Sentara Enterprises 8/8/16

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Baltimore District Office
Central Region
6000 Metro Drive, Suite 101
Baltimore, MD 21215
Telephone: 410-779-5455
Fax: 410-779-5705

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

WARNING LETTER
August 8, 2016

Linda Huffer, President
Sentara Enterprises Inc., dba Sentara Home Infusion Pharmacy Services
535 Independence Pkwy, Suite 200
Chesapeake, VA 23320

Dear Ms. Huffer,

Between July 13, 2015, to July 23, 2015, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility, Sentara Enterprises Inc., dba Sentara Home Infusion Pharmacy Service, located at 535 Independence Pkwy, Suite 300, Chesapeake, VA 23320-5176. This inspection was conducted in response to information received from the Virginia Department of Health regarding an investigation of two cases of *Leuconostoc* bacteremia in two pediatric patients after receiving Total Parenteral Nutrition (TPN) products produced by your firm.

During the inspection, the FDA investigators observed serious deficiencies in your practices for producing sterile drug products, which put patients at risk. For example, our investigators observed rust on HEPA filter grills as well as rusted vents of hoods used during aseptic production. Our investigators also observed poor aseptic practices, including an operator transferring materials into a hood without being disinfected. Furthermore, your firm failed to demonstrate through appropriate studies that your aseptic processing areas are able to provide adequate protection of the ISO 5 areas in which sterile products are processed.

FDA collected environmental samples at multiple locations in your firm, including the aseptic processing areas. Testing results of the samples identified microbial contamination in the aseptic processing areas, including spore-forming bacteria. Therefore, your products may be produced in an environment that poses a significant contamination risk.

FDA issued form FDA 483 to your firm on July 23, 2015. FDA acknowledges your firm's response to the form FDA 483, dated August 13, 2015 as well as your additional responses dated September 18, 2015, and November 25, 2015.

Based on this inspection, it appears that you are producing drugs that violate the Federal Food, Drug, and Cosmetic Act (FDCA).

A. Violations of the FDCA

Adulterated Drug Products

The FDA investigators observed that your drug products intended or expected to be sterile were prepared, packed, or held under insanitary conditions, whereby they may have become contaminated with filth or rendered injurious to health, causing them to be adulterated under section 501(a)(2)(A) of the FDCA [21 U.S.C. §351(a)(2)(A)]. For example, our investigators observed rust on HEPA filter grills as well as rusted vents of hoods used during aseptic production. Our investigators also observed poor aseptic practices, including an operator transferring materials into a hood without being disinfected. Furthermore, your firm failed to demonstrate through appropriate studies that your aseptic processing areas are able to provide adequate protection of the ISO 5 areas in which sterile products are processed.

FDA collected environmental samples at multiple locations in your firm, including the aseptic processing areas. Testing results of the samples identified microbial contamination in the aseptic processing areas, including spore-forming bacteria. Therefore, your products may be produced in an environment that poses a significant contamination risk.

Under section 301(a) of the FDCA the introduction or delivery for introduction into interstate
commerce of any drug that is adulterated is a prohibited act. Further, it is a prohibited act under section 301(k) of the FDCA [21 U.S.C. § 331(k)] to do any act with respect to a drug, if such act is done while the drug is held for sale after shipment in interstate commerce and results in the drug being adulterated.

B. Corrective Actions

We acknowledge your action taken on September 17, 2015, to cease compounding sterile drug products and voluntarily recall all sterile drug products within expiry. FDA has been informed that your firm resumed sterile compounding operations on November 26, 2015. We further acknowledge your response to the form FDA 483 Inspectional Observations, dated August 13, 2015 as well as your additional responses dated September 18, 2015, and November 25, 2015. Although several of your proposed corrective actions appear adequate, others are deficient. For example, in response to FDA's adverse environmental findings, you indicated that your rusted

hoods were removed, cleared all cleanroom areas as operational, and provided your third party environmental sampling results. However, you did not adequately investigate adverse environmental findings to identify root causes to determine how contamination was introduced to your cleanroom. As a result, you cannot demonstrate that the corrective actions you took are appropriate to prevent recurrence of the insanitary.

In addition, in response to FDA's adverse environmental findings, you indicated that you have reviewed your cleaning process and adopted a new cleaning policy. However, from review of this policy, it is not clear what the required contact time of your sporicidal agent will be to ensure adequate disinfection of the ISO 5 areas. Moreover, it is unclear if the multiple cycles of cleaning and disinfection performed by your firm, to achieve the third party environmental results described above, will be included in your updated cleaning policy.

In response to our observation of inadequate smoke studies, you stated that "All future testing with outside testing operators will be scheduled during peak dept. operations to assure full dynamic testing interpretation and functional operations meet this compliance requirement." In addition, you provided your third party certification reports. However, you did not provide adequate documentation for our review, such as a detailed description of the conditions at the time of the smoke studies or videos of the smoke studies, to show that these studies were performed under dynamic conditions.

In response to our observation of inadequate personnel monitoring, you stated, regarding fingertip testing, that "any failed 1st attempts are immediately retested due to possible improper manipulation of testing paddles." From your response, it is unclear whether you will be evaluating the ability of the operator to don gloves without contaminating them. The first samples may contain meaningful data, which your firm should be evaluating. In addition, you stated that you have established department guidelines for fingertip testing. However, you did not provide the referenced guidelines in your response; therefore, we cannot fully assess the adequacy of your response.

FDA strongly recommends that your management immediately undertake a comprehensive assessment of your operations, including facility design, procedures, personnel, processes, materials, and systems. In particular, this review should assess your aseptic processing operations. A third party consultant with relevant sterile drug manufacturing expertise could be useful in conducting this comprehensive evaluation.

C. Conclusion

The violations cited in this letter are not intended to be an all-inclusive statement of violations at your facility. You are responsible for investigating and determining the causes of the violations identified above and for preventing their recurrence or the occurrence of other violations. It is your responsibility to ensure that your firm complies with all requirements of federal law, including FDA regulations.

You should take prompt action to correct the violations cited in this letter. Failure to promptly correct these violations may result in legal action without further notice, including, without limitation, seizure and injunction.

Within fifteen working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to correct the violations. Please include an explanation of each step being taken to prevent the recurrence of violations, as well as copies of related documentation. If you do not believe that the products discussed above are in violation of the FDCA, include your reasoning and any supporting information for our consideration. If you cannot complete the corrective actions within 15 working days, state the reason for the delay and the time within which the corrections will be completed. Please address your reply to:

CDR Rochelle B. Young, RPh, MSA
Compliance Officer
FDA Baltimore District Office
U.S. Food and Drug Administration
Baltimore District Office
6000 Metro Drive, Suite 101
Baltimore, MD 21215

If you have questions regarding any issues in this letter, please contact CDR Young via email at Rochelle.Young@fda.hhs.gov or by phone at (410) 779-5437.

Sincerely,
/S/
Evelyn Bonnin
District Director
Baltimore District

cc: Virginia Department of Health
cc: Virginia Board of Pharmacy