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	10/9/2023-10/18/2023*
	FEI NUMBER 3004540906

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. S. Ravi Prakash Reddy, Senior Vice President - Operations

FIRM NAME	STREET ADDRESS
NATCO Pharma Limited	Pharma Division, Kothur Village
CITY, STATE, ZIP CODE, COUNTRY Rangareddy, Telangana, 509228 India	TYPE ESTABLISHMENT INSPECTED Sterile and Non-sterile Drug Products 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

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. The (b) (4) non-dedicated (b) (4) used in the manufacturing of finished drug product firm have not b since their installation several years ago. For example,

(b) (4)

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(b) (4)

1. On 11-Oct-2023, we observed thick build-up of (b) (4) and (b) (4) color (b) (4) materials on (b) (4) and throughout the (b) (4) ID: VS/034 located in Unit-(b) (4) while this equipment was in "CLEANED" status. Similarly, (b) (4) (b) (4) and (b) (4) material was also observed on the (b) (4) and in the (b) (4) of (b) (4) ID: VS/034. This (b) (4) is used in the manufacturing of the following potent (b) (4) drug products:

(b) (4)

On 12-Oct-2023, (b) (4) swab samples were collected from different locations of (b) (4) and (b) (4) of (b) (4) 4 and analyzed by HPLC to identify the presence of drug previously manufactured drug products. Test data revealed the presence of different (b) (4) drug substances present as high as up to about 800 times the acceptance limit (b) (4) indicating a potential risk for (b) (4) drug products cross-contamination with other drug products

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active materials (drug substances) that were manufactured using this (b) (4) Swab samples test results are tabulated as follows:

(b) (4)

Limit: N (b) (4) (b) (4)

Furthermore, the swab samples testing showed numerous unknown peaks randomly eluting at different retention times in multiple swab samples tested by HPLC. These unknown peaks were not identified and accounted for in the above table. There is a potential that the unknown peaks could be due to (b) (4) drug products pertaining to (b) (4) active materials. The residues of these active ality and Product Units management stated on 12-Oct-2023 only (b) (4) drug products (listed above from (b) (4) were manufactured using (b) (4) ID: VS/034 located in Unit (b) (4) (b) (4) However, on 16-Oct-2023 your Quality Unit provided a list that indicated (b) (4) products that were manufactured using this (b) (4)

As a result of finding out of acceptance limit results, your firm reported Field Alerts for (b) (4) Tablets (b) (4) mg (b) (4) Tablets (b) (4) for (b) (4) (b) (4) Tablets (b) (4) mg (b) (4) and (b) (4) Tablets (b) (4) mg (b) (4) (b) (4) o the FDA during the current inspection indicating the potential for cross-contamination.

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2. On 13-Oct-2023, we observed build-up of (b) (4) color (b) (4) materials (b) (4) of (b) (4) ID: T/020 located in Unit (b) (4) (b) (4) while this equipment was in "CLEANED" status. This (b) (4) is used in the manufacturing of the following (b) (4) drug products:

(b) (4)

On 13-Oct-2023, (b) (4) swab samples were collected from different locations of (b) (4) of (b) (4) ID: T/020. These swab samples were analyzed by HPLC to identify the types of d s of the previously manufactured drug products. The test data revealed the presence of different drug substances present as high as up to about 117 times the acceptance limit (for (b) (4) indicating a potential risk for drug products cross-contamination with other drug products active materials (drug substances) that were manufactured using this (b) (4) Swab samples test results are tabulated as follows:

Active materials of drug products present on (b) (4)	Sample ID	Observed Result (Limit NMT (b) (4) mcg/swab)
(b) (4)		

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(b) (4)

Furthermore, the swab samples testing showed numerous unknown peaks randomly eluting at different retention times in multiple swab samples tested by HPLC. These unknown peaks were not identified and accounted for in the above table. There is a potential that the unknown peaks could be due to drug products pertaining to (b) (4) active materials.

As a result of finding out of acceptance limit results, your firm reported Field Alerts for (b) (4) (b) (4) Tablets (b) (4) mg ((b) (4) and (b) (4) (b) (4) mg and (b) (4) mg Tablets ((b) (4) # (b) (4) FDA during the n indicating the potential for cross-contamination.

3. During the inspection your Quality Unit collected swab samples from (b) (4) of (b) (4) ID: T/058 located in Unit (b) (4) (b) (4) (b) (4) ID: XIIPD/017, located in Uni (b) (4) and (b) (4) ID: T/031 located in Unit (b) (4) The swab test result are as follows:

- (b) (4) D: T/058 (Limit: NMT (b) (4) mcg/swab)
  (b) (4) Tablets (b) (4) mg and (b) (4) mg): (b) (4) mcg/swab to (b) (4) mcg/swab, (b) (4)
  (b) (4) Tablets (b) (4) mg): (b) (4) mcg/swab
- (b) (4) ID: XIIPD/017: (Limit: NMT (b) (4) mcg/swab)
  (b) (4) Tablets (b) (4) mg): (b) (4) mcg/swab to (b) (4) mcg/swab, (b) (4)
  (b) (4) Tablets (b) (4) mg, (b) (4) mg, (b) (4) mg, (b) (4) mg) (b) (4) mcg/swab to (b) (4) mcg
- (b) (4) ID: T/031 (Limit: NMT (b) (4) mcg/swab)

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(b) (4) ((b) (4) Tablets (b) (4) mg, (b) (4) mg, (b) (4) mg, and (b) (4) mg): (b) (4) mcg/swab, (b) (4) Tablets (b) (4) mg): (b) (4) mcg/swab to (b) (4) mcg/swab.

B. There is no impact assessment performed by your firm in response to cleaning and installation of (b) (4) of non-dedicated (b) (4) ID: T/077 located in Unit (b) (4) (b) (4) For example, on 06-Jan-2023, your fi Control #15225 for procuring new equipment for (b) (4) cleaning. However, upon opening (b) (4) after about 11.4 years, your firm did not evaluate risk based on the condition of (b) (4) on the products manufactured using this (b) (4) and failed to extend the risk to other drug products manufactured using (b) (4) at your facility. Your impact assessment statement *"To improve the cleaning efficiency of* (b) (4) *Hence no impact."* is misleading since there was no cleaning mechanism in place for cleaning (b) (4) (b) (4) 11.4 years.

Your firm reported Field Alert for (b) (4) Tablets (b) (4) mg and (b) (4) mg (b) (4) to the FDA on 18-Oct-2023 indicating the potential for cross-contamination. This FAR was submitted with a delay of over nine (9) month since the initial discovery of the issue in January 2023.

C. Standard Test Procedures (STPs) used in the analyses of swab samples analyses are deficient. For example,

1. Your STPs are deficient in that there is not always mention of swab blank solution preparation. In about 73 out of (b) (4) STPs pertaining to different drug products manufactured at your site, there is no mention of swab blank solution preparation. In the absence of swab blank solution preparation procedure, your QC Analysts were testing swab diluent which does not include new swab stick which is treated similar to swab sample test solution preparation.

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2. Your STPs are deficient in that there is not always mention of the type of swab stick that should be used in collecting swab samples. For example, there is no mention of type of swab stick in about 31 out of (b) (4) STPs for different drug products that should be used in swabbing the surface and testing in QC laboratory for residual materials. In the absence of this information, your QC Analysts were not aware of whether they prepared swab samples correctly and the reliability of test results.

3. There are not adequate swab sticks available in your firm for collecting and testing swab samples. For example, on 16-Oct-2023 your Quality Assurance Unit stated that they do not have the "correct swab stick" for 41 out of (b) (4) drug products that should be used for swabbing equipment used in drug products manufacturing. The orrect swab stick" refers to the swab stick against which equipment cleaning validation was performed.

4. Your firm has not always established stability of swab sample, and standard test solutions. For example, there is no swab solution stability established for 9 products out of (b) (4) Also, there is no mention of swab solution stability in 25 out of (b) (4) STPs for different drug products.

5. Your QC Unit relies upon QA Unit for the final calculation of swab samples test results and investigating the quality event if any. For example, according to your SOP No.: GQA/060-03, Titled: QUALITY CONTROL UNIT RESPONSIBILITIES, Effective date: 30-May-2023, your QC Unit should be evaluating whether samples test results have met the specification or not. However, your QC Unit did not know the acceptance limit for swab samples testing and had no knowledge of swab samples meeting or not meeting the specification limits when swab samples pertaining to Unit (b) (4) and Unit (b) (4) samples were analyzed in your QC laboratory. Your Vice President of ARD and QC stated that upon completing of swab samples testing test results are provided to QA Unit for further calculation and evaluation if the results pass or fails the acceptance limit. There is no oversight of the QA Unit over the accuracy of test results calculated by them.

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D. Production equipment such as [(b) (4)] (equipment ID: VS-033) and [(b) (4)] (equipment ID: VS-034) in Unit [(b) (4)] area are not cleaned and maintained appropriately to prevent contamination. For example:

1. [(b) (4)] (equipment ID: VS-033) housed in Room # [(b) (4)] is not maintained appropriately to prevent contamination. On 10/9/2023, I observed that the [(b) (4)] surface is scratched, dented, and appeared to be missing pieces. Production operator stated the [(b) (4)] surface got impacted due to the use of a pair of metal ring spanners that they routinely use to open it. In order to open the [(b) (4)] one ring spanner is used to hold the nut and the other is used to [(b) (4)] However, the equipment use and clean SOP (VPD/175-05) does not have such instructions i.e., usage of ring spanners to [(b) (4)] The equipment cleaning log indicated product change over "[(b) (4)] cleaning was performed on this equipment on 10/7/2023. after [(b) (4)] tablets batch [(b) (4)] was [(b) (4)] on 10/6/2023. This equipment is a shared use equipment and is used to manufacture about [(b) (4)] or more potent products including [(b) (4)] US commercial products.

2. Major production equipment i.e., [(b) (4)] (equipment ID: VS-034) housed in Room # [(b) (4)] is not maintained appropriately to nation. During the inspection of this equipment (tagged as Clean) on 10/9/2023, I observed [(b) (4)] colored particles in the [(b) (4)] area and [(b) (4)] colored residue on the equipment gasket. Equipment cleaning log indicated product change over "[(b) (4)] [(b) (4)] cleaning was performed on this equipment on 10/7/2023 after [(b) (4)] tablets batch [(b) (4)] was compressed on 10/6/2023. This equipment is a shared use equipment and is used to manufac out [(b) (4)] highly potent products including [(b) (4)] US commercial products.

OBSERVATION 2

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

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Specifically,

Your Quality Unit lacks an oversight on the control and management of GMP documents that are critical in ensuring the drug products manufactured and tested at your site are safe and effective. For example, on 09-Oct-2023, we observed your Quality Control (QC) Microbiology Laboratory, Production, Engineering and Maintenance department's employees deviated from your SOP No.: GQA/083-1, Titled: Data Integrity Policy, Effective date: 19-Jul-2021 and SOP No.: GQA/027-06, Titled: Good Documentation Practices, Effective date: 10-Nov-2020 by destroying GMP documents by tearing it into pieces and disposing as scrap.

There is also a lack of Quality Unit oversight on employees' practices of documenting GMP data on uncontrolled white paper and later disposing these papers by tearing into pieces inside your firm's main scrapyard. Among multiple sections violated by destroying GMP documents, section 4 of SOP No.: GQA/083-1 and section 7.1 of SOP No.: GQA/027-06 refers to (b) (4) principle to ensure integrity of data and Good Documentation Practices. Further, section 7.3 of SOP No.: GQA/027-06 refers to *"All entries shall be made directly on to the original record. Do not use scrap paper."* In the scrapyard we observed torn pieces of analytical weight slips (balance printouts), sterility testing (b) (4) printouts, (b) (4) operation printouts, BET validation protocol, filter integrity test printouts, and batch manufacturing record page along with manufacturing and testing activities recorded in blue and black color ink ball point pens on uncontrolled white printing papers, tissue papers, notebook pages, and gloves. According to your firm's SOP No.: GQA/001-11, Titled: SOP on SOP, Effective date: 31-Jul-2023, section: 7.2.17 Quality Assurance personnel shall use blue color ink ball point pens for data recording and approval. Cross-function (all other departments including QC, Production, Materials, etc) teams shall use black color ink ball point pens.

Upon putting together some of the torn pieces of documents with the help of your employees, your Quality Unit management stated the torn pieces belonged to original record, raw data and meta data

pertaining to microbial testing and manufacturing and these documents should not have been destroyed.

Additionally, we observed your Quality Unit lacked an adequate oversight in ensuring the data pertaining to drug products is complete and reliable. Your Incident Investigations pertaining to missing/lost Batch Manufacturing Record (BMR) pages and QC testing documents lack integrity of data and thorough investigation to determine the root cause. For example,

A. Your Incident Investigation No.: NK/IR/V/PD/2021/009, PR ID: 2471, Product: [(b) (4)] mg [(b) (4)] Batch No.: [(b) (4)] was initiated on 03-Jun-2021 due pages 147 and 148 of [(b) (4)] These pages are used for recording [(b) (4)] manufacturing activities pertaining to [(b) (4)] vials during aseptic manufacturing of the referenced product. We observed the following issues in your incident investigation:

1. Your Quality Unit (QA) issued a second copy of BMR pages 147 and 148 of [(b) (4)] on 04-Jun-2021 to Production Unit as a result of missing BMR pages. These pages were completed simply by writing respective information under sections "Time (From and To)", "Activities (Done by and Sign and date)", "Recorded by" sections on 04-Jun-2021. There is no justification provided for "Time (From and To)" entries for total [(b) (4)] stepwise manufacturing activities after about 25 days from the date of original document was lost (Per BMR page 149, these activities were completed on 09-May-2021).

2. Investigation was not extended to evaluate potential destruction of documents by your employees (Refer to OBSERVATION 2A).

3. Your Production Manager stated that according to CAPA section of this incident investigation and "TRAINING ATTENDANCE CUM EVALUATION STATUS

RECORD", all production employees involved in the manufacturing of this batch were given awareness training and evaluated on questionnaire-based paper assessment sheet. However, one of the production operators that worked on manufacturing steps of BMR pages 147 and 148 was not trained.

4. According to your "TRAINING ATTENDANCE CUM EVALUATION STATUS RECORD", production employees scored 100% marks. However, your Production Manager was unable to provide questionnaire-based training assessment sheet as a proof of evidence to indicate the actual training was imparted and that the employees scored 100% marks. During the inspection on 10-Oct-2023, your Production Manager stated that there was no questionnaire-based awareness assessment performed and no justification was provided for giving 100% marks to production employees.

B. Your Incident Investigation No.: NK/IR/XII/QC/2023/011, PR ID: 17433, Product: (b) (4) Tablets (b) (4) mg, Batch No.: (b) (4) Test: (b) (4) was initiated on 13-Mar-2023 due to missing raw test data worksheets (Sample advise sheet), Standard and Sample weight analytical balance printouts, Laboratory Management System Record of Result (LMS ROR), Sample set, Instrument method). We observed the following issues in your incident investigation:

1. Quality Unit provided no justification for continuing with the sample analysis in the absence of the sample preparation details including analytical balance printout for sample weight. Additionally, your firm provided no justification along with supporting data for the use of (b) (4) mg as sample weight to calculate the test result and concluded testing as meeting the specification limit.

2. Investigation was not extended to evaluate potential destruction of documents by your employees (Refer to OBESRVATION 2A).

3. Your QA Manager stated that according to CAPA section of this incident investigation and "TRAINING ATTENDANCE CUM EVALUATION STATUS RECORD", QC Analysts scored 100 % marks in paper-based questionnaire on "Good Laboratory Practices" procedure for the questions that were not relevant to the issues of document lost/missing. Your firm provided no awareness and refresher training on Document Control, Good Documentation Practices and Data Integrity Policy and Procedures.

C. Your Incident Investigation No.: NK/IR/IV/PD/2022/010, PR ID: 9938 was initiated on 09-Aug-2022 as a result of missing equipment usage logbook of equipment (b)(4) (b)(4) Equipment ID: PK/060, Logbook No.: 62. We observed the following issues in your incident n:

According to your "TRAINING ATTENDANCE CUM EVALUATION STATUS RECORD", production employees scored 100% marks. However, your Production Manager was unable to provide questionnaire-based training assessment sheet as a proof of evidence to indicate the actual training was imparted and that the employees scored 100% marks. During the inspection on 10-Oct-2023, your Production Manager stated that there was no questionnaire-based awareness assessment performed and no justification was provided for giving 100% marks to production employees.

Additionally, your firm provided no documented evidence for the issuance of the original Equipment ID: PK/060, Logbook No.: 62 and the reissuance of a new logbook as a proof of evidence that the packaging activities pertaining to the referenced equipment are recorded in a logbook.

OBSERVATION 3

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

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Specifically,

Adequate procedures are not established to prevent microbiological contamination of [(b) (4)] [(b) (4)] Injections, [(b) (4)] mg/[(b) (4)] mL and [(b) (4)] mg [(b) (4)] mL that are manufactured by aseptic filling operations using filling line [(b) (4)] n Room # [(b) (4)] in Plant [(b) (4)] For example:

A. [(b) (4)] filling, stoppering, and sealing operations take place in [(b) (4)] RABS maintained as grade [(b) (4)]

The space between the [(b) (4)] and wall panel (in front of the [(b) (4)] RABS [(b) (4)] [(b) (4)] is very tight. The [(b) (4)] air supply line with its piping and filter housing is installed on the wall panel and the presence [(b) (4)] table that is used to place settle plates for environmental monitoring creates an opening of only [(b) (4)] of width for the operator. This tight space does not allow a fully gowned operator to extend his arms without touching other surfaces where he stands for almost entire time of the filling operations. On 10/10/2023, during aseptic filling of [(b) (4)] Injection batch [(b) (4)] the production operator's righ [(b) (4)] touched the [(b) (4)] of the [(b) (4)] and his left-hand [(b) (4)] touched the piping of the [(b) (4)] air supply and filter hosing multiple times and as a result he did not sanitize afterwards. Process simulation studies indicate the [(b) (4)] [(b) (4)] RABS is [(b) (4)] multiple times during routine and non-routine interventions.

B. A filling vessel (capacity [(b) (4)] L) [(b) (4)] is parked inside the [(b) (4)] (ID: VEG/072) for aseptic filling of [(b) (4)] batches. On 10/10/2023, during aseptic filling of [(b) (4)] Injection batch [(b) (4)] I observed this filling vessel [(b) (4)] was

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not parked completely [redacted] of [redacted] Instead, the [redacted] back panel was pushing the [redacted] gap of abou [redacted] and thus impacting the [redacted] in the [redacted] The site has no data from [redacted] visualization studies that the lesser [redacted] from [redacted] not being introduced into the grade A area when [redacted] are not [redacted] nd have an [redacted] of about [redacted]

C [redacted] aseptic filling operations can take place in any of the [redacted] i.e., [redacted] in Unit [redacted] Whenever, a batch is filled, the production supervisors leave the filling room (ID: V-034) after line clearance and watch the filling & stoppering operations from view window in [redacted] oom (ID: V-045) and sealing operations from view window in [redacted] ID: V047). However, either of these viewing windows do not provide full view of the entire aseptic processing areas as the [redacted] (ID: VEG/072; installed at [redacted] degrees of the filling area) blocks the view of other asepti rators in the aseptic areas call the supervisor to document any planned/unplanned interventions or significant events.

The site filled [redacted] niection [redacted] mg/ [redacted] mL batch [redacted] on 11/29/2022 and filling started at [redacted] and ended at [redacted] Production supervisor [redacted] observed the sealing operations for this batch [redacted] ID: V047). The firm does not have video cameras installed to ensure all activities are monitored and documented while these are occurring. Review of the entry/exits logs for the production supervisor indicated he was not in the room for more than half hour dung vial filling, stoppering, and sealing operations were taking place. There is no assurance that all significant incidents including interventions have been documented for this batch particularly when there is no supervisor present. The site does not have video cameras to monitor activity later on. On 12/29/2022, the firm shipped [redacted] vials of [redacted] Injection [redacted] mg/ [redacted] mL batch [redacted] (manufacturing date: [redacted] Expiration Date: [redacted] for the US market.

D. During the filling of [redacted] Injection batch [redacted] on 10/10/2023, numerous phone calls were made placed inside the filling room between the operators in the aseptic filling area and the

supervisor in the (b) (4) area. The site performs surface monitoring of the phone buttons only from the phone placed inside the aseptic processing areas. However, the environmental monitoring of the phone receiver (that is held in the operator's hand for long time) and the mouthpiece that is brought near the mouth while talking is not done.

OBSERVATION 4

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,

Your firm's Laboratory Investigations procedure (SOP No.: GQA/086-03, Effective date: 17-May-2023) pertaining to investigation of OOS test results is deficient, and the investigations are inadequate and scientifically non-justifiable. For example,

A. According to your QA Manager, R&D Unit is involved in investigating the root cause and CAPA actions for OOS investigations at Phase II and Phase III stages. However, there is no mention of R&D's "Responsibilities" in section 5.0 of your Laboratory Investigations procedure (GQA/086-03).

B. Your QC and Production Units engages with R&D Units at Phase I to Phase III OOS investigations and sends samples for retesting to R&D for identifying the root cause for failure and summarizing CAPA. Your Laboratory Investigations procedure is deficient in that there is no mention of QC and Production Unit sending sample to R&D for retesting and there is no written procedure and format established for IOC between different departments of your firm.

C. Manufacturing date given by your firm to the drug products is not a true reflection of the actual date when the drug product was manufactured. For example, according to your procedure GQA/046-06, effective date: 18-Apr-2023, section 7.6.1 *"The manufacturing date of the batch shall be the date on*

which the BMR issuing date". There have been significant delays from the date of BMR issuance to the actual date when the drug substance and components were mixed to the date of (b) (4) the batches on stability for long term, intermediate, and accelerated conditions pertaining to exhibit batches, validation batches, and (b) (4) stability batches. Quality Unit did not ensure timely charging of batches on stability and the delay of up to 150 days was observed in some cases. Further, in the event of stability OOS investigations your Quality Unit have concluded the root cause being delayed charging of a batch on stability.

OBSERVATION 5

Separate or defined areas to prevent contamination or mix-ups are deficient regarding operations related to aseptic processing of drug products.

Specifically,

Air flow visualization studies (smoke studies) performed to evaluate unidirectional laminar airflow in aseptic processing areas are deficient to provide assurance about the quality of the drug products manufactured in these areas. For example:

A. The site performed smoke studies under dynamic conditions in 11/2022 after replacement of the HEPA filters (change control # ACC/V/EN/21/024) in classified areas. Following deficiencies were observed in the smoke study videos pertaining to this study.

1. A video (about (b) (4) long) evaluating laminar airflow when the (b) (4) of the (b) (4) (b) (4) RABS (ID: VP-003 A) is (b) (4) nd at about (b) (4) significant smoke is seen being pushed from grade B area into the (b) (4) RABS. It appears this (b) (4) s (b) (4) during normal production operations as the firm has performed 4 interventions for (b) (4) (b) (4) during media fill batch # (b) (4) (b) (4) mL vial size in 2021.

2. A video (about [(b) (4)] long) evaluating laminar airflow when the [(b) (4)] of the [(b) (4)] RAB -003 B) is [(b) (4)] The smoke is seen covering the RABS [(b) (4)] in the [(b) (4)] of the video. Howeve n the RABS [(b) (4)] dense smoke is seen entering only the left side of the filling area. It appears this [(b) (4)] is [(b) (4)] during normal production operations as the firm has performed 10 interventions for [(b) (4)] RABS [(b) (4)] during media fill batch # [(b) (4)] [(b) (4)] mL vial size in 2021.

B. Since 2020, the firm performed the following air flow visualization studies:

S. No.	Protocol No.	Performed on	Dynamic or Static	Status
1	VEV/PQ/099-19	09/2020	Static	Scheduled
2	VEV/PQ/099-21	08/2021	Static	Scheduled
3	VEV/PQ/099-22	11/2021	Dynamic	Unscheduled
4	VEV/PQ/099-24	11/2022	Static	Scheduled
5	VEV/PQ/099-26	07/2023	Static	Unscheduled

The firm presented the smoke studies videos that were shot during these studies. From the presented videos pertaining to the first four smoke studies performed between 09/2020 to 11/2022 it could not be determined as on which date or year these videos have been captured as date, time, and year is not captured when these videos were shot.

OBSERVATION 6

Written records are not always made of investigations into unexplained discrepancies and the failure of a batch or any of its components to meet specifications.

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	10/9/2023-10/18/2023*
	FEI NUMBER 3004540906

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. S. Ravi Prakash Reddy, Senior Vice President - Operations

FIRM NAME	STREET ADDRESS
NATCO Pharma Limited	Pharma Division, Kothur Village
CITY, STATE, ZIP CODE, COUNTRY Rangareddy, Telangana, 509228 India	TYPE ESTABLISHMENT INSPECTED Sterile and Non-sterile Drug Products Manufacturer

Specifically,

Written records of equipment alarms are not maintained and/or investigated pertaining to the equipment used in Parenteral Manufacturing Unit (b) (4) and (b) (4) Manufacturing Unit (b) (4) For example:

A. Parenteral Manufacturing Areas: Major production equipment used in the sterile manufacturing of (b) (4) and other injectable drugs in Unit (b) (4) do not have the capability to store and print alarms ring batch manufacturing. Such equipment includes but is not limited to (b) (4) (b) (4) (b) (4)

SOP (VPD/329-00) for Categorization and Handling of Alarms for Unit (b) (4) Parenterals, requires all (b) (4) (b) (4) alarms be recorded on the logbook and rectified through Maintenance Request Form (MRF). It was observed that the firm did not report any alarm (b) (4) from all aforementioned equipment in the 2022. The site manufactured about (b) (4) batches of injectable drug products in 2022 by using this equipment.

B. (b) (4) manufacturing Areas: SOP VPD/302-01 defines the procedure for categorization and handling of equipment alarms in Unit (b) (4) (b) (4) manufacturing areas. This SOP categorized the potential alarms in (b) (4) the most serious. If a (b) (4) alarm triggers and the machine does not acknowledge the alarm when the operator tries to reset it; then it automatically becomes (b) (4) larm as it indicates there is something wrong with the equipment. The SOP requires al and (b) (4) alarms be recorded on the logbook and investigated through a deviation.

On 10/12/2023, system generated alarms om the (b) (4) machine (ID: VS/037) during the manufacturing of (b) (4) batches each of (b) (4) Tablets (batch # (b) (4) and

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(b) (4) Tablets (batch # (b) (4) were reviewed. It was observed the site observed (b) (4) a r example, following alarms were observed for (b) (4) (b) (4) g, batch (b) (4) that was (b) (4) on (b) (4)

(b) (4)

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FOOD AND DRUG ADMINISTRATION

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(b) (4)

[redacted]

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(b) (4)

[redacted]

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Saleem A Akhtar, Investigator

X Pratik S Upadhyay Investigator Signed By: Pratik S. Upadhyay -S Date Signed: 10-18-2023 07:51:

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(b) (4)

[redacted]

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(b) (4) [redacted]

Every time these alarms appear, they were acknowledged by the operator without documentation. SOP VPD/302-01 requires a deviation be initiated for all the (b) (4) [redacted] alarms. However, the firm failed to investigate these alarms or any other alarms that have been observed in other batches manufactured on this equipment. The alarm logbooks pertaining to (b) (4) [redacted] machine (ID: VS/037) for 2022 and 2023 did not have a single alarm listed for all the products manufactured by using this equipment. During the last three years, the site manufactured approximately (b) (4) [redacted] batches of products using this equipment that were shipped into the US market.

OBSERVATION 7

Appropriate controls are not exercised over computers or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel.

Specifically,

Appropriate user access controls are not exercised for (b) (4) [redacted] achine (b) (4) [redacted] equipment ID: VS-037) housed in Room # (b) (4) [redacted] Unit (b) (4) (b) (4) [redacted] area. For example,

During the inspection of this equip (b) (6) [redacted] on 10/9/2023, Production Operator (b) (6) [redacted] accessed this machine using (b) (4) [redacted] user access. (b) (6) [redacted] stated all operators use the (b) (4) [redacted] user access when

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accessing HMI of this (b) (4) (VS-037). Further investigation indicated the equipment has fifteen (b) (4) listed users and the "Operator" access is not assigned to anyone of them. The details of the listed users and their access level is as follows:

(b) (4)

Production Manager, (b) (4) area stated the equipment (b) (4) equipment ID: VS-037) does have the capabil store and print batch audit trails; however, as of 10/17/2023, the batch audit trails from this equipment are not printed and reviewed. This equipment is a shared use equipment and is used to manufacture abou (b) (4) or more (b) (4) products including commercial products for the US market.

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OBSERVATION 8

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.

Specifically,

Your firm failed to establish adequate written gowning procedures pertaining to the aseptic manufacturing areas to ensure the sterile drug products have the identity, strength, purity, and quality that they represent to possess. For example:

On 10/10/2023, during the inspection of aseptic areas in Unit (b) (4) face covers were not available in the (b) (4) (ID: V-(b) (4) . In this room street garm ts and shoes are removed and factory provided garments, cap (hair net), nose mask, and shoes are used to enter into classified areas (such as (b) (4) maintained as grade C area and aseptic processing areas, maintained as grade B and A areas) with additional gowning in the subsequent change rooms substituting the face cover with the nose mask.

The Gowning SOPs for aseptic and non-aseptic areas do not require use of mustache/beard covers to tuck facial hair; instead nose masks are used that are not intended for this purpose. More than 80 % of employees qualified to enter in aseptic processing areas (grade A and grade B) and other classified areas (grade C and D) areas in (b) (4) and drug manufacturing areas have mustaches.

***DATES OF INSPECTION**

10/09/2023(Mon), 10/10/2023(Tue), 10/11/2023(Wed), 10/12/2023(Thu), 10/13/2023(Fri), 10/16/2023(Mon), 10/17/2023(Tue), 10/18/2023(Wed)

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Rangareddy, Telangana, 509228 India	Sterile and Non-sterile Drug Products Manufacturer

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Investigator
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Investigator
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07:51:

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgment, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."