DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov	02/10/2025-02/18/2025
	FEI NUMBER 3003747558

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

A. Chandrasekar, Vice President- Operations

FIRM NAME	STREET ADDRESS
Orchid Pharma Limited	Plot Nos. 121-128, 128A-133, 138-151, 159-164, SIDCO Industrial Estate
CITY, STATE, ZIP CODE, COUNTRY Alathur, Chengalpattu District - 603110, Tamil Nadu, INDIA	TYPE ESTABLISHMENT INSPECTED API 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.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

Your firm's cleaning processes for non-dedicated equipment have not been adequately established and validated.

Specifically,

You manufacture [redacted] for the US market in your [redacted] Sterile Plant in not dedicated manufacturing equipment, including but not limited to; [redacted] (ID's # [redacted]1802, [redacted]1801), [redacted] (ID# [redacted]1801), [redacted] (ID # [redacted]1803), [redacted] (ID's # [redacted]1801, [redacted]1802), [redacted] (ID # [redacted]1801). You validated the cleaning procedure as per your cleaning validation report, Document Number CVR [redacted]/0003, Effective date 12/7/2017. Your cleaning validation did not establish the clean hold time (CHT) and sterile hold time (SHT) such that there is no assurance that your manufacturing equipment are free of/meet the specifications for microbiological and endotoxin levels at the time of manufacturing.

The [redacted] stage of the manufacturing process involves [redacted] operation in [redacted] ID # [redacted] 1801. Review of your manufacturing records confirmed that after sterilization [redacted] you held your [redacted] for [redacted] before starting the [redacted] operation (**Table 1**).

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	Rajiv R. Srivastava -S Digitally signed by Rajiv R. Srivastava -S Date: 2025.02.18 16:20:57 +05'30'	Rajiv R Srivastava, CSO	02/18/2025

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Table 1 Equipment hold time for (b) (4) 1801 (b) (4)

You do not have data to assure the sterility of (b) (4) 1801 prior to start of the manufacturing operation. Between 2021 and 2023, you manufactured and shipped at least (b) (4) batches of API, (b) (4) totaling > (b) (4) to the US market.

OBSERVATION 2

You have not established the written procedure to ensure that your process can perform effectively and reproducibly to manufacture an intermediate or API meeting its predetermined specifications and quality attributes.

Specifically,

A. You have attempted to concurrently validate the manufacturing of (b) (4) (b) (4) as per your Report No. CPVR (b) (4) /001 Effective date 6/28/2019. You (b) (4) three process validation batches in (b) (4) ach batch was loaded equally across all the (b) (4) (in (b) (4) in each (b) (4) You sampled the material for (b) (4) analysis (for in process control) as described in your procedure, In-process Sampling from (b) (4) SOP No. PRD.14.06.08 Version No. 008 Effective date 6/1/2024. The sampled materials from each (b) (4) were collected (b) (4) (b) (4) sample for the (b) (4) The (b) (4) data represents average across

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all the (b) (4) and does not provide the uniformity of the (b) (4) across all the (b) (4)

B. You have attempted to concurrently validate the manufacturing of (b) (4) as per your Report No. CPVR (b) (4) 0001 Effective date 7/28/2021. The (b) (4) of one of the intermediate, (b) (4) is caried out in (b) (4) ID # (b) (4) 701 (b) (4) and (b) (4) 704 (b) (4) Your batch records did not have information as to how much material was loaded in each (b) (4) Your Production Manager (S) stated that the (b) (4) are loaded equally as per your procedure, Operation of (b) (4) SOP No. PRD.00.01.08 Version 007 Effective date 9/1/2023.

According to your respective batch records, you used (b) (4) samples for the analysis of (b) (4) (b) (4) as per your sampling procedure, In Process Sampling Procedure SOP No. PRD.00.01.11 Version No. 006 Effective date 10/7/2024. The (b) (4) data represents average across the sampled (b) (4) and does not provide the uniformity of the (b) (4) across all the (b) (4)

OBSERVATION 3

Appropriate qualification of critical equipment and ancillary systems are not completed according to established specifications.

Specifically,

A. You (b) (4) in (b) (4) ID's # (b) (4) (b) (4) The operation qualification of these (b) (4) is achieved through (b) (4) (b) (4) studies as documented in Report No. (b) (4) Effective date 9/25/2024. The (b) (4) is carried out according to the Procedure for (b) (4)

Distribution Study in (b) (4) SOP No. PRD.14.01.43 Version No. 002 Effective date 7/1/2024. The procedure suggested that the (b) (4) was carried out without (b) (4) and the (b) (4) data logger sensors were directly fixed/placed on the (b) (4) of the (b) (4) You have used these (b) (4) in the manufacturing of (b) (4) that is used in the manufacturing of (b) (4) for the US market.

B. You attempted to validate the manufacturing of (b) (4) in a (b) (4) ID # (b) (4) 303. (b) (4) the batch at (b) (4) is one of the critical process parameters. The initial operation qualification of the (b) (4) is missing the data for (b) (4) from the corresponding OQ Report No. OCPL/PRD/ROQ (b) (4) 303/R00 Effective dated 2/6/2003. On 8/17/2022, you replaced the (b) (4) 303 with (b) (4) 716 as evidenced by closure of the respective change control, CCIF No. 067-22P. This new (b) (4) is equipped with (b) (4) You did not qualify (b) (4) 716 for the (b) (4) as evident in the corresponding operation qualification Report No. OQR (b) (4) 716/0001 Effective date 7/5/2022. You routinely manufacture (b) (4) that is used in the manufacturing of (b) (4) (b) (4) for the US market.

C. You manufacture (b) (4) in (b) (4) ID # (b) (4) 1801. The manufacturing process consists of (b) (4) the batch at (b) (4) Your Senior Manager Quality Assurance (b) (6) stated that the firm did not have initial qualification report and shared the Requalification Report No. RQR (b) (4) 1801/0001 Effective date 1/18/2022. As per the report, you verified the (b) (4) by operating the (b) (4) in (b) (4) settings; (b) (4) This verification was done without any loading and duration of each (b) (4) is not known. You also did not verify the (b) (4) with any calibrated equipment. Your Deputy Manager (b) (4) (SP) stated that he visually verified/counted the (b) (4) of the (b) (4) (b) (4)

D. You manufacture [redacted] in [redacted] ID # [redacted] 1803. The manufacturing process consists of [redacted] the batch [redacted] of manufacturing. The initial Operation Qualification Report No. OCPL/XPRD/XOQ/[redacted] 1803/R00 Effective date 3/3/2003 did not include qualification for the [redacted] Later you requalified the equipment as documented in Requalification Report No. RQR/[redacted] 1803/0001 Effective date 4/22/2021. As per the report, you verified the [redacted] by operating the [redacted] at [redacted] This verification was done without any loading and duration of each [redacted] is not known. You also did not verify the [redacted] with any calibrated equipment. Your Deputy Manager [redacted] (SP) stated that he visually verified/counted the [redacted]

OBSERVATION 4

You failed to test samples of each component for conformity with all appropriate written specifications for purity, strength, and quality. You also failed to establish the reliability of component supplier analysis on which you rely in lieu of certain tests through appropriate validation of the supplier's test result at appropriate intervals.

Specifically,

A. You use [redacted]-USP in the manufacturing of [redacted] API for the US market. The specification for endotoxin in the coming raw material is NMT [redacted] EU/mg, that is higher than the release specification for [redacted] API, NMT [redacted] EU/mg. In addition, you do not test this raw material for bioburden prior to release for manufacturing.

B. You use [redacted] in the manufacturing of [redacted] API for the US market. You do not test [redacted] for endotoxin and bioburden. You decided to remove the testing requirement for endotoxin from the specification

in 2014 based on the trend data from approved suppliers. However, you added (b) (4) new manufacturer/suppliers and continue to accept and release (b) (4) without testing for endotoxin and bioburden for the manufacturing of (b) (4) (b) (4) API.

C. You use (b) (4) in the manufacturing of (b) (4) (b) (4) API for the US market. You do not test this raw material for endotoxin and bioburden. You decided to remove the testing requirement for endotoxin from the specification in 2014 based on the trend data from the approved suppliers. Your procedure for Skip/Reduced Testing for Raw Materials SOP No. QAD.09.78 Version No. 003 Effective date 1/1/2023 does not have provision for periodic reverification/recertification of the raw materials specifications.

OBSERVATION 5

Cleaning procedures do not contain sufficient details to enable operators to clean each type of equipment in a reproducible and effective manner.

Specifically,

You do not have cleaning procedures for your manufacturing equipment. You use product specific batch records for equipment cleaning. These batch records include all the major manufacturing equipment and a summary of the unit operations for cleaning. The summary lacks details to enable operators render an effective and reproducible cleaning. E.g.

A. You manufacture (b) (4) API for the US market in (b) (4) in multiple non-dedicated equipment. Cleaning of some of the equipment is summarized in Batch Record for Cleaning of (b) (4) at (b) (4) Effective date 7/25/2023. The batch record

does not include all the steps needed to clean the [redacted] (ID # [redacted] 1801), e.g. the cleaning batch record is missing procedure/instruction to disassemble, reassemble, and list of all the different parts of the [redacted] that needs cleaning.

B. You manufacture [redacted] in [redacted] 1801. The equipment cleaning is summarized in Batch Record for Cleaning of [redacted] at [redacted] Effective date 8/7/2020. S. No. 9 includes a series of operations that reads, [redacted] **". There are no pictures for individual parts and no detail instruction to complete the operations.

C. On 2/10/2025, the Equipment Logbook [redacted] 103/2025 for [redacted] ID # [redacted] 2118 suggested that the [redacted] was rendered clean on 2/11/2025 after manufacturing of [redacted] Batch No. [redacted] an Intermediate for [redacted] The equipment cleaning is summarized in Batch Record for Cleaning of Equipment After [redacted] In [redacted] Effective date 1/27/2022. The cleaning verification for [redacted] 2118 is confirmed when no visible product residues and extraneous materials are found on the equipment surface. However, when a [redacted] cloth was rubbed against the inner surface of the [redacted] the portion of the [redacted] cloth that touched the [redacted] turned black. Your Manager [redacted] for [redacted] stated that due to the [redacted] surface of the [redacted] the operator did not see the black materials on the inner surface of the [redacted]

OBSERVATION 6

Appropriate controls are not exercised over computer or related system to assure that the changes in the master production or control records or other records are instituted only by authorized persons.

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As per your list of laboratory equipment, you have at least (b) (4) pH meters that include (b) (4) (b) (4) in your QC laboratory; ID (b) (4) I observed that the current (b) (4) calibration data was stored in the equipment memory, but no testing/measured data was present in the pH meter memory. Your QC Manager (BR) stated that the equipment was not designed to store the electronic data and hence the data could not be backed up on the server.

As per the equipment manual, the pH meter could store at least 10,000 unique measured values. Your analyst prints the result and attaches to the Analytical Work Sheet and enters the equipment use logbook with the batch number of the tested materials and date/time without a need for a second person verification of the data. The test result print out does not include identity of the analyst and the materials tested. The operating procedure, SOP No. QCD.02.116 Version No. 004 Effective date 6/1/2024 does not have provision for saving the electronic data. You use the pH meter in the QC lab to routinely test and release the raw materials, and API for US market.

OBSERVATION 7

The responsibilities and procedure applicable to the quality control unit are not in writing and/or fully followed.

Specifically, your procedure for Training and Development SOP No. HRD.01.01 Version No. 015 Effective date 11/20/2023 has a provision for periodic CGMP training at (b) (4) However, review of your training records confirmed that there were at least (b) (4) associates (out of total (b) (4) employees) whose GMP training was past due for (b) (4)

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