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	3/11/2024-3/15/2024
	FEI NUMBER 3006076314

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Parameswaran P S, Head Operations & Supply

FIRM NAME	STREET ADDRESS
Apotex Research Private Limited	Plots 1 And 2, Bommasandra Ind. Area, Jigani Link Rd; 4th Phase
CITY, STATE, ZIP CODE, COUNTRY Bangalore, Karnataka, 560099 India	TYPE ESTABLISHMENT INSPECTED Drug 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

Written records are not always made of investigations into unexplained discrepancies.

Specifically,

A) Your firm failed to investigate and identify the root cause of several low results observed for the (b) (4) data at the (b) (4) stage of (b) (4) Granules (b) (4) % for the PPQ batches. (b) (4) Granules (b) (4) % is the same (b) (4) used for all strengths of (b) (4) For example, the following mean values were recorded:

(b) (4)

[redacted]

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Jeffrey P Raimondi, Consumer Safety Officer Aditi Thakur, FDA Center Employee	X Jeffrey P Raimondi Consumer Safety Officer Signed By: Jeffrey P. Raimondi -S Date Signed: 03-15-2024 13:31:43	DATE ISSUED 3/15/2024

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	3/11/2024-3/15/2024
	FEI NUMBER 3006076314

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Parameswaran P S, Head Operations & Supply

FIRM NAME	STREET ADDRESS
Apotex Research Private Limited	Plots 1 And 2, Bommasandra Ind. Area, Jigani Link Rd; 4th Phase
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Bangalore, Karnataka, 560099 India	Drug Manufacturer

(b) (4)

[redacted]

Lots [redacted] (b) (4) were used [redacted] (b) (4) of [redacted] (b) (4) mg.

B) The root cause for investigations LIR# 1530944 and LIR#1530951 regarding anomalous results obtained at the [redacted] (b) (4) time point during dissolution [redacted] (b) (4) units) [redacted] (b) (4) units) test of [redacted] (b) (4) [redacted] (b) (4) mg_[redacted] (b) (4) dissolution testing is not adequately justified. Dissolution profile study [redacted] (b) (4)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Jeffrey P Raimondi, Consumer Safety Officer Aditi Thakur, FDA Center Employee	X Jeffrey P Raimondi Consumer Safety Officer Signed By: Jeffrey P. Raimondi -S Date Signed: 03-15-2024 13:31:43	3/15/2024

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	3/11/2024-3/15/2024
	FEI NUMBER 3006076314

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Parameswaran P S, Head Operations & Supply	
FIRM NAME Apotex Research Private Limited	STREET ADDRESS Plots 1 And 2, Bommasandra Ind. Area, Jigani Link Rd; 4th Phase
CITY, STATE, ZIP CODE, COUNTRY Bangalore, Karnataka, 560099 India	TYPE ESTABLISHMENT INSPECTED Drug Manufacturer

[redacted] was performed for [redacted] mg, Batch# [redacted] PPQ according to protocol S2-PQP-3682-001-001, Revision: 1 (intended for USA market) and anomalous results of [redacted]% were obtained in the [redacted] time point.

Based on initial investigation findings, no discrepancies were observed from the reagent, standard and sample preparations. However, the most probable cause for the observed anomalous results during dissolution test was determined to be due to contamination during test execution as it was hypothesized that the analyst did not place foil over the samples, despite the method not requiring this, and the standard spilled over onto the first row of samples only. All dissolution profile samples from other timepoints were present on the workbench at the same time observed acceptable results.

C) The root cause for investigation LIR# 1223365 regarding anomalous result observed in [redacted] sample testing for [redacted] granules [redacted]% [redacted] mg) PPQ batch [redacted] is not adequately justified.

[redacted] (Lot [redacted] resulted in a [redacted] of [redacted]% which was performed as a part of protocol # S2-PQP-3386-001-001, Revision: 1 Titled as "PPQ for Protocol [redacted] Granules [redacted]% (USA Market) (S2-PQP-3386-001). [redacted] results after [redacted] stage are "for information only" without acceptance criteria. Based on phase 1 investigation findings, no assignable cause was identified for this anomalous result. The investigation was extended to manufacturing through SME PR # 1224409 and it was concluded that manufacturing process/procedure/instructions are not the contributing factor for the reported result. The firm performed testing of the two additional replicate [redacted] samples and resulted in the assumption that the initial anomalous result is not a true result. It was hypothesized this high result to be from an addition of [redacted] solution instead of sample [redacted] into the specific [redacted] volumetric

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Jeffrey P Raimondi, Consumer Safety Officer Aditi Thakur, FDA Center Employee	X Jeffrey P Raimondi Consumer Safety Officer Signed By: Jeffrey P. Raimondi -S Date Signed: 03-15-2024 13:31:43	3/15/2024

flask unknowingly by the analyst. The root cause of this investigation is not justified and was ultimately attributed to analyst error without evidence.

OBSERVATION 2

Your firm failed to establish written procedures for production and process controls designed to assure that the drug products have the identity, strength, purity, and quality that they are purported or represented to possess.

Specifically,

A) You have not identified the specific cause for assay trending upward with each subsequent unit operation including (b) (4) granules, and (b) (4) tablets during manufacturing of each of the following PPQ batches (b) (4) of (b) (4) (b) (4) mg Tablets. For example, the following values were observed for each of the aforementioned stages:

(b) (4)

(b) (4)

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	3/11/2024-3/15/2024
	FEI NUMBER 3006076314

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Parameswaran P S, Head Operations & Supply

FIRM NAME	STREET ADDRESS
Apotex Research Private Limited	Plots 1 And 2, Bommasandra Ind. Area, Jigani Link Rd; 4th Phase
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Bangalore, Karnataka, 560099 India	Drug Manufacturer

(b) (4)

(b) (4)

B) Your firm failed to establish an acceptance criterion for the (b) (4) unit operation. (b) (4) (b) (4) testing is "for information only" despite being part of process validation.

OBSERVATION 3

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

Specifically,

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Jeffrey P Raimondi, Consumer Safety Officer Aditi Thakur, FDA Center Employee	X Jeffrey P Raimondi Consumer Safety Officer Signed By: Jeffrey P. Raimondi -S Date Signed: 03-15-2024 13:31:43	3/15/2024

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	3/11/2024-3/15/2024
	FEI NUMBER 3006076314

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Parameswaran P S, Head Operations & Supply

FIRM NAME	STREET ADDRESS
Apotex Research Private Limited	Plots 1 And 2, Bommasandra Ind. Area, Jigani Link Rd; 4th Phase
CITY, STATE, ZIP CODE, COUNTRY Bangalore, Karnataka, 560099 India	TYPE ESTABLISHMENT INSPECTED Drug Manufacturer

A) Multiple anomalous results were obtained in (b) (4) test of (b) (4) Granules (b) (4)%. Investigations (LIR) have determined the root cause to being characteristic of the product at (b) (4) (b) (4) stage, however, no CAPA has been initiated to prevent anomalous results for (b) (4) CAPA has not been implemented for the following:

LIR	Batch	Sub lot	Mean	%SD	Anomalous result
					(b) (4)

B) The Quality Unit has not ensured that all system suitability injections were performed in chromatographic sample set sequence for analyzing the degradation products for (b) (4) (b) (4) mg prior to injecting the samples. During the review of the degradation results of Batch (Stability Sample, RT (b) (4) you failed to inject the Solution (b) (4) system suitability solution) injection at the beginning of the sequence injections as a part of system suitability criteria per method degradation product (b) (4) Solution (b) (4) (system suitability solution) was injected and analyzed in separate chromatographic sequence.

C) The Quality Unit failed to establish what is considered to be an anomalous result. For example, an investigation was initiated due to a result (b) (4)% (SD (b) (4)%) for (b) (4) of (b) (4) Granules (b) (4)% lot # (b) (4) however, an investigation was not initiated due to a result of (b) (4)% (SD (b) (4)%) for (b) (4) of (b) (4) Granules (b) (4)%. There is no justification why an investigation was performed for the (b) (4)% results and not the (b) (4)% result.

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE
Jeffrey P Raimondi, Consumer Safety Officer
Aditi Thakur, FDA Center Employee

X Jeffrey P Raimondi
Consumer Safety Officer
Signed By: Jeffrey P. Raimondi -S
Date Signed: 03-15-2024
13:31:43

DATE ISSUED
3/15/2024

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	3/11/2024-3/15/2024
	FEI NUMBER 3006076314

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Parameswaran P S, Head Operations & Supply

FIRM NAME	STREET ADDRESS
Apotex Research Private Limited	Plots 1 And 2, Bommasandra Ind. Area, Jigani Link Rd; 4th Phase
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Bangalore, Karnataka, 560099 India	Drug Manufacturer

X Aditi Thakur
FDA Center Employee
Signed By: Aditi S. Thakur -S
Date Signed: 03-15-2024 13:32:09

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE

Jeffrey P Raimondi, Consumer Safety Officer
Aditi Thakur, FDA Center Employee

X Jeffrey P Raimondi
Consumer Safety Officer
Signed By: Jeffrey P. Raimondi -S
Date Signed: 03-15-2024 13:31:43

DATE ISSUED
3/15/2024