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	7/16/2024-7/26/2024* FEI NUMBER 3005124189

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Fecel Albuquerque, Vice President, Quality Assurance

FIRM NAME	STREET ADDRESS
Indoco Remedies Limited	L 32 33 - 34 I D C Verna Industrial Road
CITY, STATE, ZIP CODE, COUNTRY Vasco Da Gama, Goa, 403722 India	TYPE ESTABLISHMENT INSPECTED Sterile & Non-sterile 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

Procedures describing the handling of written and oral complaints related to drug products are deficiently written or followed.

Specifically, your firm failed to investigate following consumer complaints thoroughly.

A. Consumer complaint (PR# 166586) was received on 4/13/2024 for missing label on a vial of [redacted] (b) (4) Solution USP [redacted] (b) (4) mg/mL [redacted] (b) (4) mg/mL batch [redacted] (b) (4) The site has [redacted] (b) (4) packing lines to pack all [redacted] (b) (4) drugs for the US market. During protocol-based evaluation and challenging the packing machine (Protocol: SP/Q/24/024), the firm concluded the vials with missing label can pass through the rejection sensor under following conditions:

- When two bottles travel in close vicinity on the conveyer, it allows the bottle with missing label to pass the rejection sensor.
- In case of the machine stoppage due to an alarm, the rejection sensor will allow the bottle with missing label to pass through upon acknowledgement of the alarm and the bottle is present exactly below the product detection sensor.

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The site performed an impact assessment and inspected retain samples of various drug products for missing labels. However, during the review of the impact assessment raw data, we observed the employees' (b) (6) and (b) (6) handwriting who inspected retain samples for at least following products, did not match:

- (b) (4) Injection, USP (b) (4) mg (b) (4) mL, batch (b) (4)
- (b) (4) Solution (b) (4) % sterile, batch (b) (4)
- (b) (4) Injection, USP (b) (4) mg/ (b) (4) mL, batch (b) (4)
- (b) (4) Injection USP (b) (4) mg/mL, batch (b) (4)

Another complaint involving the same batch (b) (4) of (b) (4) (b) (4) Solution USP (b) (4) mg/ml/ (b) (4) mg/mL is discussed in bullet point C of this observation.

B. Following (not all inclusive) complaints involving US consumers, indicating container closure integrity and/or loss of sterility were received:

a. Consumer complaint PR # 100170: received on 2/10/2023 for (b) (4) (b) (4) Solution USP (b) (4) %, batch (b) (4) for missing (b) (4) of the vial.

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b. Consumer complaint PR # 115918: received on 5/24/2023 for [(b) (4)] Suspension USP [(b) (4)]%, batch [(b) (4)] for a missing [(b) (4)] the vial and [(b) (4)]

c. Consumer complaint PR # 123588: received on 7/14/2023 for [(b) (4)] Solution USP [(b) (4)]%, batch [(b) (4)] for no drug in the bottle.

d. Consumer complaint PR # 163319: received on 3/26/2024 for [(b) (4)] Solution USP [(b) (4)] mg/mL/ [(b) (4)] mg/mL, batch [(b) (4)] for no plastic seal on the vial.

e. Consumer complaint PR # 123560: received on 7/14/2023 for [(b) (4)] % sterile Suspension USP, batch [(b) (4)] for a missing [(b) (4)] the vial.

f. Consumer complaint PR # 130717: received on 8/29/2023 for [(b) (4)] Suspension USP [(b) (4)]%, batch [(b) (4)] for a missing [(b) (4)] the vial.

g. Consumer complaint PR # 43479: received on 2/15/2022 for batch [(b) (4)] of [(b) (4)] % sterile Suspension USP, for a missing [(b) (4)] the vial.

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h. Consumer complaint PR # 51087: received on 3/31/2022 for an unknown batch of [redacted] Emulsion [redacted]%, for a missing [redacted] the vial.

The firm invalidated all these complaints stating they have adequate controls in place. The Agency was not notified about these complaints.

C. The firm received about 10 complaints pertaining to [redacted] Solution USP[redacted]% and [redacted] Solution USP [redacted]mg/ml[redacted]mg/mL about the drug not coming out of the vial by [redacted] For example, a consumer complaint PR # 164073: received on 3/30/2024 for [redacted] Solution USP [redacted]mg/mL[redacted]mg/mL, batch [redacted] for drug not coming out of the [redacted] The customer took the impacted bottle to the pharmacy where they inserted a pin to try to open the bottle.

The firm management stated this issue is caused by [redacted] The firm has not initiated any corrective action to resolve the issue.

OBSERVATION 2

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile did not include adequate validation of the aseptic process.

Specifically,

A. The following discrepancies were observed during review of your Line (b)(4) smoke study (airflow visualization study) performed in June and July 2024:

-The view of critical operations, including, but not limited to, interventions and set up, was impeded due to excessive amounts of smoke being generated.

-The smoke study did not assess the airflow around the approximately (b)(4) sensors which are installed in (b)(4) locations approximately (b)(4) the (b)(4) frames in the Grade A RABS filling area.

Your firm manufactures sterile drug products on Line (b)(4) including, but not limited to, (b)(4) Injection USP (b)(4) mg (b)(4) mL and (b)(4) Solution (b)(4)% (b)(4)%.

B. Your firm uses Grade B specifications (b)(4) CFUs for alert limit and (b)(4) CFUs for action limit) for personnel monitoring samples of the mask, forehead, and chest of employees who set up the aseptic filling line and reach into the Grade A RABS with their head and chest. For example, during the manufacturing of (b)(4) Injection USP (b)(4) mg (b)(4) mL (batch number (b)(4) employees engaged in the set up and (b)(4) interventions of the batch received personnel monitoring on their face mask, forehead, and chest upon leaving the Grade A and Grade B areas. These samples were all held to Grade B specifications (b)(4) CFUs for alert limit and (b)(4) CFUs for action limit). The only samples held to Grade A specifications (no growth) are finger

dab and forearm samples collected [redacted] interventions. In addition, none of the personnel monitoring samples collected during gowning qualification activities are held to Grade A specifications (no growth). **THIS IS A REPEAT OBSERVATION**

C. Your firm has approximately [redacted] employees that are not qualified to visually inspect [redacted] glass vials according to your current qualification standards. These employees were used to visually inspect [redacted] glass vials for [redacted] Injection USP [redacted] mg [redacted] mL (including, but not limited to, batch numbers [redacted] intended for the US market. The vials were [redacted] There are typically [redacted] rejected vials per batch which are [redacted] visually inspected (total batch size is [redacted] vials). Your employees typically reject approximately [redacted] of the vials they [redacted] inspect. [redacted]

These employees were last qualified for inspecting [redacted] glass vials prior to [redacted] when the acceptance criteria for visual inspection qualification was to detect at least [redacted]% of major defects. On [redacted] your firm changed the acceptance criteria to detecting at least [redacted]% of major defects in [redacted] vials as listed in your SOP titled "Assessment and Evaluation of Personnel For [redacted] Checking" (number SOP/G2/QA/096. These approximately [redacted] employees detected between [redacted]%-[redacted]% major defects during their initial qualifications prior to [redacted] and they have not been re-qualified on [redacted] vial visual inspection as of [redacted]

OBSERVATION 3

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

Specifically, responsibilities of the quality control unit in QC Lab are not in writing and/or fully followed. For example, the following deficiencies were observed during the inspection of the QC Lab:

A. The quality control unit failed to ensure the warning and error messages in Empower message center are reviewed routinely. During review of (b) (4) Empower message center data, following warning messages were reported:

- About 33 warning notifications indicating, "Injection----cannot be altered. It belongs to a sample set which is currently being acquired".
- About 49 warning notifications indicating, "User Abort" when a run is aborted by the analyst.
- About 69 warning notifications indicating, "Data file checksum error. Possible data corruption or medication of file…..".
- About 10 warning notifications indicating, "Stop Flow key was pressed".

The QC Labs use Empower to process HPLC/GC data. However, warning and error notifications in Empower message are not reviewed by the Quality Unit. The firm's SOPs for Unit (b) (4)

(SOP/G2/QC/076), and Unit (b) (4) (SOP/G3/QA/028), "Review of Analytical Protocols and Electronic Data for Laboratory Records" do not require routine review of warning and error messages reported in Empower Message Center.

B. On 7/18/2024, the QC Lab received many (b) (4) samples including about (b) (4) of (b) (4) Lot # (b) (4) (location: unit preparation area, Line (b) (4) to test (b) (4) (b) (4) The original label (signed and dated with wet ink) pertaining to this sample for (b) (4) test was found in the laboratory trash. The analytical worksheet for this sample was blank showing analysis has not been initiated for this sample yet. However, when the (b) (4) sample was measured, it was observed to be about (b) (4) The QC Lab management failed to provide reasonable justification about missing (b) (4) of the sample and why the original sample label was thrown in the laboratory trash. This lab performs testing of (b) (4) drug products manufactured for the US market. The firm's SOP/G2/QC/173, "General Guidelines for Good Laboratory Practices", Effective Date: 5/16/2024" is deficient and does not ensure appropriate controls over signed/dated labels and (b) (4) sample reconciliation. As per the firm's test procedure SAP/RSF000017/A/S, Effective 4/1/2020, the sample needed for (b) (4) test is (b) (4) mL respectively.

C. In the QC Lab's trash bin, we observed about (b) (4) HPLC vials. These vials appeared to have been used in analysis. However, these vials were vaguely labelled such as but not limited to "(b) (4) (b) (4)", "(b) (4) "(b) (4)", "(b) (4)", "(b) (4)", and "(b) (4)" etc. Due to these vague labels, the solutions in these vials could not be traced back to the original solutions. The site does not have any control procedure in place to demonstrate traceability of test solutions that are tested in the QC Lab using glass HPLC vials.

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OBSERVATION 4

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

REPEAT OBSERVATION

Specifically, control procedures in place to prevent microbiological contamination of sterile drug products are in adequate. For example:

A. On 16 July 2024, we observed (b) (4) sensors located inside the Line (b) (4) RABS, which were located above the open bottle/vial conveyor area, the filling area, and the cap and stopper loading area. The approximately (b) (4) sensors are located approximately (b) (4) (b) (4) the (b) (4) frames and are partially blocking the first air and laminar airflow in the RABS sections they are located in. In addition, your firm does not have an SOP instructing employees how to clean and disinfect the (b) (4) sensors. Line (b) (4) is intended to be used for manufacturing sterile (b) (4) drug products including, but not limited to, (b) (4) Injection USP (b) (4) mg (b) (4) mL and (b) (4) Solution (b) (4) % (b) (4) %.

B. On 19 July 2024, we observed rough surfaces (including non-smooth (b) (4) on the interior of the top back corner of the (b) (4) Line (b) (4) Grade A RABS frame during the manufacturing of media fill, batch number (b) (4) This section of the RABS frame was located above the (b) (4)

C. On 23 July 2024, we observed (b) (4) conduits partially covering electrical wires on manufacturing tank number (b) (4) in the Grade A Line (b) (4) area. The conduits

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were approximately (b) (4) in length and did not extend to the end of the wires. An open gap was present at the ends of the conduits. The external (b) (4) surface of the conduit and the inside of the conduit appeared to be difficult to adequately clean and disinfect to meet Grade A standards. Your firm did not include these electrical wire conduits in a cleaning validation study. Line (b) (4) is intended to be used for manufacturing sterile (b) (4) drug products including, but not limited to, (b) (4) Injection USP (b) (4) mg (b) (4) mL and (b) (4) Solution (b) (4) % (b) (4) %.

D. The firm uses (b) (4) pens (material code: (b) (4) in aseptic filling areas. However, these pens are not cleaned, tracked, and monitored once they are in use in the filling areas. A pen is discarded once the pen ink is completely exhausted. On 7/19/2024, the Production Manger stated there are about (b) (4) pens in Line (b) (4) aseptic filling area which was being used to fill a media fill batch (b) (4) It could not be established for how long these pens were being used in that area.

E. During filling of media fill batch (b) (4) on 7/19/2024, one operator (b) (6) was observed repeatedly touching and resting his gloved hand on the (b) (4) surface of an HMI next to (b) (4) RABS. He did not wipe his hands and arm after repeatedly touching the (b) (4) surface. The firm's SOP/G2/PR/163, "Behavior and Aseptic Practices for Persons Working in Clean Area"; Effective: 3/9/2024, specifically restricts employees from leaning over or putting hands, arms, or fingers over the equipment. However, this employee failed to follow this control procedure.

OBSERVATION 5

Buildings used in the manufacturing, processing, packing and holding of a drug product are not maintained in a good state of repair.

Specifically,
On 16 July 2024, we observed approximately six leaks in the air handling unit service areas in Plant (b) (4) These air handling units supply your sterile manufacturing cleanrooms. There is a (b) (4) area (b) (4) the service area and the cleanrooms are (b) (4) area. The leaks were located above cleanroom locations including, but not limited to, the Line (b) (4) corridor, the Line (b) (4) corridor, and the Line (b) (4) (b) (4) zone (b) (4) unloading area) and filling area. These lines were not in operation during the current inspection due to qualification activities, but your firm plans to manufacture (b) (4) (b) (4) drug products, including, but not limited to, (b) (4) Injection USP (b) (4) mg (b) (4) mL and (b) (4) Solution, (b) (4) %, for the US market on these lines in (b) (4) (b) (4)

OBSERVATION 6

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically, routine environmental monitoring is not performed for garment washers & dryers that are used to wash gowns intended for classified areas. For example:

In manufacturing Unit (b) (4) Room (b) (4) the firm has (b) (4) garment washers & dryers (combo units; equipment ID: (b) (4) that are used to clean garments intended to be used in classified areas (b) (4) in all (b) (4) filling lines. The firm's environmental monitoring program outline in SOP/G2/MI/004 does not include routine monitoring of these washers and dryers.

The firm performed a comprehensive risk assessment of contamination hazards Document #

QRM/QA/G2/032, Effective: 12/30/2023. During this risk assessment the site failed to assess contamination hazards that potentially could be caused by these (b) (4) garment washers and dryers.

OBSERVATION 7

Determinations of conformance to appropriate written specifications for acceptance are deficient for in-process materials.

Specifically, microbiological examination of (b) (4) to determine its suitability to manufacture sterile drugs, is deficient. For example:

The site performs testing of (b) (4) as per SOP/G2/MI/123, Effective: 7/10/2024 "Microbiological Examination of (b) (4) from (b) (4) System (b) (4) On 7/16/2024, following deficiencies were observed during the inspection of incubated media plates pertaining to microbiological examination of (b) (4) used to manufacture sterile drug products:

A. (b) (4) System (b) (4) location # (b) (4) Line supporting (b) (4) The (b) (4) used for this plate was observed having some (b) (4) and was not fully touching the nutrient media in the media plate. The firm's SOP/G2/MI/003 requires that entire (b) (4) surface of the (b) (4) should be touching the nutrient surface to ensure growth; otherwise, the test is invalid. However, the Micro Lab personnel failed to follow the procedure and continued with the analysis until observed during the inspection.

B. (b) (4) System (b) (4) location- (b) (4) (ID: (b) (4) Loop: A visible (b) (4) particle (that did not

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appear as microbial growth) was observed on the (b) (4) This (b) (4) sample is handled under Grade A environment when (b) (4) The firm could not provide information about the size and possible source of this particle.

The site initiated deviations for both incidents when observed on first day of the inspection. However, the micro laboratory manager stated the site has not observed such incidents in last three years.

***DATES OF INSPECTION**

7/16/2024(Tue), 7/17/2024(Wed), 7/18/2024(Thu), 7/19/2024(Fri), 7/22/2024(Mon), 7/23/2024(Tue), 7/24/2024(Wed), 7/25/2024(Thu), 7/26/2024(Fri)

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