Triad Isotopes Inc. 3/10/15

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Southwest Region
Kansas City District
6050 Marshall Drive
Suite 205
Lenexa, Kansas 66214-1524
913-495-5100

UPS
RETURN RECEIPT REQUESTED

WARNING LETTER

CMS # 480877

March 10, 2016

Marc Pfefferle, CEO
Triad Isotopes, Inc. Corporate Headquarters
4205 Vineland Road
Orlando, FL 32811

Dear Mr. Pfefferle:

From January 5, 2015, to January 9, 2015, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility, Triad Isotopes, Inc., located at 712 Westport Road, Kansas City, Missouri.

During the inspection, the investigators observed serious deficiencies in your practices for producing sterile drug products, which put patients at risk. For example, our investigators observed that your operators processed sterile drug products wearing non-sterile gloves and non-sterile forearm covers. In addition, your firm's environmental monitoring program is inadequate to ensure that the aseptic manipulations of sterile drugs products and components in the ISO 5 hood do not compromise the sterility of the finished product. Furthermore, our investigators found the design and operation of the ISO 5 laminar flow hoods is not adequate to prevent disruption of clean unidirectional airflow during aseptic operations. Specifically, your hoods were modified to accommodate **(b)(4)** permanently mounted **(b)(4)** that are below the HEPA filters. Therefore, your products may be produced in an environment

that poses a significant contamination risk. FDA issued a Form FDA 483 to your firm on January 9, 2015. FDA acknowledges receipt of your firm's response to the Form FDA 483 dated January 29, 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 drug products in your facility that were 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 your drug products to be adulterated under section 501(a)(2)(A) of the FDCA. For example, our investigator observed that:

1. Your operators use non-sterile gloves and non-sterile forearm covers donned in an unclassified area not supplied by HEPA filtered air.

2. Your firm's environmental monitoring program is inadequate to ensure that the aseptic manipulations of sterile drugs products and components in the ISO 5 hood do not compromise the sterility of the finished product. Specifically, no viable air monitoring was conducted for a period of approximately 9 months, and personnel monitoring only occurs every **(b)(4)**, even though aseptic operations occur **(b)(4)**.

3. The design and operation of your ISO 5 laminar flow hoods are not adequate to prevent disruption of clean unidirectional airflow during aseptic operations. The inside of the working area of your hoods was modified to accommodate **(b)(4)** permanently mounted **(b)(4)** that are below the HEPA filters to the side of the critical ISO 5 area. Also, the loosely fitting plastic covers designed to protect the **(b)(4)** from sanitizing agents is not an appropriate design to facilitate cleaning.

4. There are no magnehelic gauges installed on your **(b)(4)** primary ISO 5 laminar hoods to confirm that they are operational.

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 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

In your response to the Form FDA 483 inspectional observations, dated January 29, 2015, you describe certain corrective actions you took to address the observations. Although several of your proposed corrective actions that address the identified insanitary conditions appear adequate, others are deficient. Regarding the use of

non-sterile gloves, you stated that according to a study you reference in the response, there is no difference between sterile gloves and non-sterile gloves that are repeatedly disinfected with sterile **(b)(4)**. Your response states that you believe your firm is in full compliance with USP Chapter <797>. However, USP Chapter <797> requires the use of"sterile powder-free gloves," and we believe the failure to use sterile gloves contributes to the insanitary conditions at your firm.

To address your environmental monitoring program deficiencies, you committed to complete viable air monitoring **(b)(4)** from the date of your response and to set up a **(b)(4)**. However, you only use settling plates for air sampling, and no active air samplers, and this is inadequate.

Furthermore, regarding the inadequate facility design of your ISO 5 area, you state that the area has been certified and complies with all applicable regulations. However, **(b)(4)** and other equipment in the critical ISO 5 space could pose a significant problem in the quality of air during production. Further, certification reports state that your firm has design deficiencies and is not in compliance with USP <797> requirements for sterile preparations. In addition, you did not commit to monitor the airflow in the laminar flow hoods. We believe that these conditions also contribute to the insanitary conditions observed at your facility.

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 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. Your written notification should be addressed to:

Danial Hutchison, Compliance Officer
FDA Kansas District Office
U.S. Food and Drug Administration
8050 Marshall Drive, Suite 205

Lenexa, KS 66214

If you have questions regarding any issues in this letter, please contact Mr. Hutchison via email at danial.hutchison@fda.hhs.gov or by phone at (913) 495-5154.

Sincerely,
/S/
Cheryl A. Bigham
District Director
Kansas District

cc:
Joe Huber, RPh., BCNP
Pharmacy Manager
Triad Isotopes, Inc.
712 Westport Road
Kansas City, MO 64111