production units were scrapped due to foreign matter.
ii. 171,581 production nonconformances were identified as having foreign matter.
iii. 3,066 complaints identified foreign matter in sterile devices.

B. Your firm failed to adequately investigate the cause of nonconformities relating to product, processes and the quality system, as required by 21 CFR 820.100(a)(2). For example:

a. Your firm's analysis of quality data does not allow you to detect and adequately take action to address quality problems. From June 1, 2012 to June 18, 2014, your firm identified 735,385 production nonconformances across all device families that were trended to reject definitions. However, these definitions do not identify the cause of the problem so that it can be addressed. For example:

i. Your firm identified 38,916 nonconformances as Reject Definition "506" for "Damaged," that is defined as "Flawed in some physical manner that may potentially result in loss of device function or customer dissatisfaction."
ii. Your firm identified 28,842 nonconformances as Reject Definition "340" for "Seal, Package, Incomplete" which is defined as "Sealing process did not complete its cycle resulting in an insufficient seal".

C. Your firm failed to verify or validate the corrective action to ensure that such action is effective and does not adversely affect the finished device, as required by 21 CFR 820.100(a)(4). For example:

a. Your firm took 4 corrective actions to address quality problems however, verification or validation of the corrective actions to ensure the actions were effective and did not adversely affect the finished device was not conducted for the following projects:

i. Project BM070213 changed catheter labels from a paper backing to a synthetic backing to decrease foreign matter in production.
ii. Project BMO12813 replaced a swager production machine due to multiple manufacturing problems.
iii. Project BM110612-1 improved tipping ability.
iv. Project BM061313 implemented the use of a flexor measurement.

4. Failure to establish and maintain procedures for acceptance of incoming products to ensure conformance with specified requirements, as required by 21 CFR 820.80(b). For example, your firm's receiving inspections are inadequate in that, from January through June 2014, your firm accepted pre-bifurcated grafts from raw material suppliers despite 100% of the grafts requiring reworking due to crotch stitching defects. A sample of 214 device history records (DHRs) for AAA devices manufactured using part # 290147 and 290141 revealed that all 214 of the grafts had documented crotch rework performed.

5. Failure to establish and maintain procedures to control product that does not conform to specified requirements as required by 21 CFR 820.90(a). For example, your firm's nonconformance system is inadequate in that:

A. From June 1, 2012 to June 18, 2014, your firm identified 735,385 nonconformances across all device families however; you did not evaluate and, where necessary, investigate those nonconformances. Your firm's evaluation involves associating the nonconformance with a reject definition however, the definitions do not adequately identify the cause of the problem so that it can be addressed.

B. Nonconformances found prior to Quality Control inspections are not identified and documented, and therefore, the exact number cannot be quantified. Nonconformances found prior to Quality Control Inspections are routinely taken to the group leader, who takes them to the individual responsible for the nonconformance for reworking. Devices that are reworked in this manner are not documented as nonconformances and are therefore not quantified.

C. Your firm identified 186,468 devices that were scrapped for "built incorrectly" across all device families from July l, 2012 to June 18, 2014 however; there was no identification of specifically what was built incorrectly for each device and this data could not be reconciled to the 735,385 nonconformances to ensure that all nonconforming devices were accounted for.

6. Failure to establish and maintain written sampling plans based on valid statistical rationale and that are adequate for their intended use, as required by 21 CFR 820.250(b). For example, your firm's sampling plan for incoming inspection of woven graft materials is not based on a valid statistical rationale. Your firm's procedure entitled "Incoming Inspection of Graft Material procedure, Document #QC_1660" Version 3, requires a sample size of 1 for each lot of woven graft materials, regardless of the lot size that is received. From January 19, 2014 to June 19, 2014, your firm has received 6,068 pieces of pre-bifurcated woven graft material and the size of each lot ranged from 2 to forty-one pieces.

7. Failure to establish and maintain procedures to ensure that all purchased or otherwise received product and services conform to specified requirements, as required by 21 CFR 820.50. Your firm receives woven graft material for use in your Abdominal Aortic Aneurysm (AAA) devices and accepts them, in part, under Certificates of Conformance (COC), but these COCs do not demonstrate or indicate conformance to your firm's Material Specification for Woven Graft Material (Document #MS_708, Version No.: 9). For example:

A. Your firm's Material Specification for Woven Graft Material requires suppliers to test for Gauge (Thickness) and Water Permeability. The supplier Certificate of Conformance dated 31.05.11 for pre-bifurcated graft material batch numbers 123836, 124253/2, and 124253/3 states "The devices were manufactured in accordance with Specification Number CEOO1 Revision No. 2". Review of the supplier's Specification Number CE001 Revision No. 2 revealed that Gauge (Thickness) and Water Permeability were not listed as requirements in the specification. Gauge (Thickness) and Water Permeability are not tested at incoming inspection or at any other point in the manufacturing process.

B. Your firm's Material Specification for Woven Graft Material states the Fabric Yarn Count must be 139±9 picks/inch and 146±12 ends/inch. The supplier's Specification Number CE001 Revision No.2 specifies the weave construction as 54±2 picks/cm and 40±2 ends/cm which is approximately 137±5 picks/inch and 102±5 ends/inch, respectively.

For each of the noted violations, we are unable to determine the adequacy of your firm's response dated August 7, 2014 and September 12, 2014. Your firm's response did not include documentation or evidence of the corrective actions. Also note that anticipated completion dates beyond April 2015 are unacceptable. Please reconsider those timelines.

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. 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 Governments will not be granted until the violations related to the subject devices have been corrected.

We request that you submit your plan for corrective actions based on this correspondence in writing, within fifteen (15) business days from the date you receive this letter, to the following address:

Food and Drug Administration
Detroit District Office
300 River Place, Suite 5900
Detroit, Michigan 48207

If you have any questions about the content of this letter, please contact: CDR Kimberly Martin at (317) 226-6500 ext. 116.

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 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,
/S/
Art O. Czabaniuk
Acting District Director
Detroit District Office