

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION			
DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov		DATE(S) OF INSPECTION 03/23/2023-03/28/2023 FEI NUMBER 3015345351	
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED Mr. More Santosh, Factory Manager			
FIRM NAME Zen Chemicals Pvt. Ltd.		STREET ADDRESS D-5, MIDC, Phase-2, Manpada Road	
CITY, STATE, ZIP CODE, COUNTRY Dombivili, Maharashtra, India 421203		TYPE ESTABLISHMENT INSPECTED Critical API Intermediate Manufacturer	
This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.			
<i>The observations noted in this Form FDA-483 are not an exhaustive listing of objectionable conditions. Under the law, your firm is responsible for conducting internal self-audits to identify and correct any and all violations of the quality system requirements.</i>			
DURING AN INSPECTION OF YOUR FIRM I OBSERVED: OBSERVATION 1 Equipment are not cleaned and sanitized to prevent contamination of the critical API intermediate product. Specifically, your firm failed to complete a clean and dirty hold time study and to establish clean and dirty hold times for (b) (4). Additionally, you failed to ensure that you are able to clean and remove the previous manufactured critical API intermediate with no carryover during changeover cleaning using non-dedicated equipment. On March 13 and 14, 2023, I observed, during the facility walkthrough, the following equipment used to manufacture U.S. marketed critical API intermediate were observed visibly dirty. This includes multiple critical API intermediate contact surfaces. All equipment noted below were in a cleaned state during my visual observation and are non-dedicated. In addition, you do not perform a cleaning verification (e.g. swabbing) of the equipment after material changeover cleaning. A. (b) (4) residue on the inside of the (b) (4) and (b) (4) as well as (b) (4) and (b) (4) residues on the corner of the (b) (4) were observed on product contact surface, the inside side of the (b) (4) equipment # ZEN/MC/P-56 located in the (b) (4) area. Batch to Batch cleaning was conducted on March 14, 2023.			
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- B. (b) (4) residue in the (b) (4) and below the bowl of the (b) (4) and (b) (4) and (b) (4) residue in the (b) (4) of the (b) (4) were observed on the (b) (4) equipment # ZEN/MC/P-31 located in the (b) (4) area. Batch to Batch cleaning was conducted on March 13, 2023.
- C. (b) (4) residue around the circumference of the bowl of the (b) (4) were observed on the (b) (4) equipment # ZEN/MC/P-62 located in the (b) (4) area. Batch to Batch cleaning was conducted on March 13, 2023.
- D. Rust like residue on the (b) (4) and shaft were observed on product contact surface, of the (b) (4) equipment # ZEN/MC/P-44 located in the (b) (4) area. The equipment completed a Batch to Batch cleaning on March 13, 2023.
- E. Rust like residue on the inside and outside of the (b) (4) were observed on product contact surface of the (b) (4) equipment # (b) (4) located in the (b) (4) area. Both the equipment completed a Batch to Batch cleaning on March 25, 2023
- F. On March 25 and 26, 2023, (b) (4) replicate swab samples of the residue from the cleaned, non-dedicated (b) (4) (equipment # (b) (4) (equipment # ZEN/MC/P-56), (b) (4) (ZEN/MC/P-44) and (b) (4) (equipment # (b) (4) were collected and analyzed for (b) (4) and (b) (4). The (b) (4) samples were analyzed on March 25 and 26, 2023. On March 26, 2023, the results of the analysis were as provided, and they are as follows:

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Sample No	Equipment Used	Equipme nt No	Found Product Name	Concentrati on Observed	Limit (Product to	Last Product Manufactu
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(b) (4)

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(b) (4)			
OBSERVATION 2 No investigations are conducted to evaluate all potential root causes of multiple sample results. Specifically, in reviewing your firm HPLC and GC computerized analytical data from 2021 -2023, you failed to investigate the following: A. Three (3) separate analysis were rerun on HPLC equipment # QC/INST/09. 1. The first set of samples consisted of (b) (4) injections which were analyzed on December 7-8, 2021 for calibration. The (b) (4) injections were rerun due to wrong vial number. 2. The second set of samples consisted of (b) (4) injections and were analyzed on June 2, 2022 for stability of (b) (4). The (b) (4) injections were rerun due to wrong preparation of sample. 3. The third set of samples consisted of (b) (4) injections which were analyzed on February 5, 2023 for stability of (b) (4). The (b) (4) injections were rerun due to wrong column was used for analysis. According to Assistant QC Manager, the samples were reanalyzed due to analysts error and no investigation was conducted. B. According to a QC Officer, the Gas Chromatograph (equipment # QC/INST/09) sporadically generates more files than the actual analysis that is performed. Therefore, the analyst selects the (b) (4) samples that are generated from the analysis and uses the selected files as the final samples. The QC Officer			
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added that they do not know why this occurs and when the extra files are generated, and no investigation was conducted for this occurrence (s).

OBSERVATION 3

Appropriate controls governing computer acquired data and/or related systems have not been established to assure that changes and access to computerized software for the laboratory control system is accessed only by authorized personnel.

Specifically, on March 23 and 27, 2023, I observed,

- A. UV which uses software UV Probe 2.70 (equipment # QC/INST/13) does not have audit trail capabilities. This equipment is used for the identification of (b) (4) which is shipped to the US.
- B. GC which uses Chrome 2004 crt software (equipment # QC/INST/08) has a common user name and password shared by four (4) employees. The GC is used for analyzing the purity of solvents.
- C. HPLC which uses Chromeleon 6.80 software (equipment # QC/INST/09) has a user name "cmadmin" that is used by at least two (2) employees. This user name gives the employee the ability to change the rights of users; which includes the ability of data deletion. This equipment is used for Assay & (b) (4) impurity content for (b) (4) and related substances of (b) (4) which is shipped to the US.
- D. Your firm's back up of electronic data is inadequate and does not conform to your firm's Data backup procedure QC/SOP/GEN/59, document titled, 'Standard Operating Procedure for Backup of Electronic Data', with issued date January 30, 2020.
 - Your firm uses unprotected portable hard drives to store electronic data for HPLC, GC and UV.
 - According to Administrator Manager / IT the electronic data that is backed up on to the portable hard drive is overridden each time a backup is conducted. The previous data is lost.

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- ### OBSERVATION 4

Specifically,

According to section 7.8.4 of your SOP, QA/SOP/GEN/39, document titled, 'Standard Operating Procedure for Qualification of Facility / Equipment's / System' states, that QA in coordination with user department and Engineering department shall conduct PQ.

OBSERVATION 5

Employees are not trained in cleaning procedures.

Specifically,

Your firm failed to train your employees who perform cleaning, verify that cleaning is adequate and recheck and approve cleaning equipment and sign final cleaning batch to batch or product to product documentation. In reviewing employee's training records, approximately six (6) employees were deficient in training on cleaning SOP, TR/15/05/013. During the inspection, six (6) equipment were found with product residue. This includes equipment such as the (b) (4) and (b) (4)

***DATES OF INSPECTION**

03/23/2023 (Thu), 03/25/2023 (Sat), 03/26/2023 (Sun), 03/27/2023 (Mon), 03/28/2023 (Tue)

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgment, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."