Vipor Chemicals Private Ltd. 1/29/19

U.S. FOOD & DRUG ADMINISTRATION

10903 New Hampshire Avenue
Silver Spring, MD 20993

Via UPS
Return Receipt Requested

Warning Letter 320-19-11

January 29, 2019

Mr. Popatlal S. Patel
Chairman and Managing Director
Vipor Chemicals Private Ltd.
#301, Ivory Terrace, R.C. Dutt Road
Baroda, 390007
India

Dear Mr. Patel:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Vipor Chemicals Private Ltd. at 218 GIDC Makarpura, Vadodara, Gujarat, from February 21 to 24, 2018.

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

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your drugs 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 have not received a response from your firm regarding corrective actions for the deviations identified during the inspection.

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

1. Failure to transfer all quality or regulatory information received from the API manufacturer to your customers.

Your quality unit omitted the name and address of the original manufacturer of your API on certificates of analysis (COA) you issued to your customers. For example, the COA for **(b)(4)**, batch number **(b)(4)**, does not list the name and address of the original API manufacturer, Basic Pharma Life Science Private Ltd., Ankleschwar (Gujarat), India.

FDA placed this supplier on Import Alert 99-32 for refusing an FDA foreign establishment inspection on October 10, 2017. You should be aware of your suppliers' regulatory status prior to purchasing and distributing API from them. Customers and regulators rely on COA for information about the quality and source of drugs and their components. Omitting information from COA compromises supply chain accountability and traceability and may put consumers at risk.

See **Guidance for Industry *ICH Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients* (https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073497.pdf)** for more information on how API from original manufacturers as well as API repackagers and relabelers should be labeled, and clearly identify the original API manufacturer as the API moves through the supply chain. The guidance can be found at the following website: **http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/U (https://www.fda.gov/downloads/Drugs/.../Guidances/ucm073497.pdf)CM073497.pdf. (https://www.fda.gov/downloads/Drugs/.../Guidances/ucm073497.pdf)**

In response to this letter, provide:

- A written procedure regarding generation of COA, including controls you have implemented to demonstrate that the COA you generate and issue include the required information about original manufacturers.
- A retrospective review to determine how your failure to provide required information may have affected drug quality.
- Any actions you have taken or will take, such as notifying customers, recalling drugs, or invalidating previously issued COA for any drugs still within their labeled retest dates; and a recently issued COA that includes the required information, as well as a batch certificate.

2. Failure to have the procedures and processes necessary to ensure the API manufactured at your facility meet established specifications for quality and purity.

Batch Control
You do not have a procedure to control the issuance, usage, and reconciliation of batch manufacturing records (BMRs). Your production personnel record manufacturing activities in personal notebooks or on draft BMRs. Production managers then transcribe the data onto another BMR, which is then circulated to the production operators and supervisors for their signatures. Production management stated that drafts are incinerated in a wood burner. Your firm's representative asked our investigator why such a practice was problematic.

Investigations
You do not have procedures to investigate deviations, out-of-specification (OOS) results, out-of-trend (OOT) results, and stability failures.

In response to this letter, provide:

- A comprehensive, independent risk assessment of production records including but not limited to a thorough review of the documentation to determine the completeness, consistency, and accuracy of reported data. Indicate how you

determined that the data you used to release drugs was attributable, legible, contemporaneously recorded, an original or true copy, and accurate.

- A complete assessment of documentation systems used throughout your manufacturing and laboratory operations to determine where documentation practices are insufficient. Include a detailed corrective action and preventive action (CAPA) plan that comprehensively remediates documentation practices and ensures you retain complete, contemporaneously prepared, and accurate records.
- A comprehensive assessment of your system for investigating deviations, discrepancies, complaints, OOS results, and stability failures. Also include a retrospective review of manufacturing and laboratory records for all drugs shipped to the U.S. market. If discrepancies are found, provide the associated investigation, root cause analysis and product impact assessment.

3. Failure to establish and follow adequate written procedures for cleaning equipment and its release for use in the manufacture of API.

The cleaning procedure posted on the wall in the API manufacturing area indicated only water is used for cleaning. Your production manager stated this cleaning method is common for API manufacturing equipment. You did not have data to show that this is adequate.

Our investigator observed production equipment you use to manufacture **(b)(4)** API tagged as "**(b)(4)**," even though it was visibly encrusted with black, **(b)(4)**, and **(b)(4)** residue. We also observed rust on filtration unit and mixing tank surfaces that come into contact with API, as well as other equipment and facility cleaning and maintenance issues.

In response to this letter, provide:

- A comprehensive plan to evaluate the adequacy of cleaning procedures, practices, and validation studies for each piece of manufacturing equipment used to manufacture more than one product.
- Scientific rationale for your cleaning validation strategy to ensure the efficacy of your cleaning procedures is adequately assessed.
- A summary of your cleaning validation protocol which incorporates conditions identified as worst case. This should include but not be limited to evaluating drugs that are of highest toxicity, drugs that are lowest solubility in their cleaning solvents, drugs that have characteristics that make them difficult to clean, and swabbing of various equipment locations that are most difficult to clean.

4. Failure to demonstrate that the water used in the manufacture of your API is suitable for its intended use.

You have not validated your **(b)(4)** water system which was installed more than **(b)(4)** ago. Your firm has not demonstrated that you can effectively control, maintain, sanitize, and monitor the system so it consistently produces pharmaceutical-grade water that, at a minimum, meets the USP monograph for **(b)(4)** water. You use water from this unvalidated system as a component in your drugs.

Your limited testing of the water produced by this system is inadequate. It is imperative that you routinely test water for chemical properties, such as total organic carbon and conductivity, and microbiological attributes.

In response to this letter, provide a plan and timeframes for validating your water system and ensuring appropriate design, control, maintenance, and monitoring of your water system.

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. We also recommend that

the qualified consultant perform a comprehensive audit of your entire operation for CGMP compliance and evaluate the completion and effectiveness 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.

Conclusion

Deviations cited in this letter are not intended as an all-inclusive list. You are responsible for investigating these deviations, for determining the causes, for preventing their recurrence, and for preventing other deviations.

FDA placed your firm on Import Alert 66-40 on July 11, 2018.

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

Failure to correct these deviations may also result in FDA continuing to refuse admission of articles manufactured at Vipor Chemicals Private Ltd. at 218 GIDC Makarpura, Vadodara, Gujarat, into the United States under section 801(a)(3) of the FD&C Act, 21 U.S.C. 381(a)(3). Under the same authority, articles 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 (mailto:CDER-OC-OMQ-Communications@fda.hhs.gov)** or mail your reply to:

W. DeVore Irick
Compliance Officer
U.S. Food and Drug Administration
White Oak Building 51, Room 4235
10903 New Hampshire Avenue
Silver Spring, MD 20993
USA

Please identify your response with FEI 3003090962.

Sincerely,
/S/
Francis Godwin
Acting Director
Office of Manufacturing Quality
Office of Compliance
Center for Drug Evaluation and Research

More in Warning Letters

(/ICECI/EnforcementActions/WarningLetters/default.htm)