DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Food and Drug Administration 1240 Parklawn Drive Room 2032 Rockville, MD 20857 ORAPharm1_responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	09/23/2024-09/27/2024 FEI NUMBER 3004086884

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Sridhar Surat, Associate Vice President Operations

FIRM NAME	STREET ADDRESS
Apitoria Pharma Private Limited	Survey No. 10 & 13, Gaddapotharam VillageIda-Kazipally, Jinnaram Mandal
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Sanga Reddy District, Telangana, India	API Manufacture

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/WE OBSERVED:

OBSERVATION 1

Equipment used in the manufacturing of drug substances and intermediates is not of adequate upkeep to facilitate operations for its cleaning and maintenance.

Specifically, during the day one walkthrough of Building (b) (4) on 23 September 2024, the following was observed in the non-dedicated equipment used to manufacture drug substances for US market.

A. Visible scratch marks and dents on the equipment surface of direct product contact were observed on the bottom section of (b) (4), equipment ID# (b) (4) 004 and the sides of (b) (4) equipment ID# (b) (4) 003. Your (b) (4) maintenance check lists don't record the checking for scratch marks and dents. The latest preventive maintenance for (b) (4) (equipment ID# (b) (4) 004) and (b) (4) (equipment ID# (b) (4) 003) was performed on 02 September 2024 and 26 August 2024, respectively.

B. We observed a white residue buildup and what appeared to be scratch marks on the (b) (4) surface of "ready to use/ clean" (b) (4) equipment ID# (b) (4) 009 (capacity (b) (4) last cleaned on 22 September 2024) and equipment ID# (b) (4) 015 (Capacity (b) (4) last cleaned on 17 September 2024). We also observed white and (b) (4) stains on the inside wall near the left hatch of "ready to use/ clean" (b) (4) equipment ID# (b) (4) 00 (Capacity: (b) (4) last cleaned on 12 September

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Pushpa S. Jayasekara -S Digitally signed by Pushpa S. Jayasekara -S Date: 2024.09.27 18:06:14 +05'30' — Pushpa Suresh Jayasekara, CSO Khalid M. Khan -S Digitally signed by Khalid M. Khan -S Date: 2024.09.27 08:43:26 -04'00' — Khalid M. Khan Chemist	09/27/2024

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Food and Drug Administration 1240 Parklawn Drive Room 2032 Rockville, MD 20857 ORAPharm1_responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	09/23/2024-09/27/2024
	FEI NUMBER 3004086884
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Sridhar Surat, Associate Vice President Operations	
FIRM NAME	STREET ADDRESS
Apitoria Pharma Private Limited	Survey No. 10 & 13, Gaddapotharam VillageIda-Kazipally, Jinnaram Mandal
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Sanga Reddy District, Telangana, India	API Manufacture

2024). These (b) (4) and (b) (4) were used to manufacture several drug substances including (b) (4) for US customers.

OBSERVATION 2

Failure to establish adequate manufacturing instructions in the production records for drug substances and intermediates. Specifically,

A. During the day two walkthrough on 24 September 2024, we covered Block (b) (4) Module (b) (4) the (b) (4) API stage for BPCR Number (b) (4) Batch number (b) (4) In Step (b) (4) of the batch record, it states to " (b) (4) (b) (4)". Management stated that per SOP UIIMF0057, an operator visually checks the (b) (4) (b) (4) (b) (4) However, such (b) (4) instructions are not reflected in the manufacturing batch records.

B. Your batch record for (b) (4) drug substance (BPCR# (b) (4) Version (b) (4) for which drug substance manufacturing stage, which step) does not include the (b) (4) of the (b) (4) equipment (ID# (b) (4) 005). This (b) (4) can be run at variable (b) (4)

C. Your cleaning records for product change-over cleaning (Type-II cleaning) of (b) (4) (ECR# ECR/381/PCO/007) from (b) (4) drug substance (Batch# (b) (4) to (b) (4) drug substance (Batch# (b) (4) and periodic batch to batch cleaning (Type- III

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Pushpa S. Jayasekara -S Digitally signed by Pushpa S. Jayasekara -S Date: 2024.09.27 18:06:36 +05'30' — Pushpa Suresh Jayasekara, CSO	09/27/2024
	Khalid M. Khan -S Digitally signed by Khalid M. Khan -S Date: 2024.09.27 08:44:25 -04'00' — Khalid M. Khan Chemist	

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Food and Drug Administration 1240 Parklawn Drive Room 2032 Rockville, MD 20857 ORAPharm1_responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	09/23/2024-09/27/2024
	FEI NUMBER 3004086884
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Sridhar Surat, Associate Vice President Operations	
FIRM NAME Apitoria Pharma Private Limited	STREET ADDRESS Survey No. 10 & 13, Gaddapotharam VillageIda-Kazipally, Jinnaram Mandal
CITY, STATE, ZIP CODE, COUNTRY Sanga Reddy District, Telangana, India	TYPE ESTABLISHMENT INSPECTED API Manufacture

cleaning) of [redacted] (b) (4) (ECR# ECR/381/PCO/003) for [redacted] (b) (4) drug substance (Batch# [redacted] (b) (4) did not include the instructions, documentation and results for the cleanliness visual inspection checks on operation No [redacted] (b) (4)

OBSERVATION 3

Failure to ensure training is regularly conducted by qualified individuals and covers, at a minimum, the particular operations that each employee performs and CGMP as they relate to the employee's functions. Specifically,

A. Your firm fails to train your manufacturing personnel on how to perform swab sampling (at the most difficult clean area of [redacted] (b) (4) equipment ID# [redacted] (b) (4) 005 and [redacted] (b) (4) equipment ID# [redacted] (b) (4) 016 for cleaning verification after product-to-product change over cleaning (Type-II cleaning) and periodic batch to batch cleaning (Type- III cleaning)

B. Your firm fails to train your QC analysts on how to assess microbial growth in a growth promotion test using [redacted] (b) (4) media.

OBSERVATION 4

Failure of your quality unit to review and approve all appropriate quality-related documents. Specifically,

[redacted] (b) (4) API (Lot# [redacted] (b) (4) has a change control (ID # CRF-UII-000693) due the size reduction of this batch from reduced batch size [redacted] (b) (4) instead of standard batch size [redacted] (b) (4) and was approved on 16 July 2024. BPCR review check list for this batch was reviewed and verified by manufacturing and

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Pushpa S. Jayasekara -S Digitally signed by Pushpa S. Jayasekara -S Date: 2024.09.27 18:06:59 +05'30' — Pushpa Suresh Jayasekara, CSO	09/27/2024
	Khalid M. Khan -S Digitally signed by Khalid M. Khan -S Date: 2024.09.27 08:45:45 -04'00' — Khalid M. Khan Chemist	

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Food and Drug Administration 1240 Parklawn Drive Room 2032 Rockville, MD 20857 ORAPharm1_responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	09/23/2024-09/27/2024
	FEI NUMBER 3004086884

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Sridhar Surat, Associate Vice President Operations

FIRM NAME	STREET ADDRESS
Apitoria Pharma Private Limited	Survey No. 10 & 13, Gaddapotharam VillageIda-Kazipally, Jinnaram Mandal
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Sanga Reddy District, Telangana, India	API Manufacture

quality assurance on 27 July 2024. However, manufacturing and quality assurance personnel has signed the BPCR check list stating that any changed controls document was not initiated for this (b) (4) API (Lot# (b) (4) and have attached to the final batch records. No quality assurance related deviation or investigation was initiated for not adequately reviewing quality documents.

OBSERVATION 5

The (b) (4) water system design and the water sampling method to assure quality of (b) (4) water are not adequate. Specifically,

A. The (b) (4) tank used in preparation of (b) (4) solution is of inappropriate design. It is located in an unprotected open environment without a sealed lid or a cover to protect the prepared (b) (4) solution from rain and other contaminants in the open air.

B. During the (b) (4) water sampling demonstration, your operator did not demonstrate proper sampling technique. Specifically:
   1. The operator failed to maintain disinfected clean state of the hose while touching the exposed ends of the hose, and at one point, dropping the hose such that the open end touched the floor. Later, the hose connectors were disinfected before sampling.
   2. Your analyst failed to collect the (b) (4) water sample immediately after the removal of the (b) (4) protective covers from the sampling hose to prevent sample contamination.
   3. While sampling at point (b) (4) water was leaking from the (b) (4) connector due to a missing seal in the (b) (4) connector.

OBSERVATION 6

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Pushpa S. Jayasekara -S Digitally signed by Pushpa S. Jayasekara -S Date: 2024.09.27 18:07:34 +05'30'	Pushpa Suresh Jayasekara, CSO	09/27/2024
	Khalid M. Khan -S Digitally signed by Khalid M. Khan -S Date: 2024.09.27 08:46:55 -04'00'	Khalid M. Khan Chemist	

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Food and Drug Administration 1240 Parklawn Drive Room 2032 Rockville, MD 20857 ORAPharm1_responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	09/23/2024-09/27/2024
	FEI NUMBER 3004086884
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Sridhar Surat, Associate Vice President Operations	
FIRM NAME	STREET ADDRESS
Apitoria Pharma Private Limited	Survey No. 10 & 13, Gaddapotharam VillageIda-Kazipally, Jinnaram Mandal
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Sanga Reddy District, Telangana, India	API Manufacture

Failure to establish and follow written procedures for investigating critical deviations or the failure of intermediates and API batches to meet specifications. Specifically,

A. Your firm's change control request is inadequate and does not include risk evaluation and risk mitigation strategy. (b) (4) batch (b) (4) was manufactured following a planned deviation under Change Control Request CRF-UII-000286 (No. DE-UII-000018) for reduced batch size of approximately (b) (4) due to terminal batch of the campaign. Despite the reduced batch size, the process parameters and general process of (b) (4) established and validated for (b) (4) (b) (4) batch size were utilized that resulted in OOS for particle size. The change control request neglected the fact that the manufacturing process for batch size of (b) (4) had been previously validated which was more suitable for the subject batch.

B. Deviation DE-U08-001180 was initiated for scaled up tech transfer batch of (b) (4) from R&D to Batch No. (b) (4) on 28 March 2023. The deviation reported that multiple unspecified impurities appeared in the chromatogram which cumulatively exceeded the specification limit of NMT (b) (4) % for the total unknown impurities. The most probable cause of (b) (4) degradation was assigned as the root cause without confirmation at the proposed scale up batch size of (b) (4)

OBSERVATION 7

Your equipment are not adequately qualified. Specifically,

A. The Laminar Flow Hood (Property ID QLAM003) located in Microbiology lab is primarily used for preparation of (b) (4) water samples for microbial count. It was qualified initially in 2019 and then recently in 2024. The smoke studies conducted do not show laminar flow but instead the smoke streams are observed with downward trajectory from back end of the cabinet to the front.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Pushpa S. Jayasekara -S Digitally signed by Pushpa S. Jayasekara -S Date: 2024.09.27 18:07:59 +05'30' Pushpa Suresh Jayasekara, CSO Khalid M. Khan -S Digitally signed by Khalid M. Khan -S Date: 2024.09.27 08:47:56 -04'00' Khalid M. Khan Chemist	09/27/2024

B. The operating, cleaning and re-validation procedure (SOP UIIQC281) does not include the equilibration period after initial startup and disinfection of the Laminar Flow Hood (Property ID QLAM003).

OBSERVATION 8

Your equipment cleaning validation protocol is inadequate. Specifically,

Your firm uses non-dedicated equipment for manufacturing US and non-US products. During the product-to-product changeover equipment cleaning (Type II cleaning) validation of non-US product (b) (4) API in Block (b) (4) module (b) (4) and US product (b) (4) Block (b) (4) Module (b) (4) following discrepancies were noted.

Non-US product (b) (4) API in Block (b) (4) module (b) (4) product to product changeover equipment cleaning validation was completed in 18 May 2021 (protocol # P-CLV-H1P-CIV-C1022560-01-00). For Swab limit (ppm), you have calculated total surface area (TSA) (m^2) of the equipment chain by addition of all the equipment surface area and (b) (4) % of the equipment surface area (area of pipes, tubes, spatulas, etc.). During the (b) (4) Block (b) (4) Module (b) (4) product to product changeover, equipment cleaning validation was completed on 19 June 2024 (protocol # P-CLV-381-AII-C1182430-01-00). However, for Swab limit (ppm), you have calculated total surface area (TSA) (m^2) of the equipment chain by addition of all the equipment surface area and (b) (4) % of the equipment surface area (area of pipes, tubes, spatulas, etc.). In the latter case, instead of using (b) (4) % for additional surface area, you have reduced the additional surface area to (b) (4) % which, ultimately reduced the TSA. Your calculation of Swab limit is inversely proportional to the TSA. Your firm does not have any supporting documents

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Food and Drug Administration 1240 Parklawn Drive Room 2032 Rockville, MD 20857 ORAPharm1_responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	09/23/2024-09/27/2024 FEI NUMBER 3004086884

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Sridhar Surat, Associate Vice President Operations	
FIRM NAME Apitoria Pharma Private Limited	STREET ADDRESS Survey No. 10 & 13, Gaddapotharam VillageIda-Kazipally, Jinnaram Mandal
CITY, STATE, ZIP CODE, COUNTRY Sanga Reddy District, Telangana, India	TYPE ESTABLISHMENT INSPECTED API Manufacture

for justification, change controls or SOP (Equipment cleaning validation, CQA045) to support the above change in equipment cleaning validation protocol.

OBSERVATION 9

Failure to ensure that new and modified facilities and equipment are qualified. Specifically,

A. During the review of installation qualification and mapping of refrigerator (b) (4) (Model# (b) (4) (Set point 2°C to 8°C; performed on 17 March 2021), we noticed that your firm has not conducted the temperature mapping for worst case (i.e. fully loaded) condition.

B. SOP CQA020, titled "Calibration of humidity, cooling incubators and deep freezers", effective date 6 October 2023 stated that mapping of cooling incubators should be done (b) (4) However, loading conditions have not been specified in the SOP.

OBSERVATION 10

Failure of your quality unit to establish a system to release or reject raw materials, intermediates, packaging and labeling materials. Specifically,

Your firm has generated labels for "retest due" without any information on the label for warehouse use and these labels were issued outside from the established ERP (Enterprise resource plan). No date of issue logs and label reconciliation process was in place for these labels.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Pushpa S. Jayasekara -S Digitally signed by Pushpa S. Jayasekara -S Date: 2024.09.27 18:08:57 +05'30' — Pushpa Suresh Jayasekara, CSO Khalid M. Khan -S Digitally signed by Khalid M. Khan -S Date: 2024.09.27 08:51:42 -04'00' — Khalid M. Khan Chemist	09/27/2024

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Food and Drug Administration 1240 Parklawn Drive Room 2032 Rockville, MD 20857 ORAPharm1_responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	09/23/2024-09/27/2024
	FEI NUMBER 3004086884

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Sridhar Surat, Associate Vice President Operations

FIRM NAME	STREET ADDRESS
Apitoria Pharma Private Limited	Survey No. 10 & 13, Gaddapotharam VillageIda-Kazipally, Jinnaram Mandal
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Sanga Reddy District, Telangana, India	API Manufacture

*DATES OF INSPECTION

09/23/2024, 09/24/2024, 09/25/2024, 09/26/2024, 09/27/2024, 0

APPEARS THIS WAY ON ORIGINAL

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE

Pushpa S. Jayasekara -S — Digitally signed by Pushpa S. Jayasekara -S Date: 2024.09.27 18:09:26 +05'30' — Pushpa Suresh Jayasekara, CSO

Khalid M. Khan -S — Digitally signed by Khalid M. Khan -S Date: 2024.09.27 08:52:25 -04'00' — Khalid M. Khan Chemist

DATE ISSUED
09/27/2024