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	9/19/2022-9/28/2022*
	FEI NUMBER 3005029956

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Ashish Rajarnis, Vice President (Works)

FIRM NAME	STREET ADDRESS
Torrent Pharmaceuticals Limited	Taluka-Kadi, Ahmedabad Mehsana Highway
CITY, STATE, OR COUNTRY, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Indrad, Gujarat, 382721 India	Finished Product and API Manufacturer (Non-sterile)

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

Equipment and utensils are not cleaned and maintained at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product.

Specifically,

A. Your manual cleaning procedure for non-dedicated manufacturing equipment is inadequate in that does not ensure the removal of residues from the previously manufactured product to avoid cross-contamination.

For example,

On 19 September 2022, we observed residues of white powder [e.g., flakes] on different surfaces of cleaned (b) (4) GR-122, located in manufacturing Suite (b) (4) This (b) (4) equipment is used to manufacture tablet products for the US market.

The residues were observed in the following areas:

1. lower plenum (b) (4)
2. lower plenum bottom area
3. extension of the (b) (4) inside wall next to (b) (4) port

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Jose E Melendez, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Investigator - Dedicated Drug Cadre	X	9/28/2022

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	9/19/2022-9/28/2022*
	FEI NUMBER 3005029956

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Mr. Ashish Hajarnis, Vice President (Works)	
FIRM NAME Torrent Pharmaceuticals Limited	STREET ADDRESS Taluka-Kadi, Ahmedabad Mehsana Highway
CITY, STATE, ZIP CODE, COUNTRY Indrad, Gujarat, 382721 India	TYPE ESTABLISHMENT INSPECTED Finished Product and API Manufacturer (Non-sterile)

4. extension of the (b) (4) inside wall next to (b) (4)

5. (b) (4) valve of the (b) (4)

Additionally, a fine white to off-white color powdery layer was also observed on the (b) (4) of the (b) (4) and on the wall of the room behind the equipment.

On the same day, swab samples of the referenced equipment locations were collected and tested. Test results indicated the presence of (b) (4) residues. In addition, test results from the swab sample collected from the (b) (4) valve of the (b) (4) showed the presence of residues of previous product that contain (b) (4) API (FP Batch Number: (b) (4) manufactured on 10 August 2022. Post manufacturing of this product, your firm was in continuous campaign manufacturing of (b) (4) Between 10 August 2022 to 19 September 2022, your firm conducted approximately (b) (4) cleaning product changeover activities. The acceptance criteria for cleaning product changeover is that no visible residue should be observed on the equipment after cleaning.

B. Your analytical cleaning method used to monitor the effectiveness/reproducibility of your manual cleaning process of the non-dedicated production equipment is inadequate.

Specifically, after the cleaning sample is collected from a predefined equipment area, the swab sample is placed in a test tube and transferred to the Quality Control laboratory for further analysis. In the laboratory, the sample is saturated with (b) mL of extraction diluent where the analyte to be analyzed and measured is extracted into the diluent.

On 19 September 2022, during the cleaning sample preparations of (b) (4) GR-122, we observed that none of the samples swab heads were completely immersed in the extraction diluent. It was observed that approximately 70 % of the swab head was in contact with the extraction diluent. In addition, it was also found that the (b) (4) process of these cleaning samples was inadequate because the test tubes were placed in a plastic rack, preventing them from being completely immersed in the (b) (4) to

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Jose E Melendez, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Investigator - Dedicated Drug Cadre	X	9/28/2022

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	9/19/2022-9/28/2022*
	FEI NUMBER 3005029956

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Mr. Ashish Hajarnis, Vice President (Works)	
FIRM NAME Torrent Pharmaceuticals Limited	STREET ADDRESS Taluka-Kadi, Ahmedabad Mehsana Highway
CITY, STATE, ZIP CODE, COUNTRY Indrad, Gujarat, 382721 India	TYPE ESTABLISHMENT INSPECTED Finished Product and API Manufacturer (Non-sterile)

have a homogeneous extraction process.
This deficiency may leave extractable residues of monitoring active ingredient on the swab head leading to inaccurate cleaning results.

C. The validation study conducted in accordance with Protocol AMVCV/ST/P/003/01, entitled, "Protocol For Cleaning Validation Study of Glassware Washing Procedure By Glassware (b) (4) (b) (4) "; approved 17 May 2022 is inadequate.
Specifically, the validation strategy of the QC laboratory automated glassware (b) (4) does not consider different load configurations, including range of glassware sizes, quantity, location, and orientation to group larger and smaller sizes and confirm which of these load configurations represents the worst case.
Since April 2019, your Quality Control laboratory has initiated a substantial number of laboratory incident reports (approximately 70), including some OOS investigation reports associated to the presence of unknown peaks in chromatographic analyses.

D. On 19 September 2022, we observed your non-dedicated (b) (4) Tank ID: GR-149 encrusted with fine white to off-white color powder residues and flakes in product contact areas. This tank was located inside Room ID: (b) (4) tagged in "CLEANED" status and ready for use. Subject tank was last used in the manufacturing of (b) (4) Tablets USP (b) (4) ng, Batch No. (b) (4) on 02 August 2022 and was in the room during the manufacturing of (b) (4) pellets. Tank GR-149 has been used in the preparation of drug solution, which is later used in (b) (4) ID: GR-122. This equipment had been through line clearance check on 02 August 2022. The same tank GR-149 has been previously used in the drug solution preparation for several batches of (b) (4) Pellets and (b) (4) Tablets USP. (Pictures taken to demonstrate the observed issues).

E. On 20 September 2022, we observed your (b) (4) ID: GR-31 located inside Room ID: (b) (4) was tagged in "CLEANED" status while the flooring of (b) (4) chamber was covered with white to off-white

	EMPLOYEE(S) SIGNATURE		DATE ISSUED
SEE REVERSE OF THIS PAGE	Jose E Melendez, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Investigator - Dedicated Drug Cadre	X	9/28/2022

color pellets and fine powder traces. This chamber also contained a thread like material completely covered in powder. It resembled this thread like material was soaked at some point in white powder solution and later due to (b) (4) conditions inside (b) (4) chamber it (b) (4) and became hard. GR-31 was previously used for (b) (4) Pellets. (Pictures taken to demonstrate the observed issues).

F. On 20 September 2022, we observed your (b) (4) ID: GR-110 located inside Room ID: (b) (4) was tagged in "CLEANED" status while a randomly selected (b) (4) was observed encrusted with white color power residues in product contact areas. This (b) (4) was last used in (b) (4) of (b) (4) (b) (4) excipient. (Pictures taken to demonstrate the observed issues).

G. On 20 September 2022, we observed dent and scratch marks all over inside your non-dedicated (b) (4) ID: GR-92 in the product contact areas. This (b) (4) was located in (b) (4) area and was previously used in the manufacturing of (b) (4) Tablets USP (b) (4) mg on 19 September 2022. Your Production Operators stated the reason for dent marks due to hammering the equipment using a (b) (4) hammer. Your (b) (4) hammer appeared to be breaking into pieces. Also, the (b) (4) shaped area of (b) (4) appeared to have significantly changed in shape due to hammering of the equipment over the period of use. (Pictures taken to demonstrate the observed issues).

These issues pertaining to dent marks and changes in the shape of equipment was concerning to ensure the overall integrity of this equipment in manufacturing of drug products, validation of process and equipment cleaning. Your Production Head acknowledged the issues however the equipment was used in production on subsequent days during this inspection on 21 and 22 September 2022. Your manufacturing and quality unit failed to identify these manufacturing equipment issues and deviated from line clearance checklist ANNEXURE-II, CHECK LIST FOR (b) (4) EQUIPMENT/AREA per SOP No.: T.01.57.27 in section 15 *"Check for any crack and damage on product contact parts of* (b) (4) (b) (4) '. In this (b) (4) refers to (b) (4)

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	9/19/2022-9/28/2022*
	FEI NUMBER 3005029956

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Mr. Ashish Hajarnis, Vice President (Works)	
FIRM NAME Torrent Pharmaceuticals Limited	STREET ADDRESS Teluka-Kadi, Ahmedabad Mehsana Highway
CITY, STATE, ZIP CODE, COUNTRY Indrad, Gujarat, 382721 India	TYPE ESTABLISHMENT INSPECTED Finished Product and API Manufacturer (Non-sterile)

H. Your (b) (4) equipment Cleaning Verification for (b) (4) is deficient for the following reasons:

1. Your manual equipment cleaning program for product change over cleaning based on visual assessment for equipment cleaning is not scientifically justifiable and not supported with documented evidence.

2. There is no mention of type of swabs to be used in swabbing from pre-determined locations in your equipment cleaning verification protocols and reports.

3. Swab samples were not tested within swab sample solution validity of (b) (4) For example:

Equipment/Swabbing location	Date swab sample collected	Date swab sample tested	Total days swab sample not tested
(b) (4)	23/11/2020	(b) (4)	
	26/11/2020		
	8/1/2022		

Dates are in Indian format (Date/Month/Year)

Your firm collected the above swab samples in a clear glass test tube after manufacturing of (b) (4) (b) (4) pellets which is a light sensitive molecule. There is a potential for degradation of residual active

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Jose E Melendez, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Investigator - Dedicated Drug Cadre	X	9/28/2022

present on the swab sticks leading to unreliable test results as these swab samples were tested outside of the swab sample stability of (b) (4)

OBSERVATION 2

There is a failure to thoroughly review any unexplained discrepancy and the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

Specifically,

A. There is a cascade of failure in your firm's laboratory investigations pertaining to extraneous and unknown peaks. Your firm frequently invalidated out-of-specification (OOS) and laboratory incident investigations without an adequate investigation leading to the potential root cause(s) of manufacturing equipment and laboratory glassware cleaning issues. For example, but not limited to:

Laboratory Incidents - Unknown & Extraneous peaks source not identified:

N/A PSV 09/28/2022

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	9/19/2022-9/28/2022*
	FEI NUMBER 3005029956

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Ashish Hajarnis, Vice President (Works)

FIRM NAME	STREET ADDRESS
Torrent Pharmaceuticals Limited	Taluka-Kadi, Ahmedabad Mehsana Highway
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Indrad, Gujarat, 382721 India	Finished Product and API Manufacturer (Non-sterile)

Sr. No.	Date	Lab Incident Number	Name of Product	Batch number	Test	Description of Lab incident	Conclusion
1	1/4/2021	85613	(b) (4) Tablets USP	(b) (4)	Assay	Unknown peak observed in Sample preparation (b) (4)	Glassware contamination and source of contamination not identified
2	6/5/2021	90366	(b) (4) Tablets USP (b) ng		Dissolution	Extraneous peak observed in sample Unit (b) (4)	Glassware contamination and source of contamination not identified
3	28/05/2021	93788	(b) (4) Tablets (b ng)		Content Uniformity (CU)	Extraneous peak observed in injection no (b) (4)	Glassware contamination and source of contamination not identified
4	7/2/2020	LI/I/F/20/0189	(b) (4) Tablets USP		CU	Extraneous peak observed in CU Tablets (b) and (b	Glassware contamination and source of contamination not identified
5	29/06/2020	LI/I/F/20/0800	(b) (4) Tablets		BU	Unknown peak observed in blend uniformity sample (b) (4)	Glassware contamination and source of contamination not identified
6	5/8/2020	LI/I/F/20/0974	(b) (4) (b) (4) Pallets		Dissolution	Unknown peak observed in 1 Hrs dissolution sample	Glassware contamination and source of contamination not identified
7	26/09/2020	LI/I/F/20/1233	(b) (4) Tablets USP		Dissolution	Extraneous peak observed in test injection	Glassware contamination and source of contamination not identified
8	3/4/2019	LI/I/F/19/0752	(b) (4) Tablets		Assay	Extraneous peak observed in sample injection	Glassware contamination and source of contamination not identified

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE
Jose E Melendez, Investigator - Dedicated Drug Cadre
Pratik S Upadhyay, Investigator - Dedicated Drug Cadre

JSM
X

DATE ISSUED
9/28/2022

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	9/19/2022-9/28/2022*
	FEI NUMBER 3005029956

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Mr. Ashish Hajarnis, Vice President (Works)	
FIRM NAME Torrent Pharmaceuticals Limited	STREET ADDRESS Taluka-Kadi, Ahmedabad Mehsana Highway
CITY, STATE, ZIP CODE, COUNTRY Indrad, Gujarat, 382721 India	TYPE ESTABLISHMENT INSPECTED Finished Product and API Manufacturer (Non-sterile)

9	10/4/2019	LI/I/F/19/0802	(b) (4) Capsules USP	(b) (4)	CU	Extraneous peak observed in content uniformity test unit (b)	HPLC Vial contamination during handling and source of contamination not identified
10	15/06/2019	LI/I/F/19/1169	(b) (4) (b) (4) Tablets		BU	Extraneous peak observed in test injection BU-8.	Glassware contamination and source of contamination not identified
11	7/8/2019	LI/I/F/19/1476	(b) (4) (b) (4) Tablets		Dissolution	Extra peak observed in sample solution injection unit (b) (4) (b) (4)	Glassware contamination and source of contamination not identified
12	11/10/2019	LI/I/F/19/1839	(b) (4) Tablets		Assay	Extra peak observed in Assay	Cross contamination and source of contamination not identified

Dates are in Indian format (Date/Month/Year)

*Laboratory Incidents - Unknown & Extraneous peaks **might be** due to Glassware contamination*

NIA PSU 09/28/2022

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Jose E Melendez, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Investigator - Dedicated Drug Cadre	J.G.M X	DATE ISSUED 9/28/2022

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	9/19/2022-9/28/2022*
	FEI NUMBER 3005029956

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Ashish Hajarnis, Vice President (Works)

FIRM NAME	STREET ADDRESS
Torrent Pharmaceuticals Limited	Taluka-Kadi, Ahmedabad Mehsana Highway
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Indrad, Gujarat, 382721 India	Finished Product and API Manufacturer (Non-sterile)

Sr. No.	Date	Lab Incident Number	Name of Product	Batch number	Test	Description of Lab incident	Conclusion
1	12/5/2022	151578	(b) (4) Tablets	(b) (4)	BU	Unknown peak observed at RT (b) n injection BU 5-8 .	Cross contamination during (b) lution and Source of contamination is (b) (4)
2	20/06/2022	157553	(b) (4) Tablets		Dissolution	Unknown peak observed in Dissolution (1Hrs) unit-6 at RRT (b) (4)	Glassware contamination and source of contamination is (b) (4)
3	21/01/2021	76351	(b) (4) Tablets USP		Assay	Extraneous peak observed at RT (b) (4) Assay sample preparation-(b	Glassware contamination and source of contamination might be a (b) (4)
4	2/8/2021	105661	(b) (4) Tablet		Dissolution	Extraneous peak observed in Sample preparation Unit 3 of Dissolution test.	External contamination and Source of contamination is (b) (4)
5	5/10/2021	116602	(b) (4) capsules		BU	Extraneous peak observed in Blend uniformity test.	Glassware contamination and source of contamination is (b) (4)
6	9/7/2020	LI/I/F/20/0847	(b) (4) Tablets USP		CU	Extraneous peak observed in (Tab (b) & (b) (Tab (b)	Glassware contamination and source of contamination might be (b) (4) or (b) (4)
7	10/7/2020	LI/I/F/20/0850	(b) (4) Tablets USP		CU	Extraneous peak observed in (b) (Tab (b) & (b) (Tab (4) (4)	Glassware contamination and source of contamination might be (b) (4)

Dates are in Indian format (Date/Month/Year)

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE
Jose E Melendez, Investigator - Dedicated Drug Cadre
Pratik S Upadhyay, Investigator - Dedicated Drug Cadre

X

DATE ISSUED
9/28/2022

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	9/19/2022-9/28/2022*
	FEI NUMBER 3005029956

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Mr. Ashish Hajarnis, Vice President (Works)	
FIRM NAME Torrent Pharmaceuticals Limited	STREET ADDRESS Taluka-Kadi, Ahmedabad Mehsana Highway
CITY, STATE, ZIP CODE, COUNTRY Indrad, Gujarat, 382721 India	TYPE ESTABLISHMENT INSPECTED Finished Product and API Manufacturer (Non-sterile)

OOS Investigations - Unknown & Extraneous peaks

Sr. No.	Date	OOS Number	Name of Product	Batch number	Test	Description of OOS	Conclusion
1	19/05/2022	OOS/B/ST/22/037	(b) (4) Capsules (b) mg	(b) (4)	Related Substances by HPLC	25°C/60%RH at 3M sample was found to have unknown peak in test sample solution. According to investigation, this peak was corresponding to (b) (4)	Root cause was due to contaminated HPLC vial. (b) was classified as "Invalid" and the batch was released in the USA Market
2	5/2/2021	OOS/B/FP/21/008	(b) (4) (b) Tablets USP		Related Substances by HPLC	Unknown peak observed was not identified and investigated to determine to source of contamination.	Root cause was due to contaminated HPLC vial. This OOS was classified as "Valid" and the batch was rejected.

Dates are in Indian format (Date/Month/Year)

Review of the firm's OOS investigation revealed that the firm's investigation practices continuous to be deficient. For the above two (2) OOS investigations pertaining to the similar issues of unknown peak observed in sample test solution of respective batches in Related Substances by HPLC test, your firm invalidated test result for (b) (4) Capsules (b) mg (Batch (b) (4) and released the batch into the US market. Whereas classified the OOS as "valid" in case of (b) (4) Tablets USP (b) (4) and rejected the batch. Your Executive Director of Quality stated *"if the unknown peak would have been detected in sample stock solution, they would not have rejected the batch but in this case since the unknown peak was found in HPLC vial they had to reject the batch"*. Whereas your Vice President of Quality and QC Head stated *"unknown peak observed at RRT (b) (4) in case of (b) (4) Capsules (b) (4) mg could be identified as (b) (4) peak through PDA and LC-MS test whereas the unknown peak in case of (b) (4) Tablets USP was not identified. Hence the later drug product batch (b) (4) was rejected"*. Both rationales lacked

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Jose E Melendez, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Investigator - Dedicated Drug Cadre	J.E.M. X	9/28/2022

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	9/19/2022-9/28/2022*
	FEI NUMBER 3005029956

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Mr. Ashish Hajarnis, Vice President (Works)	
FIRM NAME Torrent Pharmaceuticals Limited	STREET ADDRESS Taluka-Kadi, Ahmedabad Mehsana Highway
CITY, STATE, ZIP CODE, COUNTRY Indrad, Gujarat, 382721 India	TYPE ESTABLISHMENT INSPECTED Finished Product and API Manufacturer (Non-sterile)

scientific justification supported with documented evidence.

For each of the above tabulated laboratory incident and OOS investigations, your firm pointed root cause(s) due to contaminated glassware and CAPA taken was to give awareness training to analyst associated with the investigation. Substantial number of examples were found for multiple drug product testing where the original unfavorable results were invalidated without a scientifically sound and justifiable root cause, and results of passing re-test results were reported as the result of record.

The above tabulated OOS and laboratory incidents are few examples of issues observed in the USA marketed products. However, there are many such examples for the domestic and ROW marketed products.

B. Protocol TPL-P-001-19 entitled "(b) (4) Review of Invalidated OOS Investigations for US-Marketed Products Within Expiry" was approved on 25 October 2019 to document the process that third party should use for conducting a retrospective review of all generated invalidated out-of-specifications (OOS) investigation reports for USA marketed products that were within expiry as on October 8, 2019.

Per Protocol TPL-P-001-19, the third party should assess adequacy of investigations and evaluate whether the scientific justification and evidence relating to the invalidated OOS result conclusively or inconclusively demonstrates causative laboratory error. Your Quality Unit committed to amend all investigations that your third party did not find to be in compliance. However, it was observed that some of the amended investigation reports (e.g., OOS/IN/F/FP/19/052, OOS/IN/F/FP/19/054 and OOS/IN/F/FP/19/055) do not clearly establish an unequivocal root cause to invalidate the unexpected OOS results. These amended investigation reports were not subsequently evaluated by your third party. Therefore, this raises the concern that you did not always adequately address the gaps identified in your investigations to support the proposed root causes with scientific justification.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Jose E Melendez, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Investigator - Dedicated Drug Cadre	J.E.M. X	9/28/2022

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	9/19/2022-9/28/2022*
	FEI NUMBER 3005029956

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Mr. Ashish Hajarnis, Vice President (Works)	
FIRM NAME Torrent Pharmaceuticals Limited	STREET ADDRESS Taluka-Kadi, Ahmedabad Mehsana Highway
CITY, STATE, ZIP CODE, COUNTRY Indrad, Gujarat, 382721 India	TYPE ESTABLISHMENT INSPECTED Finished Product and API Manufacturer (Non-sterile)

OBSERVATION 3

Written records of investigation of a drug complaint do not include the findings of the investigation and the follow-up.

Specifically,

Your product quality complaint investigation was deficient for the following drug product:

Product Name: (b) (4) Tablets USP (b) mg, NDC Code: (b) (4) Pack: (b) (4) count
Complaint Number: MC/B/19/141, Date of receipt of complaint: (b) (6)
Batch No.: Unknown, Product shelf life: (b) (4)
Issue: *Contamination of* (b) (4) *Tablets USP* (b) (4) *mg and with* (b) (4)
FAR filed on: 12 June 2019.

A. The complainant (b) (6) was tested positive for (b) (4) through a testing conducted by (b) (6) in (b) (6). The complainant had no history of taking (b) (4). He had taken Torrent Pharmaceutical's drug product named (b) (4) *Tablets USP* (b) (4) *mg* a day prior to getting tested by (b) (6). According to the investigation, Complainant provided the same batch of (b) (4) Tablets USP (b) (4) mg to (b) (6) for testing and it confirmed positive for (b) (4) presence in the (b) (4) Tablets USP (b) (4) mg. Your firm's Quality Unit confirmed the product through pictures of tablet and pharmacy bottle with your firm's name sent by the complainant however the entire investigation was limited to evaluation of documents and trend of this particular drug product.

In your investigation, your Quality Unit kept referring to lack of batch number details as a limiting factor in conducting a thorough investigation. However, your Quality Unit has deviated from the

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Jose E Melendez, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Investigator - Dedicated Drug Cadre	J.E.M. X	9/28/2022

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	9/19/2022-9/28/2022*
	FEI NUMBER 3005029956

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Mr. Ashish Hajarnis, Vice President (Works)	
FIRM NAME Torrent Pharmaceuticals Limited	STREET ADDRESS Taluka-Kadi, Ahmedabad Mehsana Highway
CITY, STATE, ZIP CODE, COUNTRY Indrad, Gujarat, 382721 India	TYPE ESTABLISHMENT INSPECTED Finished Product and API Manufacturer (Non-sterile)

following section of procedure SOP No.: CQA-145-07, Titled: "Procedure For Handling Of Product Quality Complaints", Effective Date: April 08, 2022, Section 4.6.7 *"If complaint samples* ***are not available*** */ not in good condition / of insufficient quantity for desired analysis,* ***then retain sample can be considered for analysis****"*. Your firm tested no retain sample to identify the potential cross-contamination issues. Your firm engaged with third party consultant that also identified the gap of not testing retain samples of (b) (4) Tablets USP (b) (4) mg. Your firm disregarded the recommendation of the third party consultant. Furthermore, your firm failed to evaluate the following:

1) Trend of laboratory incidents pertaining to unknown and extraneous peaks in (b) (4) Tablets USP (b) (4) mg
2) Trend of OOS investigations (valid and invalid) pertaining to presence of unknown and extraneous peaks in (b) (4) Tablets USP (b) (4) mg
3) Product changeover equipment cleaning procedure and practices
4) Suitability of swab and swab sample collection and testing practices

During this inspection, we observed systemic failure in your manufacturing equipment cleaning validation and inadequate laboratory investigations conducted by your firm **(Refer to OBSERVATIONS 1 and 2)**.

B. As a result of above consumer complaint (MC/B/19/141), your firm carried-out a protocol-based evaluation of placebo and excipients by LCMS/MS test method.

Protocol No.: MISP/0414/00, Effective date: October 23 2019; and
Report No.: MISR/0414/00, Effective date: December 23 2019

We observed the following deficiencies:

1) There was no reference of the above protocol-based evaluation in your complaint investigation

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Jose E Melendez, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Investigator - Dedicated Drug Cadre	J.E.M. X	9/28/2022

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	9/19/2022-9/28/2022*
	FEI NUMBER 3005029956

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Mr. Ashish Hajarnis, Vice President (Works)	
FIRM NAME Torrent Pharmaceuticals Limited	STREET ADDRESS Taluka-Kadi, Ahmedabad Mehsana Highway
CITY, STATE, ZIP CODE, COUNTRY Indrad, Gujarat, 382721 India	TYPE ESTABLISHMENT INSPECTED Finished Product and API Manufacturer (Non-sterile)

MC/B/19/141 that revealed trace level of (b) (4) active presence in Plain Placebo (b) (4) (b) (4) (b) (4) and (b) (4) are key excipients used in the manufacturing of several drug products.

- (b) (4) is used in manufacturing of (b) (4) drug products (under different finished good code) of which about (b) (4) are approved for commercialization in the USA market.
- (b) (4) is used in the manufacturing of about (b) (4) drug products (under different finished good code) of which about (b) (4) % are approved for commercialization in the USA market.

2) Upon identifying (b) (4) active in (b) (4) and (b) (4) your firm simply closed the protocol-based evaluation confirming the presence of (b) (4) in Plain Placebo, (b) (4) (b) (4) However, your firm did not extend the investigation to the supplier of (b) (4) and (b) (4) to identify the root cause for the presence of (b) (4) in their supplied materials to the firm.

C. Your Pharmacovigilance (PV) Unit has provided Medical Assessment Report with a significant delay. For the product contamination Complaint No.: MC/B/19/141, your Pharmacovigilance Unit received complaint on 06 June 2019 however the Medical Assessment was done December 31 2019 i.e. a delay of over six (6) months in assessing whether there is any impact and risk as a result of reported complaint while your product was in the USA market. Your AGM-QA stated that reason for delay being PV team requested site level investigation closure report prior to the issuance of Medical Assessment Report.

Subsequent evaluation of trend in the issuance of Medical Assessment Report revealed that your firm has always received Medical Assessment Report upon closure of the site-based complaint investigation.

D. Your firm has deviated from procedure SOP No.: CQA-111-03, Titled: "Reporting Of Field Alert

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Jose E Melendez, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Investigator - Dedicated Drug Cadre	X	9/28/2022

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	9/19/2022-9/28/2022*
	FEI NUMBER 3005029956

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Mr. Ashish Hajarnis, Vice President (Works)	
FIRM NAME Torrent Pharmaceuticals Limited	STREET ADDRESS Taluka-Kadi, Ahmedabad Mehsana Highway
CITY, STATE, ZIP CODE, COUNTRY Indrad, Gujarat, 382721 India	TYPE ESTABLISHMENT INSPECTED Finished Product and API Manufacturer (Non-sterile)

Report For Drug Products". Effective date: March 31 2022, Section 4.5 that requires submitting the FAR within (b) (4) Your firm received Complaint No.: MC/B/19/141 on 06 June 2019. However, the complaint was filed on (b) (4) - A delay by one (1) day.

***DATES OF INSPECTION**
9/19/2022(Mon), 9/20/2022(Tue), 9/21/2022(Wed), 9/22/2022(Thu), 9/23/2022(Fri), 9/26/2022(Mon), 9/27/2022(Tue), 9/28/2022(Wed)

Pratik S Upadhyay
Investigator - Dedicated Drug Cadre
Signed By: Pratik S. Upadhyay -S
Date Signed: 09-28-2022 05:35:10

X

N/A PSU 09/28/2022

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Jose E Melendez, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Investigator - Dedicated Drug Cadre	X	9/28/2022