Biomedix, Inc. 6/14/13

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Detroit District
300 River Place
Suite 5900
Detroit, MI 48207
Telephone: 313-393-8100
FAX: 313-393-8139

WARNING LETTER
2013-DET-18

June 14, 2013

VIA UPS

Myra J. Bender
President
Biomedix, Inc.
3895 West Vernal Pike
Bloomington, IN 47404

Dear Ms. Bender:

During an inspection of your firm located in Bloomington, Indiana,on February 5, 2013, through March 4, 2013, investigators from the United States Food and Drug Administration (FDA) determined that your firm manufactures the Select-3 Intravenous (IV) Administration Set. Under section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 321(h), this product is a device because it is intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or it is intended to affect the structure or function of the body.

This inspection revealed that this 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, its 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 Myra J. Bender, President, dated March 21, 2013, 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, in relation to each of the noted violations. We have also received your update to your FDA 483 response dated May 16, 2013. This update will be collectively considered as, in part, to this warning letter.

The violations found during the inspection and subsequent review, include, but are not limited to, the following:

1. Failure to establish and maintain adequate procedures to control the design of the device as required by 21 CFR 820.30, for example:

A. Your firm has not established and maintained procedures to control the design of the device in order to ensure that specified design requirements are met, as required by 21 CFR 820.30(a).

B. Your firm has made design changes to the SELEC-3 IV Administration Set without establishing and maintaining procedures for the identification, documentation, validation or where appropriate, verification, review and approval of the changes before implementation, as required by 21 CFR 820.30(i).

C. You have not maintained a design history file that documents the design changes made during the

life of your SELEC-3 IV Administration Set, as required by 21 CFR 820.30(j).

Your firm's response dated March 21, 2013, is not adequate as objective evidence of implementation of corrective action was not submitted for review.

2. Failure to establish and maintain adequate procedures for implementing corrective and preventive actions, as required by 21 CFR 820.100(a). For example, your firm's CAPA system is inadequate in that:

A. From January 1, 2010 to December 31, 2012, your firm documented **(b)(4)** scrapped components from your SELEC-3 IV Set manufacturing process (excluding barrel tubes) however, this data has not been analyzed or investigated to determine the cause or if there are any existing or potential quality problems in your manufacturing process.

The adequacy of your response, dated March 21, 2013, cannot be determined at this time. Your response states you will further revise CAPA Procedure Q8034-OA to include the sources of data that will be reviewed and the frequency of review by June 28, 213. However, you should also ensure your CAPA policy includes all of the elements included in 21 CFR 820.100 to include the statistical methodology that will be utilized to analyze quality data where necessary, the implementation and recording of changes in methods and procedures needed to correct and prevent identified quality problems, and ensuring that information related to quality problems or nonconforming product is disseminated to those directly responsible for assuring the quality of the product or prevention of the problems.

3. Failure to adequately ensure that, where the results of a process cannot be fully verified by subsequent inspection and testing, the process shall be validated with a high degree of assurance and approved according to established procedures, as required by 21 CFR 820.75(a). For example:

A. Your firm utilizes **(b)(4)** as the method of sterilization for your SELEC-3 IV Administration Sets, but you have not validated the sterilization process to determine the parameters that would consistently achieve the desired Sterility Assurance Level without negatively impacting the product.

B. Your firm produces your SELEC-3 IV Administration Sets on semi-automated processes that have not been validated, using the following equipment:

1. **(b)(4)**
2. **(b)(4)**
3. **(b)(4)**
4. **(b)(4)**
5. **(b)(4)**
6. **(b)(4)**
7. **(b)(4)**

The adequacy of your response, dated March 21, 2013, cannot be determined at this time. Your response states you have initiated the process of reviewing a validation protocol and will implement validation of the sterilization process and equipment by June 28, 2013. Your response also indicates you will begin **(b)(4)** dose auditing to substantiate the sterilization dose by **(b)(4)**.

4. Failure to establish and maintain adequate procedures to control product that does not conform to specified requirements, as required by 21 CFR 820.90(a). For example, from January 2, 2012 to December 21, 2012, your firm documented **(b)(4)** scrapped components from the SELEC-3 IV Administration Set manufacturing process, however, no evaluation of the scrapped components was conducted to determine the need for an investigation and notification of the persons or organizations responsible for the nonconformance.

Your firm's response dated March 21, 2013, is not adequate as objective evidence of implementation of corrective action was not submitted for review.

5. Failure to establish and maintain process control procedures that describe any process controls necessary to ensure conformance to specifications, as required by 21 CFR 820.70(a). For example:

A. Your firm has not established procedures for equipment settings to be utilized during the manufacturing of your Select-3 IV Administration Sets and the settings of equipment used in your production area are not consistent across similar pieces of equipment. For example, for the gluers utilized to apply adhesive to the barrel tube and allow the selectable drop chamber to be assembled **(b)(4)** had input settings of **(b)(4)** seconds at **(b)(4)** psi **(b)(4)** had settings of **(b)(4)** seconds at **(b)(4)** psi, and **(b)(4)** had settings of **(b)(4)** seconds at **(b)(4)** psi.

B. You are not following your standard operating procedures to ensure that a device conforms to specifications. For example, the **(b)(4)** procedure, M3001-0A Rev. 5, states the conveyor speed should be set "**(b)(4)**". During this inspection, the investigator observed the **(b)(4)**, to be set at a speed setting of **(b)(4)** during manufacturing on February 5, 7, and 8, 2013. According to your production supervisor, who stated she was the only one authorized to make changes in the conveyor speed, she was told to use the speed of 2.5 years ago and has done so every since, despite the existence of the conflicting setting in your **(b)(4)**.

Your firm's response dated March 21, 2013, is not adequate as objective evidence of implementation of corrective action was not submitted for review.

6. Failure to establish and maintain adequate schedules for the adjustments, cleaning, and other maintenance of equipment to ensure that manufacturing specifications are met. Maintenance activities including the date and individual(s) performing the maintenance activities, shall be documented as required by 21 CFR 820.70(g)(1). For example:

A. Your "Facility and Equipment -Maintenance and Housekeeping" procedure, S8016-0A, states that all maintenance tasks must be recorded in the Monthly Maintenance Form, F8016-0A, and performed with the frequency stated in F8016-0A. Instead, according to your firm's officials, maintenance activities have been performed "as needed" and have been recorded on a loose-leaf paper log in the production area.

B. Your firm does not calibrate equipment as required. Calibration stickers and documentation for the **(b)(4)** burst tester (Serial: cannot be determined), **(b)(4)**, and **(b)(4)** (Serial: **(b)(4)**) state the equipment was due for annual calibration on " 7/16/2008", "8/9/2011", and "1/29/2003" respectively however, there is no documentation to demonstrate this equipment was calibrated on or since those dates.

Your firm's response dated March 21, 2013, is not adequate as objective evidence of implementation of corrective action was not submitted for review.

7. Failure to establish and maintain procedures to ensure that all purchased or otherwise received products or services conform to specified requirements, as required by 21 CFR 820.50(a). For example, you have not established requirements, including quality requirements that must be met by your suppliers and have not documented your evaluation of suppliers.

Your firm's response dated March 21, 2013, is not adequate as objective evidence of implementation of corrective action was not submitted for review.

8. Failure to establish and maintain procedures for quality audits and to 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. These quality audits shall be conducted by individuals who do not have direct responsibility for the matters being audited, as required by 21 CFR 820.22. For example: your Quality Audits procedure (Q8029-0B, Rev. 1) states "A 'Quality Audit is to be conducted on a **(b)(4)** schedule to review and evaluate the effectiveness of the Biomedix Quality System," however, according to your firm's officials, you have not conducted a quality audit since 2002.

Your firm's response dated March 21, 2013, is not adequate as objective evidence of implementation of corrective action was not submitted for review.

9. Failure of management with executive responsibility to review the suitability of the quality system at defined intervals and with sufficient frequency according to established procedures, as required by 21 CFR 820.20(c). For example: your Management Responsibility procedure (Q8029-0A Rev. 1) is inadequate in that it does not include provisions for management review or govern the management review process. In addition, management with executive responsibility has not reviewed the suitability and effectiveness of your firm's quality system at defined intervals and with sufficient frequency to ensure that it satisfies the quality system regulation.

Your firm's response dated March 21, 2013, is not adequate as objective evidence of implementation of corrective action was not submitted for review.

10. Failure to establish and maintain procedures to control all documents that are required by 21 CFR § 820.40 (a). Specifically, your firm did not document the approval date or the signature of the approving official for your "Reclamation and Reprocessing of Spike Lines (SLA) and Patient side lines (PSA)" and "Biomedix Raw Material Inventory Control" procedures. Also, procedure "S8016-OA" specifies maintenance and housekeeping requirements for your firm's equipment and facility however, the procedure was not available at a location for which it was designated, used, or otherwise necessary. Furthermore, any changes to these documents have not been recorded as required by 21 CFR § 820.40 (b).

The adequacy of your response, dated March 21, 2013, cannot be determined at this time. Your response states your firm is currently reviewing your firm's procedures, to include your document control procedure, updating or making them obsolete as appropriate, and this will be completed by September 30, 2013. Your response also states your "Biomedix Raw Material Inventory Control" memorandum will be replaced with an updated procedure by June 28, 2013.

Our inspection also revealed that the Selec-3 Intravenous (IV) Administration Sets are 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 (IDE) under section 520(g) of the Act, 21 U.S.C. § 360j(g). The Selec-3 Intravenous (IV) Administration Sets are also misbranded under section 502(o) the Act, 21 U.S.C. § 352(o), because your firm did not notify the agency of its 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), 21 U.S.C. § 360(k), and 21 C.F.R. 807.81(a)(3)(i). Specifically, your firm has modified the Selec-3 Intravenous (IV) Administration Sets originally cleared under K901949, K925645 and K961928 by providing customers with an ordering system to alter the device through various options and configurations. Our review of your website revealed a provision for selectable length of IV tubing, an optional vented spike, optional luer activated y-sites, and optional needleless luer y-sites. These features were not part of the original 510(k). Depending on the configuration of the new components and

customization, the functionality of the device can change beyond what was 510(k) cleared. These combinations of features can alter the performance of the device and require a new 510(k) submission. For a device requiring premarket approval, the notification required by section 510(k) of the Act, 21 U.S.C. § 360(k), is deemed satisfied when a PMA is pending before the agency [21 C.F.R. 807.81(b)]. The kind of information you need to submit in order to obtain approval or clearance for your device is described on the Internet at http://www.fda.gov/cdrh/devadvice/3122.html. The FDA will evaluate the information you submit and decide whether your product may be legally marketed.

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. 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.

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 (including any systemic corrective actions) 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 should be sent to: CDR Kimberly Y. Martin, Compliance Officer at Food and Drug Administration, Detroit District Office, 300 River Place, Suite 5900, Detroit, Michigan 48207. CDR Martin can be reached at 317-226-6500 ext. 116 if you have any questions about this correspondence.

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/
Glenn T. Bass
District Director
Detroit District Office

Page Last Updated: 07/03/2013
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
Ph. 1-888-INFO-FDA (1-888-463-6332)
Email FDA