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	1/19/2023-1/27/2023*
	FEI NUMBER 3004610460

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Rishikesh Jaiwant, Senior Director Manufacturing & Operations

FIRM NAME	STREET ADDRESS
Baxter Pharmaceuticals India Pvt Ltd	Village Vasana Chacharwadi, Taluka Sanand
CITY, STATE, ZIP CODE, COUNTRY Ahmedabad, Gujarat, 382213 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

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.

1. The (b) (4) automatic visual inspection machine was used to visually inspect commercial batches for the US market for clear and amber vials, (b) (4) mL to (b) (4) mL in size, for particles, glass fragments, fibers, low/high volume, miscolored and empty vials. As part of a response to the May 2022 FDA 483, particles of known size were acquired to appropriately qualify the machine. During evaluation of the newly acquired known defect vials on the (b) (4) automatic visual inspection machine, the machine failed to reject all defective vials using the existing commercial machine recipe. The existing machine recipes were found to be inadequate for further qualification work.

   There was no non-conformance investigation opened to evaluate the impact of this failure on previously released product within expiry that used the deficient visual inspection process, evaluate whether a field alert was necessary, or evaluate the impact for the continuing use of the (b) (4) visual inspection equipment. Despite the failure of the existing recipes during challenge tests, the same instrument recipes were used in continuing visual inspection until October 13, 2022, for batches released to the US market.

   a. After the (b) (4) ml amber vials failed the challenge test using the commercial machine recipe, rejecting (b) (4) %, (b) (4) %, and (b) (4) % of the defective vials on July 6, 2022, the same deficient machine recipe continued to be used for visual inspection of (b) (4) Injection (b) (4) ml USP batches (b) (4) that were shipped to the US market.

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	Justin A Boyd, Investigator Pratik S Upadhyay, Investigator - Dedicated Drug Cadre	X Justin A Boyd Investigator Signed By: 2000358686 Date Signed: 01-27-2023 13:11:18	1/27/2023

b. After the (b)(4) ml amber vials failed the challenge test using the commercial machine recipe, rejecting (b)(4) %, (b)(4) %, and (b)(4) % of the defective vials on July 12, 2022, the same deficient machine recipe continued to be used for visual inspection of (b)(4) Injection (b)(4) ml USP batches (b)(4) that were shipped to the US market.

c. After the (b)(4) ml clear vials failed the challenge test using the commercial machine recipe, rejecting (b)(4) %, (b)(4) %, and (b)(4) % of the defective vials on September 11, 2022, the same deficient machine recipe continued to be used for visual inspection of (b)(4) Injection USP (b)(4) ml batches (b)(4) that were shipped to the US market.

d. No challenge tests using the existing (b)(4) machine recipes were initiated for other vial configurations for US market products inspected with the (b)(4) including: (b)(4) ml fill in (b)(4) ml clear vials used for (b)(4) Injection USP, (b)(4) ml fill in (b)(4) ml clear vials for (b)(4) Injection USP, and (b)(4) ml fill in (b)(4) ml clear vials for (b)(4) Injection USP.

On October 5, 2022, FDA requested the site: "*Provide complete qualification reports and data for the automatic visual inspection system*". During communications with FDA, information presented by your firm's management stated: "(b)(4) *Automated Visual Inspection System adequately detects defects in inspected units*". Information was not provided to FDA about the development runs and qualification runs that had already produced data showing the existing machine recipes could not reliably detect defective vials. The suspension for using the (b)(4) came after an FDA request on October 5, 2022. The last batch for the US market visually inspected on the (b)(4) was (b)(4) Injection (b)(4) ml batch (b)(4) on October 13, 2022.

2. **OOS PR ID**: 2147828, Product: (b)(4) Inj. USP (b)(4) % w/v) in (b)(4) w/v)

Result: > (b)(4) um/ml: (b)(4) particles/ml, OOS classification: Invalid OOS

Limit: NMT (b) (4) particles/ml
Date OOS Investigation Logged: 01-Jun-2021
Date OOS Investigation Closed: 15-Jun-2021
Root cause: Usage of rusted scissor to cut open sample bag that may have shed in the sample.

On 01-Jun-2021, your QC Laboratory obtained failing results for sub-visible particulate matter in (b) (4) Inj. USP (b) (4) % w/v) in (b) (4) % w/v), Batch Number: (b) (4) Your investigation is inadequate, and it lacked scientific justification provided with documented evidence. You did not characterize particles present in your referenced product. You identified the rusted scissor used to open the bag as the root cause. However, your QC Analysts used the same rusted scissor to cut open other lots of the same product and the other tested lots met the acceptance limit.

Furthermore, while the investigation was underway, your QC Analyst continued to use the same scissors in subsequent analysis of the same product on a subsequent day. This analysis found passing result, not supporting your claim of the rusted scissor being the root cause for OOS result for sub-visible particulate matter.

3. There is no process to perform any routine identification of particulate identified during the visual inspection process that would allow for evaluation of particulate sources. Over the last two years, none of the "black particles" identified during visual inspection on the (b) (4) and (b) (4) lines have been further identified.

4. **OOS PR ID:** 2300482, Product: (b) (4) Injection USP, (b) (4) mg, Batch Number: (b) (4)

Result: Individual unknown impurity at RT (b) (4) %
Limit: NMT (b) (4) %
Final OOS classification: Invalid OOS,

Date OOS Investigation Logged: 10-Jan-2022
Date OOS Investigation Closed: 23-Feb-2022
Root cause: (b) (4) functioning of the HPLC

On January 10, 2022, your QC laboratory obtained failing result for individual unknown impurity at RT (b) (4) which you confirmed through hypothesis test on the original HPLC ID: EQP/QC/418 and ruled-out any issue with HPLC instrument, analyst and retention times, theoretical plates and tailing factor. Your QC laboratory changed HPLC systems without any scientific justification to "repeat" the analysis using freshly prepared mobile phase, standard and sample test solutions. Your firm attempted to complete "repeat" analysis on different HPLC systems for multiples days, however the repeat analysis was aborted at the system suitability stage due to incidents as mentioned below:

-HPLC ID: EQP/QC/304, Dated analysis initiated: 25-Jan-2022, Incident: (b) (4) peak not eluted/missing in standard
-HPLC ID: EQP/QC/308, Dated analysis initiated: 31-Jan-2022, Incident: Improper peak shape of (b) (4) peak

In the above two (2) cases, your firm deviated from SOP Document No.: CF/QCD/002, Revision: C, Titled: "*Handling of Laboratory Incidences"*. Your firm did not log the incident to investigate the issues pertaining to missing (b) (4) peak and for improper peak shape of (b) (4) peak.

The overall assessment of OOS logged for the US market in years 2021 and 2022 revealed three (3) out of fifty-two (52) OOS having laboratory incidents during OOS investigation. However, your firm did not log a separate LIR to investigate the root cause. Furthermore, in the same period of years 2021 and 2022, your firm changed the HPLC instrument in seven (7) OOS investigations without any scientific justification and invalidated the original failing results

through repeat analysis.

5. No further CAPA actions are initiated when there are repeated Laboratory Incidence Reports (LIR's) that identify the same root cause, unless there are (b) (4) associated with the same analyst in a (b) (4) For example, there were 10 LIR's in 2022 that identified pipetting errors during BET analyses, but no further action was identified in the LIR investigations.

   Additionally, in communications with the FDA in October 2022 your site stated there were "*No OOS due to Pipetting error post implementation of CAPA Jan 2022*" as it related to a review of BET testing. This response did not consider the continuing LIR's that were opened for pipetting errors during BET testing. The response to the FDA also provided a graph demonstrating decreasing BET OOS investigations with the statement "…*the site has implemented significant enhancements related to BET testing by KTA. As a result, the site has consistently reduced the number of OOS BET results for the KTA method, from 66 in 2017 to two through October 2022, and none since April 2022*." However, since November 2020, investigations that were previously classified as OOS were instead identified as LIR. The LIR data from 2021 and 2022 was not considered in this trend analysis.

6. On October 25, 2022, FDA communicated to your firm that the identified root cause for OOS investigations 2345266 and 2349143 for BET were not scientifically based. The investigations have not been further evaluated since that time.

7. Since July of 2022 there have been 16 LIRs opened for cracked/desiccated media observed at the end of sample collection or during plate reading. A comprehensive investigation of media handling at this site was not conducted. An investigation provided by the media supplier on December 1, 2022, identified that the root cause may be due to the type of (b) (4) used and that the supplier would switch to providing an (b) (4) with a low (b) (4) No action was taken for the existing supplies of (b) (4) still in inventory prior to this change by the supplier.

OBSERVATION 2

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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.

1. We observed change parts for the (b) (4) filling and capping lines were damaged in ways that may generate particulate or make them difficult to clean. Change parts were observed encrusted with black, brown, and (b) (4) color materials. The details are included as follows:

   a. (b) (4) on Filling Machine (b) (4) This change part is installed on (b) (4) filling line. It was observed encrusted in parts with brown and black color spots, cracked, chipped, scratch marks and rough surface due to damage to the (b) (4) on many areas while it was tagged in "CLEANED" status. Upon wiping areas of this change part using clean white color wipes, we observed stains of black and (b) (4) color materials on the wipes.

   b. Filling machine (b) (4) These change parts are installed on (b) (4) filling line. These were observed encrusted in parts with brown and black color spots, cracked, chipped, scratch marks and rough surface due to damage on the (b) (4) on many areas while it was tagged in "CLEANED" status. Upon wiping areas of this change parts using clean white color wipes, we observed stains of black and (b) (4) colors materials on the wipes.

   c. Filling machine (b) (4) This change part is installed on (b) (4) filling line and used for carrying vials towards (b) (4) It was observed cracked, chipped, and encrusted in parts with brown and black color stains on many areas while tagged in "CLEANED" status.

d. Capping machine (b) (4) along with (b) (4) guide: These change parts are installed on (b) (4) filling line. These were observed encrusted in parts with brown and black color spots, scratch marks and rough surface due to damage of the (b) (4) on many areas while these were tagged in "CLEANED" status.

e. (b) (4) towards capping machine: This change part is installed on (b) (4) illing line. It was observed encrusted in parts with brown and black color spots, cracked, chipped, scratch marks and rough surface due to damage to the (b) (4) on many areas while it was tagged in "CLEANED" status.

f. Filling machine (b) (4) and (b) (4) guide (b) (4) ml): These change parts are installed on (b) (4) filling line. These were observed encrusted in parts with brown and black color spots, cracked, chipped, scratch marks and rough surface due to damage to the (b) (4) on many areas while these were tagged in "CLEANED" status.

g. Filling machine (b) (4) This change part is installed on (b) (4) filling line. It was observed encrusted in parts with brown and black color spots, cracked, chipped, scratch marks and rough surface due to damage to the (b) (4) on many areas while it was tagged in "CLEANED" status.

h. Filling machine (b) (4) This change part is installed on (b) (4) filling line. It was observed cracked, chipped, scratch marks and rough surface on many areas while it was tagged in "CLEANED" status.

i. Filling machine (b) (4) This change part is installed on the (b) (4) filling line. It was observed to have chips and a rough surface. Areas on the (b) (4) had an unknown sticky substance.

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Rishikesh Jaiwant, Senior Director Manufacturing & Operations	
FIRM NAME Baxter Pharmaceuticals India Pvt Ltd	STREET ADDRESS Village Vasana Chacharwadi, Taluka Sanand
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2. We observed defects on your (b) (4) line filling machine: EQP/PRD/57 while it was tagged in "CLEANED" status on January 26, 2023. This is a non-dedicated filling line, and it is used the manufacturing and filling of (b) (4) Injection USP, (b) (4) mg/ml, (b) (4) ml glass vials for the USA market. The details are as follows:

   a. (b) (4) sheet below the (b) (4) plate was found damaged and missing piece of (b) (4) sheet. Additionally, the (b) (4) sheet was observed cracked and with black color spots across multiple areas.

   b. (b) (4) below filling station: White color powder stains indicative of leakage from the pipe due to spillage.

   c. (b) (4) The color coating on the base of this equipment was peeling-off in many parts along with scratch marks and improper closure at the point of (b) (4) sheet.

   d. (b) (4) we observed scratch and sign of (b) (4) color material deposition. Upon wiping the area of the (b) (4) we observed (b) (4) color spots on the white wipes.

   e. Bulk solution holding tank (ID: EQP/PRD/06) - (b) (4) Lit.: We observed white color spots at the bottom of the tank in the product contact areas after the tank had been cleaned.

3. We observed defects on your (b) (4) Filling machine: EQP/PRD/117 while it was tagged in "CLEANED" status on January 26, 2023. This is a non-dedicated filling line, and it is used the manufacturing and filling of following products for the USA market: (b) (4) Injection USP

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(b) (4) mg/ml (b) (4) ml and (b) (4) ml); (b) (4) Injection USP (b) (4) mg/ml (b) (4) ml; (b) (4) (b) (4) Injection USP (b) (4) mg/ml) (b) (4) ml (b) (4) Injection USP, (b) (4) mg/ml (b) (4) ml

a. Black color spots on (b) (4) and (b) (4)

b. Scratches on the machine (b) (4) back side of filling machine)

4. The (b) (4) located directly above the open vials at the (b) (4) for the (b) (4) filling line uses a threaded bolt that is moved and tightened along the (b) (4) (b) (4) On January 19, 2023, it was observed that this activity appeared to create wear on the (b) (4) creating a rough surface and potential (b) (4) particulate.

5. On January 19, 2023, gaps were observed between the laminar air flow units and the wall where vials exit the (b) (4) on the (b) (4) filling line.

6. On December 14, 2022, during an IPQA evaluation of the (b) (4) filling line, the IPQA identified inadequate sealing/damage at the door for LAF guard on right side of the line. Service request 42676 was created on December 16, 2022. As of January 19, 2023, no work order had been created to address the unsealed areas on the (b) (4) line.

OBSERVATION 3

Written procedures are not established for the cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing or holding of a drug product.

1. The procedure B1/PRD/018 for the (b) (4) filling line has no instructions for cleaning the change parts that are removed from the (b) (4) filling line. These non-dedicated parts are changed for different vial sizes, but after removal from the line they are put in a storage cupboard

without any cleaning. The parts are wiped with (b) (4) during the transfer back into the filling area and wipe with (b) (4) after installation. On January 26, 2023, when these parts were taken out of the cupboard, they were found to have unidentified materials on them and some parts had an unknown sticky residue.

2. The procedure B1/PRD/025 for the (b) (4) line has no detailed instruction for cleaning change parts of different sizes, shapes, and surface materials to completely remove any potential contaminants. Operators reported they wipe with (b) (4) and do the cleaning inside of the filling room. There is no cleaning verification to ensure this process is adequate and on January 26, 2023, "cleaned" change parts were observed encrusted in places with unknown black and (b) (4) (b) (4) color materials.

3. Point 1 of your line clearance checklist states: "Check all the change part for correct format size and ensure no damage". Your production operators select "Not damaged" option even though change parts were found damaged when inspected on January 26, 2023.

OBSERVATION 4

Equipment used in the manufacture, processing, packing or holding of drug products is not of appropriate design to facilitate operations for its intended use and cleaning and maintenance.

1. The filling rooms and capping rooms for both the (b) (4) and (b) (4) filling lines used for US market product are not designed to permit operators to move freely to the required areas. Manufacturing operators are required to go underneath the line to get back and forth to the different sides of the machine to perform routine interventions during filling, such as adding stoppers to the stopper bowl.

2. After vial washing on the (b) (4) line, vials move via conveyor to the (b) (4) The barrier installed to protect the vials as they move on the conveyor has gaps, exposing the vials to the Grade D environment after vial washing.

3. The (b) (4) filling line is not designed to permit viewing from windows or cameras from outside of the aseptic gowning areas. Entry records show QA is not providing routine oversight during filling operations.

4. There is a drain line below the filling station on the (b) (4) line to capture spilled product or product from broken vials. This drain line has not been designed to facilitate cleaning.

OBSERVATION 5

Your firm failed to establish adequate 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.

1.During the manual visual inspection of (b) (4) ml batch (b) (4) and (b) (4) ml batch (b) (4) on January 20, 2023, as well as visual inspection of (b) (4) ml batch (b) (4) and (b) (4) ml batch (b) (4) on January 23, 2023, there were visual inspectors that did not follow procedure B1/PRD/064 "Manual Visual Inspection of Filled Products". These visual inspectors did not inspect against (b) (4) for a minimum of (b) (4)

2.Review of completed visual inspection records found B1/PRD/064 "Manual Visual Inspection of Filled Products" could not have been followed because more units were inspected in the documented time periods than would have been reasonably possible if the procedure had been followed.

a. On September 23, 2022, during visual inspection of batch (b) (4) (b) (4) the inspectors averaged an overall speed of (b) (4) per bag. The procedure requires at least (b) (4) to inspect the (b) (4) at least (b) (4) to inspect on (b) (4) Additionally, time is needed to pick-up and put down bags and physically remove and categorize defective bags.

b. On December 10, 2022, during manual visual inspection of (b) (4) of (b) (4) Injection USP (b) (4) mg/ml (b) (4) ml, the inspectors averaged (b) (4) per (b) (4) vials. For inspection of (b) (4) vials, the procedure first requires inspection of the caps and batch printed data, a step observed to take (b) (4) when viewed on January 23, 2023. This is followed by a minimum inspection time of (b) (4) Additionally, time is needed to pick-up or put down vials, physically place defects into bins, or move the inspected (b) (4) outside of the visual inspection room.

3. There is a lack of scientific rationale for eliminating vials containing (b) (4) particles of known sizes from the kits used to qualify the manual visual inspectors. (b) (4) is used in the manufacturing area and there was apparent wear on (b) (4) observed directly above open vials on the (b) (4) filling line. During the initial qualification of the defect kit, (b) (4) defects were detected at a lower rate than other particle types.

4. There is a lack of scientific rationale for establishing the acceptance criteria for manual visual inspectors of not less than (b) (4) % by combining type A defects (including particulates) and type B defects (including empty vials and wrong color). Further, change control 2531727 has approved changing the acceptance criteria for vials with particulates to at least (b) (4) % without a scientific rationale for how this limit was chosen. The ranging study for the known particle defects showed a probability of detection at (b) (4) % or above for all particles down to (b) (4) µm for glass particles, stopper particles, fibers, and hairs. The manual inspector qualification test kits contain these

types of defects at (b) (4) µm of greater size.

5. The acceptance criteria for light intensity during visual inspection was changed from (b) (4) to not less than (b) (4) lux for all products on October 5, 2019, but lacked a rationale for why the change was made. This limit applies to vials in clear vials and amber vials inspected for the US market. There was no evaluation of whether amber vials require higher light intensity or whether the clear vials should have an upper limit.

   On January 23, 2023, measurements in the (b) (4) visual inspection area for EQP/PRD/443 showed variation within the area. Booth (b) (4) had a reading of (b) (4) lux taken at the (b) (4) while booth (b) (4) had a reading of (b) (4) lux taken from the (b) (4) On that day, (b) (4) ml batch (b) (4) was being visually inspected, which is a clear liquid inside of a clear vial. Amber vials are also visually inspected using the same visual inspection booths.

OBSERVATION 6

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established.

1. For (b) (4) Injection USP (b) (4) mg/ml (b) (4) ml, the bulk bioburden sample is collected from the manufacturing tank. The product is subsequently transferred to the holding tank through a (b) (4) (b) (4) There is no established hold time limit the product can remain in the holding tank before (b) (4) is started. For example, during batch (b) (4) the time between (b) (4) (b) (4) bioburden sampling and the end of (b) (4) was approximately 11 hour ere is no bioburden sampling data from the holding tank. The product is transferred through a (b) (4) (b) (4) prior to filling and the (b) (4) bioburden is tested using filled vials.

2. An operator working in the filling room of the (b) (4) line on January 19, 2023, during the filling of (b) (4) batch (b) (4) was observed with exposed skin on their forehead.

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OBSERVATION 7

Procedures for the preparation of master production and control records are not followed.

Your Quality Unit lacks adequate oversight on the control and management of GMP documents. For example,

1. On 19-Jan-2023, we found torn pieces of analytical balance weight printout in a transparent plastic scrap bag located inside your (b) (4) QC Laboratory. The torn pieces were pertaining to Balance ID: EQP/QC/503, balance printout dated: 18-Jan-2023 and belonged to test sample of (b) (4) mg/ml (b) (4) Batch Number: (b) (4) Test: Assay and Weight/ml. Your QC Analyst stated the weight printout was destroyed due to the sample preparation issue.

   Your QC Analyst deviated from the following procedures due to destruction of balance printout (Original Raw Data)

   - Document No.: CF/CQA/002, Titled: Document Control, Revision: L, Effective date: 09-Sep-2022, Section: 5.3.2 - Document Destruction Process
   - Document Number: CF/CQA/003, Titled: Good Documentation Practices, Revision: E, Effective date: 05-Jan-2023
   - Document Number: GQP-04-04, Titled: Data Integrity, Revision: C, Effective date: 29-Jul-2021

   Furthermore, the sample weighing, and analytical balance printout destruction activities occurred during the (b) (4) that has no (b) (4) Supervisory oversight.

2. On 19-Jan-2023, we observed your production unit employees destroyed GMP documents signed under “Done By” section by tearing into pieces. These torn pieces were found inside a truck

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carrying scrap materials outside of your facility. Destruction of this document was in deviation of your procedure Document No.: CF/CQA/002, Titled: Document Control, Revision: L, Effective date: 09-Sep-2022, Section: 5.3.2 - Document Destruction Process.

3. Documents used to record raw GMP data are not controlled. On January 23, 2023, stacks of form GQF-03-01-05 "Course to Employee Training Roster" and Exhibit EX/CF/CQA/024.03 "Worker Training Questionnaire" were observed in a cabinet in the room used to qualify visual inspectors. They were identified as GMP records. There is no process to reconcile how many are printed, used, and submitted as GMP records.

   There are approximately 69 exhibits from site procedures that are used for recording GMP data that can be printed by any employee or filled out in Team Center Unified using a Microsoft word format. An additional 28 global quality forms used for recording GMP data are maintained on a computer system available to all employees for printing.

OBSERVATION 8

The batch production and control records are deficient in that they do not include in-process control results.

1. Original data is not being maintained and reviewed. The (b) (4) visual inspection machine has the capability to save electronic data or generate printouts, but neither was utilized.

   Only during qualification data was saved electronically, but not reviewed. Therefore, quality personnel did not identify unreported data. On July 5, 2022, a challenge identified as "test1" was intended to be the first challenge of "bad vials" as part of protocol MIS/BA1/159. After inspecting vials, it was found three of the (b) (4) cameras on the visual inspection machine were not functioning. There was no investigation initiated to determine the cause and assess whether it could have impacted other batches. The original data was not reported and no explanation was

documented.

2. Data integrity assessments for production equipment have not evaluated which equipment generates and maintains electronic data or printouts that need to be retained and reviewed.

OBSERVATION 9

Laboratory controls do not include the establishment of scientifically sound and appropriate test procedures designed to assure that drug products conform to appropriate standards of identity, strength, quality and purity.

1. Your firm has not established any written procedure pertaining to Analytical Method Validation (AMV) and Method Verification. Your firm has relied upon on your ADL (Analytical Development Laboratory) – R&D Unit for AMV and Method Verification activities. Your Quality Unit (QA and QC) has no oversight on the AMV and Method Verification conducted at your ADL – R&D Unit to determine the adequacy of analytical test method according to cGMP regulations for testing of drug products sold to the USA market. The AMV and method verification protocols and reports were signed and dated under "Prepared By", "Reviewed By", and "Approved By" sections by your ADL – R&D Unit that is a separate entity located about 15 km from your site and it is not registered with the USFDA.

   Your ADL-R&D Unit provides AMV and Method Verification support to (b) (4) additional sites of Baxter Pharmaceuticals and about (b) (4) CMO sites for Baxter Pharmaceuticals. Your Senior Specialist of the site Quality Unit and Senior Manager of ADL-R&D stated that ADL-R&D Unit has never been internally audited by any of the Baxter sites.

   From April 2022 to 19-Jan-2023, your firm performed thirty-five (35) AMV and ten (10) analytical method verification at ADL-R&D and has routed back two (2) analytical methods though CAPAs for "root cause analysis" and method improvement leading to "revalidation"

because of OOS investigations. The details are as follows:

a.Product: (b) (4) Injection USP (b) (4), CAPA PR ID: 2309629, Date opened: 25-Jan-2022, NCR PR ID: 2249526, OOS PR ID: 2190369

b.Product: (b) (4) Injection BP (b) (4) CAPA PR ID: 2298423, Date opened: 05-Jan-2022, NCR PR ID: 2236278, OOS PR ID:2103182

2.Your firm has no written procedure established for Analytical Method Transfer (AMT). The analytical methods transferred to your site from ADL-R&D is inadequate as it does not ensure the suitability of analytical method to perform the respective analysis of drug product. For example,

Your firm transferred analytical method from ADL-R&D Unit to your site QC based on system suitability and intermediate precision validation parameter as an acceptance criterion only for all products sold into the USA market.

3.Your Raw Material Standard Test Procedures (STPs) pertaining to "Identification by FTIR" are deficient in that there is no mention of background check using (b) (4) instrument method to be used for analysis, quantity, and procedure to prepare sample and standard (b) (4) disc. For example,

Your Raw material STP Document No.: RT/QC/91c/100001511, Tilted: (b) (4) USP, Effective date: 02-Mar-2020 refers to *"Take the Infrared spectrum of the sample as well as* (b) (4) *working standard using the FTIR Spectrophotometer. Examine the substance prepared as* (b) (4)

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	1/19/2023-1/27/2023*
	FEI NUMBER 3004610460

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Rishikesh Jaiwant, Senior Director Manufacturing & Operations

FIRM NAME	STREET ADDRESS
Baxter Pharmaceuticals India Pvt Ltd	Village Vasana Chacharwadi, Taluka Sanand
CITY, STATE, ZIP CODE, COUNTRY Ahmedabad, Gujarat, 382213 India	TYPE ESTABLISHMENT INSPECTED Drug Manufacturer

The following issues were observed:

-Your SOP Document No.: CF/QCD/034 establishes acceptance criteria as a correlation of standard and sample spectra at NLT (b) (4) However, your QC Laboratory provided no scientific justification for establishing NLT (b) (4) limit for FTIR analysis. As such, the overlay of standard and sample spectrums for (b) (4) USP dated 19-Oct-2022 was not identical and has areas with spikes. Your firm did not investigate the issues pertaining to variability in the FTIR spectrum.

-The procedure explained by your QC Analyst included running a background scan using (b) (4) and compare the blank spectrum with representative spectrum included in the respective STP. However, there was no representative spectrum included in the STP and as such there is no mention of (b) (4) and running a background scan using it.

-There is no assurance over the consistency in sample and standard preparation since there is no mention of the quantity of test sample and standard to be used for preparing a separate disc with (b) (4) in your above referenced STP. Your QC Analyst stated that there is "no exact quantity, just use small amount of sample and standard to prepare discs with (b) (4) whereas your QC Supervisor referred to the ratio of (b) (4) for sample/standard and (b) (4) However, your SOP Document No.: CF/QCD/034, Titled: "Fourier Transformed Infrared Spectrometer (FTIR)", Revision: D refers to "sample (b) (4) to (b) (4) % of (b) (4) quantity".

-There is no mention of the instrument method to be used for scanning the sample and standard.

-There is no mention of a technique that is used for preparing sample and standard disc with (b) (4)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Justin A Boyd, Investigator Pratik S Upadhyay, Investigator - Dedicated Drug Cadre	X Justin A Boyd Investigator Signed By: 2000358686 Date Signed: 01-27-2023 13:11:18	1/27/2023

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
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Rishikesh Jaiwant, Senior Director Manufacturing & Operations

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Ahmedabad, Gujarat, 382213 India	Drug Manufacturer

*DATES OF INSPECTION

1/19/2023(Thu), 1/20/2023(Fri), 1/23/2023(Mon), 1/24/2023(Tue), 1/25/2023(Wed), 1/26/2023(Thu), 1/27/2023(Fri)

X Pratik S Upadhyay
Investigator - Dedicated Drug Cadre
Signed By: Pratik S. Upadhyay -S
Date Signed: 01-27-2023 13:11:46

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Justin A Boyd, Investigator Pratik S Upadhyay, Investigator - Dedicated Drug Cadre X Justin A Boyd Investigator Signed By: 2000358686 Date Signed: 01-27-2023 13:11:18	1/27/2023