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	08/26/2024-09/06/2024
	FEI NUMBER: 3002806978

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Roland Holmqvist, CEO

FIRM NAME	STREET ADDRESS
Rechon Life Science AB	Soldattorpsvagen 5
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Limhamn, Skane Lan, 216 13, Sweden	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

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

There is no assurance that the current flow of personnel through the different rooms in the aseptic area in Building (b)(4) is designed to prevent microbial contamination in the aseptic core. Your current procedures require personnel to leave the aseptic processing room and its critical areas and travel through the shared corridors to perform activities during manufacturing operation.

1. Your environmental monitoring (EM) for the Grade A & B for investigations and deviations are inconclusive, as evidenced by continuous recovery of gram-negative organisms and spore formers in the gowning stage room (b) (4) This area directly precedes production filling lines, meaning that personnel could transfer these contaminants to critical production areas. Additionally, your follow up investigations are inconclusive to show a state of control for Room (b) (4) which connects directly to the production lines.

For example:

- Deviation 2023-341 showed (b)(4) CFU growth of gram-negative Moraxella osloensis recovered from air sample located in Room # (b) (4) Line (b)(4) on 11/06/2023.
- Deviation 2023-359 showed on Line (b) (4) for personal monitoring, showed the operator had growth recovery of (b)(4) CFU that included gram negative Brevimdimonas spp. and a gram-positive Staphylococcus saprophyticus organisms.

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- Deviation 2023-389 includes multiple environmental deviations that show an increased trend for gram negative rods (Moraxella osloensis) in aseptic area (Grade B and Grade A) that were identified in November 2023.

2. SOP-2202 version 5.0, Effective date 2024-05-01, procedure for "Instruktion för in- och utpassage klass B (b) (4) zon) Instruction for in and out passage of grade B (b) (4) zone)", requires personnel to replace gloves immediately in the (b) (4) change room only located in the entrance of the aseptic area in room (b) (4) To change gloves, personnel must leave the aseptic processing room and the critical areas and enter the shared corridors to the (b) (4) change room. The corridors are uncontrolled areas and personnel working in different rooms cross paths in the corridors.

3. SOP-2202 version 5.0, Effective date 2024-05-01, procedure for "Instruktion för in- och utpassage klass B (b) (4) Instruction for in and out passage of grade B (b) (4) zone)" requires personnel to exit the aseptic area to replace hoods, coveralls, or boots and re-gown. Operators must leave the aseptic processing rooms and critical area and travel to shared corridors to the exit room (room (b) (4)) where they will degrown and enter the grade D area to renter the gowning area. Although entry and exit to the aseptic area is recorded, you do not document the reasons for exit including if your operators left the aseptic area due to gowning issues.

The distance between the fill rooms to the (b) (4) gowning room (b) (4) and exit gowning room (b) (4) is below:

Aseptic Processing Room	Room #	Exit Gown (b) (4)	distance (meters) (b) (4)

This trending does continue in through April 2024. Although multiple actions have been taken these are not sufficient to prevent reoccurrence.

OBSERVATION 2

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

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1. Your firm failed to continuous monitoring HEPA air velocity in critical areas to decrease contamination risk and ensure aseptic processing line suitability.

For example:

A. Aseptic connection of bulk solution tank in Line (b)(4) Vials (b)(4) is performed in a Grade A area without continuous monitoring of the HEPA-filtered air velocity.

B. The aseptic filling process on Line (b)(4) ampoules line) is carried out without continuous monitoring of the HEPA-filtered air velocity in the aseptic core.

Deviation 444 outlines multiple air velocity deviations for HEPA filters in Line (b)(4) and Line (b)(4) Your most recent (b)(4) airflow re-qualification study documented on 07/30/2024 describes the failure of the air velocity range parameters for the following Grade A locations:

- Line (b)(4) 03-(b)(4) LAF01 corresponding to Aseptic connection of bulk solution tank.
- Line (b)(4) 03 (b)(4) LAF01 corresponding to filling line aseptic core.
- Room (b)(4) 3-(b)(4) LAF02 and 03-(b)(4) LAF03 corresponding to material storage area (e.g., (b)(4) equipment parts and tooling).

Additionally, your frequency of checking air velocity is (b)(4) schedule. This does not provide assurance that the Grade A conditions, including flow laminarity and air changes are continuously kept during commercial aseptic filling.

2. Inadequate aseptic behavior during set-up process for commercial filling of (b)(4) mcg/mL, lot (b)(4) on Line (b)(4) Ampoule line).

Specifically,

A. We observed at the end of the assembly process the manufacturing operator touching the (b)(4) of the (b)(4) (b)(4) with the palm of the gloved hand.

B. We observed two (2) manufacturing operators performing the setup process within the aseptic core area (Grade A) of the ampoule filling line. Operator A, who was in front of the filling line, was responsible for the

assembly of the filling line equipment parts, while Operator B, who was on the right side of the line, was responsible for transferring all equipment parts and tooling through an open (b) (4) of the aseptic core. We observed both manufacturing operators continually touching the (b) (4) located at the front of the line (Operator A) and the (b) (4) of the aseptic core (Operator B) with the back of their heads.

Per your Risk Assessment Report QGL-1015-02 titled "Identification of critical monitoring locations for viable and non-viable particles on the ampoule filling line", approved on 04/02/2024, no swab or contact surface samples are collected from the referenced areas.

C. We observed a manufacturing operator performing the intervention identify as (b) (4) (b) (4) This (b) (4) is located at the back of the ampoule line within the aseptic core. During this set-up intervention, we observed the manufacturing operator touching the internal surfaces next to the filling zone of the ampoule line with the chest, waist, and forearms.

3. The air flow pattern study [a.k.a. smoke studies] conducted in accordance with Report: "Visualisation of air movements under static and dynamic conditions in the ampoule line (b) (4), approved on 12/18/2023, is inadequate.

The smoke study does not simulate the filling line assembly intervention identified as (b) (4) (b) (4) This (b) (4) is located at the back of the ampoule line within the aseptic core. To perform this intervention, the manufacturing operator extends the arms, so that the upper part of the body is also inside the aseptic core. There is no evaluation of the impact of the air flow during this aseptic manipulation.

4. There is no assurance that the interventions (i.e., routine and non-routine), carried out during the aseptic process simulations (APS) on Line (b) (4) vial (b) (4) Line (b) (4) ampoule) and Line (b) (4) and the frequency of such interventions, are based on a thorough retrospective evaluation of the commercial filling process.

Your firm approved Risk Assessment Report QGL-0046-01 titled "Risk assessment regarding interventions to be performed during media fills"; approved on 08/31/2023. This report lists all (b) (4) opening/closing interventions (i.e., routine and non-routine) that were carried out in the commercial processes of the filling lines (Line (b) (4) Line (b) (4) and Line (b) (4) The period covered by this assessment is from 01/01/2023 to 05/19/2023. Your Quality Unit has been approving additional APS studies based on the outcome of Risk Assessment Report QGL-0046-01. However, this report does not document how many commercial batches were assessed or the frequency that each

intervention was performed on each batch. Therefore, your current media fill program does not ensure that the simulated interventions and their frequency are representative of conditions that may occur during commercial filling.

OBSERVATION 3

Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the equipment to produce aseptic conditions.

Your procedure SOP 2181 version 2.0, Effective date: 2023-11-09 (b) (4) Dekontaminering av lokaler på Bulk Production (b) (4) Sanitization - Decontamination of rooms at Bulk Production" for the (b) (4) decontamination and sanitization of Grade A and Grade B production areas using (b) (4) (b) (4) is inadequate.

Your firm failed to validate and assess the effectiveness, distribution, and reproducibility of (b) (4) to ensure it can safely achieve state of control in aseptic rooms against objectionable microorganisms.

Additionally, your use of biological indicators (BIs) to demonstrate state of microbial control has been ineffective as evidenced by the results from 2024. Specifically, the BIs showed microbial growth in (b) (4) (b) (4) indicating a failure to maintain the required level of decontamination/sanitization/disinfection.

(b) (4)

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OBSERVATION 4

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

Risk Assessment Report QGL-1015-02 titled "Identification of critical monitoring locations for viable and non-viable particles on the ampoule filling line", approved on 04/02/2024, justifies the environmental monitoring locations of ampoule filling line.

On 08/26/2024, during our assessment of the filling line assembly operations for the commercial filling of (b) (4) (b) (4)mcg/mL, lot (b) (4) we found that only (b) (4) air next to the filling zone is monitored.

Your Risk Assessment Report QGL-1015-02 did not consider other critical locations within the aseptic core that could be monitored. For example, your EM monitoring does not include the placement of settling plates on the right side of the line where the transfer of most equipment parts and tooling occurs. The distance from the settling plate located next to the filling zone to the area where most activities occur during line assembly is approximately (b) (4)

OBSERVATION 5

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.

A. Laboratory Investigation AV 2023-348 for (b) (4) mg/ml, (b) (4) ml vial, lots (b) (4) Exp. Dates (b) (4) and (b) (4) was initiated on 11/23/2023 due to out-of-trend (OOT) and out-of-specifications (OOS) assay results.

Specifically, OOT and OOS test results were obtained during the GC analysis performed for the determination of (b) (4) content in (b) (4) Injection of lots (b) (4) and (b) (4) (release).

For lot (b) (4) individual samples were prepared (b) (4) and each sample was injected (b) (4) (b) (4)

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For lot (b) (4) only (b) (4) individual samples were prepared. Each sample was injected (b) (4) (b) (4)

The specification range is (b) (4) mg/ml.

Re-analysis of lots (b) (4) and (b) (4) was carried out using new standard and sample preparations and after changing the GC injector needle. The results obtained were: lot (b) (4) (b) (4) Lot (b) (4) (b) (4)

Your QC laboratory invalidated the initial OOT and OOS results based on passing results from re-testing analysis. No manufacturing assessment was carried out. The investigation report states that the initial OOT and OOS results occurred due to (1) GC injector was not properly working, (2) degradation of the samples as they were prepared (b) (4) before testing, even though they were still within the (b) (4) period after preparation. However, these presumptive root causes are not scientifically proven nor substantiated in the investigation report.

B. Laboratory Investigation AV 2023-041 for (b) (4) mg/ml, (b) (4) ml vial, lot (b) (4) Exp. Date (b) (4) was initiated on 08/02/2023 due to out-of-specifications (OOS) assay result. The OOS test result was obtained during the GC analysis performed for the determination of (b) (4) content in (b) (4) Injection of lot (b) (4) (release). (b) (4) individual samples were prepared (b) (4) (b) (4) and each sample was injected (b) (4) (b) (4)

Assay Results (mg/mL); Lot (b) (4)

(b) (4)

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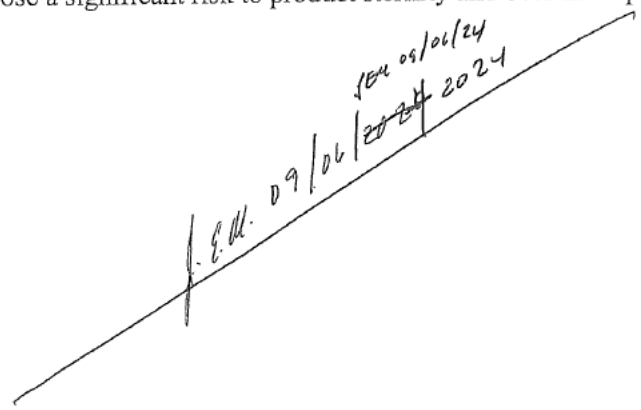
All results obtained were within specifications except for (b) (4) Injection (b) (4) which showed an OOS result of (b) (4) mg/mL. The specification range is (b) (4) mg/ml.
Re-test of (b) (4) was carried out using original sample preparations and after changing the GC injector needle. (b) (4) were not re-tested based on the satisfactory results. The re-test results were Injection (b) (4) mg/mL) and Injection (b) (4) mg/ml).

Your QC laboratory invalidated the initial OOS result for lot (b) (4) based on passing results from re-testing analysis. The investigation report states that the initial OOS result occurred due to GC injector was not properly working. However, this root cause is not scientifically justified in the investigation report.

OBSERVATION 6

Your firm failed to maintain buildings used in the manufacture, processing, packing or holding of drug products in a good state of repair.

During the walking tour of your aseptic processing areas, the walls of the production Rooms (b) (4) and (b) (4) and the floor of the Room (b) (4) in the Grade D aseptic areas were observed to be sticky to the touch. This condition suggested inadequate cleaning and maintenance practices within the controlled environment to potential microbial contamination of the room and the floor. Sticky surfaces can harbor particulate and microorganism, which can pose a significant risk to product sterility and overall aseptic processing integrity.



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