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	02/11/2025-02/17/2025
	FEI NUMBER 3008763768

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Dr Satyajit Tillu, Site Head and Senior General Manager

FIRM NAME	STREET ADDRESS
Piramal Pharma Limited	Plot C-43 TTC Industrial Area; Thane Belapur Rd
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Navi Mumbai, Maharashtra, 400703, India	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 I OBSERVED:

QUALITY SYSTEM

OBSERVATION 1

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

Specifically,

A. On February 11th, 2025, I conducted a walkthrough of [redacted] Room [redacted] used to [redacted] API. At approximately 1:10 pm, I observed [redacted] liquid present throughout the floor of the [redacted] Room [redacted] and visually leaking from the adjacently connected [redacted] Vessel [redacted] 17 used to store the [redacted] unit 03 was last used for [redacted] of [redacted] intended for [redacted] Batch # [redacted] No operator or supervisor was present in the room at the time of the observed incident. According to the Site Head, the operator responsible for stopping the [redacted] unit had gone to lunch and the leaking was likely due to the gasket on the [redacted] vessel being loose. However, there was no documentation of the operator activity or his presence within the room. In addition, the equipment logbook nor line clearance checklist include a check for the [redacted] vessel gasket. Lastly, the [redacted] time frame is not defined or appropriately document within the equipment usage logbooks or associated activity form.

B. On February 11th, 2025, I conducted a walkthrough of the [redacted] Production area and the associated Production Office. I observed that dispensing material weigh sheets and Line Clearance

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Checklist for Dispensing of Raw Materials associated with (b) (4) (non-U.S API product), Batch No. (b) (4) was stored directly between pages of executed batch manufacturing record (BMR) of Crude (b) (4) Batch Size: (b) (4) Batch No. (b) (4) The Production Officer responsible for storing away the comingled records stated that he recently signed off the Check By sections for (b) (4) steps involving Crude (b) (4) and raw material dispensing steps for (b) (4) Batch No. (b) (4) (b) (4)

C. The (b) (4) 09 (b) (4) software used to control and monitor the (b) (4) step for APIs had the following alarms reported throughout (b) (4) API batches (b) (4) between October 24, 2024 - December 25, 2024:

(b) (4)

[redacted]

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(b) (4)

However, there was no investigation or documented explanation as to why the (b) (4) gauge alarm and (b) (4) Alarm remained present and unacknowledged for multiple hours throughout the API batch (b) (4) process. In addition, the equipment alarms have not being challenged as part of Installation, Operation, and Performance Qualification (IQ/OQ/PQ).

D. The (b) (4) software used to control and monitor the (b) (4) process step for APIs had the following alarms reported throughout (b) (4) Batch # (b) (4) API batch processed between February 08, 2025, and February 11, 2025:

1. Approximately six (6) (b) (4) alarms
2. One (1) (b) (4) alarms
3. Approximately eleven (11) (b) (4) (b) (4) warning alarms
4. Approximately two (2) warning alarms

However, there was no investigation or documented explanation as to why the alarms remained present and unacknowledged for multiple hours throughout the API batch (b) (4) process. This is despite the (b) (4) vendor Operating Instructions manual categorizing (b) (4) alarms and (b) (4) alarms as - Type 10 alarm: Stop the device. In addition, the equipment alarms have not being challenged as part of Installation, Operation, and Performance Qualification (IQ/OQ/PQ).

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OBSERVATION 2

Written records of investigation of an active pharmaceutical ingredient (API) do not include follow-up.

Specifically,

A. Four (4) deviations were reported between March 06 - March 18, 2024, for (b) (4) (b) (4) 09, due to the (b) (4) steps of (b) (4) batches being stuck at No. (b) (4) cycle. The first incident occurred on March 06, 2024, for (b) (4) Batch No. (b) (4) the second incident occurred on March 09, 2024, for (b) (4) Batch No. (b) (4) the third incident occurred on March 12th, 2025 for (b) (4) Batch No. (b) (4) and the fourth incident occurred on March 17, 2024 for (b) (4) Batch No. (b) (4) which was further reprocessed into (b) (4) The following deficiencies were noted concerning the deviations:

1. There is no documented quality risk assessment performed to determine continued manufacturing operations of subsequent (b) (4) batches on the same (b) (4) (b) (4) 09, while the investigation remained open for the deviation involving batch, (b) (4) Batch No. (b) (4)
2. There was no investigation report opened at the time incident involving (b) (4) Batch No. (b) (4) cycle being stuck at Step No. (b) (4) on March 09, 2024. Batch No. (b) (4) was documented as being investigated after the decision to manufacture the next batch, Batch No. (b) (4) Start Date: March 12, 2024, with the same equipment. Batch No. (b) (4) subsequently had the similar reported deviation on March 15, 2024.
3. There is no documentation of service engineering activities and maintenance checks required to be performed for the repeated (b) (4) 09 issues involving (b) (4) Batch No. (b) (4) and (b) (4) Batch No. (b) (4)
4. (b) (4) Batch No. (b) (4) Batch No. (b) (4) and Batch No. (b) (4) (b) (4) have not been evaluated for stability throughout batch product expiry despite deviation from the validated (b) (4) setpoint of (b) (4) for the (b) (4) stage of the (b) (4) process. The (b) (4) deviated to approximately (b) (4) (b) (4) for approximately (b) (4)

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B. Deviation DV/LA-22-023 was initiated on May 23, 2022, due to the [redacted] step [redacted] activities) for [redacted] Batch No. [redacted] being stuck at Step No. [redacted] and therefore being manually promoted to step No. [redacted] of the [redacted] cycle. The [redacted] remained between [redacted] (Specification: [redacted] after being manually promoted to the [redacted] step and while maintenance was simultaneously being performed on the [redacted] between May 22 - 25, 2022. According to the investigation, having a [redacted] outside the validate limit of [redacted] may impact API water content and [redacted] content. [redacted] API batch No. [redacted] Retest Date: April 2025 was released to the U.S market on [redacted] after having passing yield and quality results for purity, assay, and water content. However, the batch was not monitored for stability throughout its API Retest Date, despite deviation from the validated [redacted] process and [redacted] specification.

OBSERVATION 3

Written records of investigation of an API complaint do not include adequate follow-up.

Specifically,

Customer Complaint CC-22-06 was initiated on May 21, 2022, due foreign particles being observed for [redacted] USP, Batch No [redacted] Retest Date: May 2024. Samples from another API batch, Batch No. [redacted] was used to test traces of potential foreign/metallic particles. However, there was no documented attempt to retrieve and test the customer complaint sample. In addition, retention samples of the sample batch were not tested. According to the Quality Control Head, there was not enough retention samples available to test the sample complaint batch. This is despite [redacted] units of [redacted] samples for Batch No [redacted] being documented as retain within the Control Sample Register at the time of the investigation. However, there is no documented reasoning as to how the control same size necessary to conduct the complaint investigation was determined. According to SOP CIC/QA/11 Handling of Customer Complaints, Version 10, Effective Date: February 22, 2022, Section 5.5, the Quality Control unit must examine the retain sample of the complaint batch and check for physical parameters. In addition, compare the retain sample with the sample, if received along with the complaint.

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FACILITIES AND EQUIPMENT SYSTEM

OBSERVATION 4

The cleaning of equipment is inadequate.

Specifically,

A. Cleaning procedures have not been validated for shared equipment used to manufacture and process crude APIs for the U.S and other global markets. For example, the following shared equipment have not been evaluated as part of a cleaning validation program:

1. [redacted] was used for [redacted] step involving [redacted] Activity Date: December 31, 2024, to January 02, 2025, and [redacted] December 28, 2024, to December 31, 2024. The same batch was previously used for [redacted] step involving [redacted] Batch No. [redacted] Activity Date: December 25, 2024, to December 26, 2024.
2. [redacted] was used for [redacted] step involving [redacted] Activity Date: November 28, 2024, to December 01, 2024, and [redacted] from November 27 - 28, 2024. The same [redacted] was also previously used for [redacted] step involving [redacted] Batch No. [redacted] Activity Date: November 24, 2024, to November 25, 2024.
3. [redacted] was used for [redacted] involving [redacted] Activity Date: October 12, 2024, to October 14, 2024. The same [redacted] was also previously used for [redacted] involving [redacted] Activity Date: October 07, 2024, to October 13, 2024.
4. [redacted] was used [redacted] involving [redacted] Activity Date: September 26, 2024 - September 28, 2024. The same [redacted] was also previously used for [redacted] involving [redacted] Batch No. [redacted] Activity Date: September 19 - 20, 2024 and Batch No. [redacted] Activity Date: September 16 - 18, 2024.

B. During the inspection walkthrough on February 11th, 2025, I observed a partially torn (b) (4) based material stored directly within the (b) (4) vessel of (b) (4) 06), which was most recently used to process (b) (4) Batch No. (b) (4) step. During the inspection, the Site Head and QA Head identified the material as (b) (4) for (b) (4) used during (b) (4) operations of the previous batch. However, (b) (4) 06 was documented as being cleaned within the Batch Equipment Cleaning Record (BECR) and had a clean equipment status, completed on: February 10, 2025, and valid up until (b) (4)

PRODUCTION SYSTEM

OBSERVATION 5

Master production and control records lack complete manufacturing and control instructions, written specifications, and precautions to be followed.

Specifically,

A. Section 8.18 of the Master Batch Manufacturing Record (BMR) of Crude (b) (4) requires the operator to (b) (4) However, MBR steps include sections for (b) (4) as per the MBR instructions. In addition, the (b) (4) step has greyed start and end time sections and checked by sections. Therefore, operators are not able to appropriately document the cycle start and end time. For example:
   1. The executed BMR for Crude (b) (4) Batch No. (b) (4) included documentation of (b) (4) cycles instead of the (b) (4) instructed by the master BMR. No written deviation has been initiated for the change in the validated procedure.
   2. The executed BMR for Crude (b) (4) Batch No. (b) (4) included the following written remark on the back page: (b) (4) end time column is shaded hence end time written in remark column.

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3. The executed BMR for Crude [redacted] (b) (4) Batch No. [redacted] (b) (4) included the following written remark on the back page: End time of [redacted] (b) (4) has recorded in remark Column. End time Column is shaded.

B. Operators are required to perform [redacted] (b) (4) as per the Master Batch Manufacturing Record (BMR) of Crude [redacted] (b) (4) However, Version 03 (Effective Date: December 14, 2024) of the master BMR has greyed out the Start and End Time sections and Checked By sections for [redacted] (b) (4) steps. Executed BMRs do not include documentation of [redacted] (b) (4) step requiring a [redacted] (b) (4) time.

MATERIALS SYSTEM

OBSERVATION 6

There is a failure to handle and store components, key starting materials, API containers, and closures at all times in a manner to prevent contamination and ensure satisfactory conformance to the identity and strength of each active ingredient.

A. According to the Site Head and QA Head, Key Starting Materials (KSMs) used to manufacture APIs for the U.S market and that are labelled with frozen and refrigerated storage label requirements are shipped and received at the firm via room temperature conditions. This includes the following KSMs transported at room temperature for multiple days (more than 24 hours) and shipped without any assurance of cold chain custody:

[redacted] (b) (4)

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B. On February 11th, 2025, I observed (b) (4) foreign matter within the (b) (4) of (b) (4) API, Batch No. (b) (4) held within (b) (4) Vessel, (b) (4) During the inspection, the (b) (4) matter was isolated from the (b) (4) and sent for external laboratory testing. The identification testing demonstrated that the foreign matter stemmed from the (b) (4) drum used processing activities.

***DATES OF INSPECTION**

02/11/2025 (Tue), 02/12/2025 (Wed), 02/13/2025 (Thu), 02/14/2025 (Fri), 02/17/2025 (Mon).

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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."