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	5/6/2024-5/17/2024*
	FEI NUMBER 3008255419

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Biju Mathew Thomas, Site Head and Head of Injectables Manufacturing-Complex 3

FIRM NAME	STREET ADDRESS
Mylan Laboratories Limited	Plot No 14, Sipcot II; Krishnagiri Road
CITY, STATE, ZIP CODE, COUNTRY Hosur, Tamil Nadu, 635109 India	TYPE ESTABLISHMENT INSPECTED 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:

PRODUCTION SYSTEM

OBSERVATION 1

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

Specifically,

Your firm performs re-qualification of your aseptic areas (b) (4) . During re-qualification activities of the aseptic areas which may last several weeks, aseptic operations are not performed. According to your Senior Director of Quality, a sterile preparation of (b) (4) is prepared (b) (4) and biological indicators were used to demonstrate that the (b) (4) agent was effective during initial qualification performed back in 2016. However, since then the firm has performed re-qualification of the aseptic areas sixteen times, performed equipment/modification changes to the (b) (4) ine and has never challenged the (b) (4) of the aseptic areas biological indicators to ensure that the aseptic areas are adequately sanitized prior to resumption of aseptic operations. In addition, the firm has never performed maintenance on their (b) (4) as listed in the manufacturer's manual. Approximately (b) (4) batches of aseptically filled drug products manufactured on the (b) (4) Line and (b) (4) Vial Line were shipped to the United States since the last re-qualification initiated on (b) (4)

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	Patty P Kaewussdangkul, Investigator Kevin P Regan, Investigator	X Patty P Kaewussdangkul Investigator Signed By: Patty P. Kaewussdangkul -S Date Signed: 05-17-2024 12:20:36	5/17/2024

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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,

1) We watched videos of your firm's airflow visualization studies conducted on your (b) (4) ine performed in August 2023 and (b) (4) Vial Line performed in January 2024 used du ptic production of sterile drug prod hat are distributed in the United States. Deficiencies we observed include but not limited to:

   a) Smoke studies of the (b) (4) Line and Vial Line are not fully performed under dynamic conditions. Inherent/c e actions and open/closed door interventions were simulated however filling activities were not always performed to simulate routine manufacturing activities.
   b) Transfer of (b) (4) stoppered aseptically filled drug products to be (b) (4) from aseptic line to (b) (4) under continuous Grade A env as not clearly demonstrated by your dynamic smoke studies performed on the (b) (4) ine.
   c) (b) (4) (b) (4)
   d) aseptic line to reach a lever to move the (b) (4) Vial Line.
   e) An aseptic technician failed to sanitize the (b) (4) RABS (b) (4) that were

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exposed to the Grade B environment during (b) (4) movement of the (b) (4) Line upon return to Grade A environment.

f) HEPA unidirectional airflow was blocked during (b) (4) inherent intervention of replenishment of (b) (4) on the (b) (4) Line.

g) A scalpel was not sanitized prior to introduction to Grade A environment to cut open a bag of (b) (4) stoppers that was (b) (4) Vial Line.

Sterile drug products such as but not limited to were aseptically manufactured and distributed to the United States:

- (b) (4) Injection, USP
- (b) (4) njection, USP

2) We reviewed CCTV video of post-production cleaning of the (b) (4) ill line after production of (b) (4) Injection USP (b) (4) mg/mL] [(b) (4) mL] (Batch No: (b) (4) with (b) (4) (b) (4) . On Form-000610094 *Equipment Cleaning Log* there is no assignment of responsibility for what has been cleaned within the (b) (4) estricted access barrier system ((b) RABs) (Grade A). The following deficiencies were noted du CCTV review of post-production cleaning within the (b) (4) ABs but are not limited to due to the limited view of the (b) (4) camera angles in the (b) (4) ine filling room:

a) From (b) (4) , a post-production cleaner touched locations on the (b) (4) line after it was cleaned. The post-production cleaner did not sanitize the touched areas and no further cleaning occurred on the (b) (4) line (where touched).

b) At (b) (4) the post-production cleaner rests their forearm across the (b) (4) during (b) (4) cleaning (line disassembly) of (b) (4) fill line.

c) (b) (4) cleaning (line disassembly) was still occurring on the (b) (4) of the (b) (4) line while cleaning already commenced in the filling area of (b) (4) line. Per SOP-000565893 *Operation and Cleaning of* (b) (4) *Vial Filling Machine and General Procedure to Clean the Machines in Aseptic Area*, e March 25, 2024, version 24.0, (b) (4)

(b) (4)

d) Sterile wipes are not being changed or folded at the frequency established in SOP-000565893 for (b) (4) the (b) (4) RABs.

e) Locations in the (b) (4) of the (b) (4) RABs are being missed during cleaning. Additionally, post-production cleaners do not follow the sequence of cleaning from high to low-risk areas established in SOP-000565893. At (b) (4) it was observed that a cleaner went from cleaning the (b) (4) of the (b) RABs (b) (4) with the same wipe.

Upon review of Form-000610094 *Equipment Cleaning Log* from Jan 2024 to present, there was routine cleaning of the (b) (4) filling line with equivalent conditions of (b) (4) that took (b) (4) (b) (4) while the CCTV video that we reviewed of post batch cleaning took (b) (4) Your equipment cleaning logs do not provide insight into the wide range of equipment cleaning times within your (b) (4) RABs.

3) During video review of filling of (b) (4) Injection USP [(b) mg/mL] [(b) (4) mL] (Batch No: (b) (4) , we observed at ~16:36 that the aseptic production operator failed to use slow and deliberate movement of the (b) (4) line while restarting the filling activity after line stoppage for an inheren (b) (4) intervention "Removal of (b) (4) ." Additionally, the (b) (4) RABs (b) (4) were improperly cleaned before returning to use.

QUALITY SYSTEM

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OBSERVATION 3

Written records are not made of investigations into unexplained discrepancies.

Specifically,

Burkholderia cepacia, was isolated thirteen times during routine monitoring of your (b) (4) system in the Hosur Steriles Facility since March 13, 2021. According to your Qu *Burkholderia cepacia* is not considered an objectionable organism and no investigation was performed to determine the impact of recovering *Burkholderia cepacia,* a gram negative microorganism in your (b) (4) system. Your (b) (4) used to clean non-dedicated equipment such as filling (b) (4) ma ffer tanks used in the aseptic production of sterile drug products. Furthermore, (b) (4) is a raw component used in the manufacture of (b) (4) (b) (4)

OBSERVATION 4

An (b) (4) ield Alert Report was not submitted within three working days of receipt of information con g a failure of one or more distributed batches of a drug to meet the specifications established for it in the application.

Specifically,

Your firm failed to submit an (b) (4) Field Alert Report (FAR) within three working days upon awareness of an OOS failure during the 9M assay stability testing for (b) (4) Injection Suspension USP (b) (4) mg (b) (4) ml Batch # (b) (4) hat was distributed in the United States. The investigation PRID #3341427 was initiated on November 25, 2023. Your Quality Director evaluated the investigation and determined that a FAR was not required. However, a Phase (b) (4) manufacturing investigation was initiated and was not completed until January 11, 2024.

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LABORATORY SYSTEM

OBSERVATION 5

Deviations from written test procedures are not justified.

Specifically,

Your SOP entitled, "BACTERIAL ENDOTOXINS TEST", SOP-000565827, Version 13.0, Effective March 20, 2024 states to (b) (4) (b) (4)

on 5/13/2024, during endotoxin testing of (b) (4) samples, I observed your microbiologist fail to follow written test procedures as the tubes were not (b) (4) and tubes were (b) (4) during reading which resulted in one of two duplicate positive product control (PPC) samples being negative during testing which invalidated the test. Your firm routinely tests (b) (4) or endotoxin which used in the manufacturing of aseptically filled drug products.

***DATES OF INSPECTION**

5/06/2024(Mon), 5/07/2024(Tue), 5/08/2024(Wed), 5/09/2024(Thu), 5/10/2024(Fri), 5/13/2024(Mon), 5/14/2024(Tue), 5/16/2024(Thu), 5/17/2024(Fri)

X Kevin P Regan
Investigator
Signed By: 2003098957
Date Signed: 05-17-2024 12:21:11

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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."