WARNING LETTER

Vega Life Sciences Private Limited

MARCS-CMS 604469 — JUNE 17, 2020

Delivery Method:

VIA UPS

Product:

Drugs

Recipient:

Mr. Venkata Reddy Kurre

Managing Director

Vega Life Sciences Private Limited

Plot Number D-15, 16, 21 & 22, Phase-I, I.D.A. Pashamylaram
Patencheru 502307 Telangana
India

Issuing Office:

Center for Drug Evaluation and Research | CDER

United States

Warning Letter 320-20-39

June 17, 2020

Dear Mr. Kurre:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Vega Life Sciences Private Limited, FEI 3015658387, at Plot No. D-15, 16, 21 & 22, Phase-I, I.D.A. Pashamylaram, Patencheru (M), Sangareddy District, Telangana, from November 25 to 28, 2019.

This warning letter summarizes significant deviations from current good manufacturing practice (CGMP) for active pharmaceutical ingredients (API).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your API are adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B).

We reviewed your December 19, 2019, response to our Form FDA 483 in detail and acknowledge receipt of your subsequent correspondence.

During our inspection, our investigators observed specific deviations including, but not limited to, the following.

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1. Failure to control and monitor solvent recovery procedures to ensure that solvents meet

appropriate standards before reuse in API manufacturing.

Our inspection found that your firm acts as a contract solvent recovery facility for your customer's **(b)(4)** API manufacturing operations. Solvents recovered at your facility include **(b)(4)**.

Your firm failed to establish and follow procedures to evaluate and control impurity risks associated with your solvent recovery operations. For example:

Inadequate Testing of Recovered Solvents

Your firm failed to follow your gas chromatography (GC) test method procedure for recovered **(b)(4)**. The procedure requires use of a standard for ensuring the batch meets the Identification by GC recovered solvent specification. We reviewed analytical data packages for approximately **(b)(4)** batches of recovered **(b)(4)** processed by your firm in 2019 and found they lacked chromatograms representing the use of a standard. Furthermore, your firm stated to the investigators that standards were never run during GC analysis of recovered **(b)(4)** in 2018 and 2019.

In your response, you provided no explanation for this deviation and made no commitment to investigate the scope of this deficiency to determine if other test methods or procedures were not followed. Your response also lacked a risk assessment to determine potential product impact.

Failure to Establish an Impurity Profile for Recovered Solvents or Investigate Extraneous Peaks in Chromatograms

Your firm failed to establish an impurity profile for recovered solvents and maintain appropriate oversight of your operations for the control of unknown impurities. Extraneous peaks were observed in more than **(b)(4)** batches of recovered **(b)(4)** processed at your facility between 2018 and 2019. The batches were released by your firm without investigation and you failed to inform your customer of any potential impurities. You stated that your customer instructed you to focus only on the peak representing the recovered solvent, however this is not adequate. Unknown peaks observed in chromatograms of recovered solvents may represent unanticipated impurities that can impact the quality of your customer's API and should be thoroughly investigated.

Your response is inadequate. Your evaluation of the extraneous peaks observed in recovered solvent chromatograms was not comprehensive and did not include a thorough manufacturing evaluation to determine if your solvent recovery operations contributed impurities to the recovered solvent.

During the inspection, your firm provided a written statement indicating that you had terminated processing recovered solvents for customers. However in your response you indicated that all future customer products would include quality agreements, which suggests that you may resume such operations in the future. Your firm has not provided sufficient details or procedures to demonstrate the capability of predicting, controlling, testing, and preventing impurities or cross contamination associated with your solvent recovery processes.

In response to this letter, provide the following:

• A comprehensive investigation into your firm's failure to follow internal procedures including test methods. Include a detailed description of the scope and root causes of your lapses and list all associated corrective actions with timeframes for completion.

• A detailed plan describing how you will implement an ongoing program for evaluating the effectiveness of your solvent recovery operations monitoring process control to ensure stable manufacturing and prevention of unanticipated impurities during solvent recovery operations.
Vega Life Sciences Private Limited, Telangana FEI 3015658387 page 3

• A procedure requiring an impurity profile analysis and risk assessment for all solvent recovery operations. The scope of the procedure should include recovered solvents for internal and external use.

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• An updated procedure for handling unknown peaks in chromatograms.

2. Failure to have adequate cleaning procedures to prevent contamination or carry-over of a material that would alter the quality of the API.

The cleaning of your nondedicated manufacturing equipment used to recover customer solvents including **(b)(4)** is inadequate. Your firm failed to ensure that your cleaning procedure was sufficient to prevent carryover or contamination for nondedicated equipment used to recover spent solvents. Your firm stated during the inspection that these requirements were not met. Additionally, your firm stated that there were no records to document cleaning of nondedicated equipment used to process recovered solvents including product changeover cleaning.

In your response, you provided examples of equipment cleaning records but did not include an explanation or justification regarding why you told our investigators during the inspection that these documents did not exist.

Your response also failed to include a thorough evaluation designed to ensure that all equipment including nondedicated storage, receiving, and charging tanks were properly cleaned according to approved procedures.

In response to this letter, provide the following:

• A corrective action and preventive action (CAPA) plan, based on the retrospective assessment, that includes appropriate remediations to your cleaning processes and practices, and timelines for completion. Provide a detailed summary of vulnerabilities in your process for lifecycle management of equipment cleaning. Describe improvements to your cleaning program including enhancements to cleaning effectiveness, improved ongoing verification of proper cleaning execution for all products and equipment, and all other needed remediations.

• Appropriate improvements to your cleaning program, with special emphasis on incorporating conditions identified as worst case in your drug manufacturing operation. In addition, describe the steps that must be taken in your change management system before introduction of new manufacturing equipment or new manufacturing operations.

• A summary of updated SOPs that ensure an appropriate program is in place for cleaning procedures for products, processes, and equipment.

• A comprehensive investigation into your firm's CGMP documentation practices. Include a detailed description of the scope and root causes of your documentation lapses and list all associated corrective actions with timeframes for completion.

3. Failure to exercise sufficient controls over computerized systems to prevent unauthorized access or changes to data and failure to have adequate controls to prevent omission of data.

Your firm failed to implement adequate controls to ensure the integrity of data generated at your facility including:

• Missing raw data files associated with recovered solvent testing were observed in folders on the local hard drive of the operating system connected to the GC instrument. Your firm indicated that the files appear to have been deleted.

• Quality Control analysts shared the same username and password for the operating system on each workstation and the analytical software for the GC.

• Recovered solvent data on the stand-alone computerized system for the GC were not backed up as required per your approved procedure.

• Your firm did not have a procedure governing the audit trail or its retention. During the inspection, the GC analytical software was configured to retain the audit trail for only **(b)(4)**.

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Your firm failed to include a comprehensive, systematic plan for evaluating your practices and procedures to ensure data integrity controls are applied throughout your firm. Additionally, you failed to conduct a risk assessment addressing potential impacts to product as a result of the inadequate data integrity controls.

Data Integrity Remediation

Your quality system does not adequately ensure the accuracy and integrity of data to support the safety, effectiveness, and quality of the drugs you manufacture. See FDA's guidance document *Data Integrity and Compliance With Drug CGMP* for guidance on establishing and following CGMP compliant data integrity practices at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/data-integrity-and-compliance-drug-cgmp-questions-and-answers-guidance-industry (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/data-integrity-and-compliance-drug-cgmp-questions-and-answers-guidance-industry).

We strongly recommend that you retain a qualified consultant to assist in your data integrity remediation. In response to this letter, provide the following:

• A comprehensive investigation into the extent of the inaccuracies in data records and reporting including results of the data review for drugs distributed to the United States. Include a detailed description of the scope and root causes of your data integrity lapses.

• A current risk assessment of the potential effects of the observed failures on the quality of your drugs. Your assessment should include analyses of the risks to patients caused by the release of drugs affected by a lapse of data integrity and analyses of the risks posed by ongoing operations.

• A management strategy for your firm that includes the details of your global CAPA plan. The detailed corrective action plan should describe how you intend to ensure the reliability and completeness of all data generated by your firm including microbiological and analytical data, manufacturing records, and all data submitted to FDA.

CGMP Consultant Recommended

Based upon the nature of the deviations we identified at your firm, we strongly recommend engaging a consultant qualified to evaluate your operations and to assist your firm in meeting CGMP requirements if your firm intends to resume manufacturing drugs for the U.S. market. We also recommend that the qualified consultant perform a comprehensive audit of your entire operation for CGMP compliance and that the consultant evaluates the completion and efficacy of your corrective actions and preventive actions before you pursue resolution of your firm's compliance status with FDA.

Your use of a consultant does not relieve your firm's obligation to comply with CGMP. Your firm's executive management remains responsible for resolving all deficiencies and systemic flaws to ensure ongoing CGMP compliance.

Solvent Recovery Operations Terminated

We acknowledge your commitment to terminate processing recovered solvents for customers at this facility for the U.S. market. If you plan to resume producing recovered solvents for the U.S. supply chain, notify this office in writing.

Conclusion

The deviations cited in this letter are not intended to be an all-inclusive list of deviations that exist at your facility. You are responsible for investigating and determining the causes of these deviations and for preventing their recurrence or the occurrence of other deviations.

FDA placed your firm on Import Alert 66-40 on April 14, 2020.

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Until you correct all deviations completely and we confirm your compliance with CGMP, FDA may withhold approval of any new drug applications or supplements listing your firm as a drug manufacturer.

Failure to correct these deviations may also result in the FDA continuing to refuse admission of articles manufactured at Vega Life Sciences Private Limited at Plot No. D-15, 16, 21 & 22, Phase-I, I.D.A. Pashamylaram, Patencheru (M), Sangareddy District, Telangana into the United States under section 801(a)(3) of the FD&C Act, 21 U.S.C. 381(a)(3). Articles under this authority may be subject to refusal of admission, in that the methods and controls used in their manufacture do not appear to conform to CGMP within the meaning of section 501(a)(2)(B) of the FD&C Act, 21 U.S.C. 351(a)(2)(B).

After you receive this letter, respond to this office in writing within 15 working days. Specify what you have done since our inspection to correct your deviations and to prevent their recurrence. If you cannot complete corrective actions within 15 working days, state your reasons for delay and your schedule for completion.

Send your electronic reply to CDER-OC-OMQ-Communications@fda.hhs.gov

Please identify your response with FEI 3015658387 and ATTN: Rory Geyer.

Sincerely,
/S/

Francis Godwin
Director
Office of Manufacturing Quality
Office of Compliance
Center for Drug Evaluation and Research

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