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	11/4/2019-11/15/2019*
	FEI NUMBER 3011033544

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
AVS Ravi Shankar, Head - Operations & Manufacturing

FIRM NAME	STREET ADDRESS
MSN Laboratories Private Limited (Formulations Division, Unit-II)	Survey # 1277, 1319-1324, Nandigama (Village & Mandal)
CITY, STATE, ZIP CODE, COUNTRY Rangareddy District, Telangana, 509228 India	TYPE ESTABLISHMENT INSPECTED Manufacturer of Human Drug Products

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 I OBSERVED:

OBSERVATION 1

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

Specifically,

1) The following two conditions were observed during the review of the smoke study videos conducted in the filling and sealing room (# (b) (4)) and the filtration room (# (b) (4) of the firm's Aseptic Production Area (APA) in Production Block (b) :

a) The airflow pattern video recorded to evaluate the airflow when (b) (4) stoppers are introduced into the (b) (4) (fixed) LAF and from there loaded into the (b) (4) stopper (b) (4) (located within the filling-line's (b) RABs) failed to represent the conditions observed during routine aseptic filling operations. During aseptic filling operations, the (b) (4) stoppers are placed in a LAF cart and transferred directly into the (b) (4) (fixed) LAF connected to the (b) RABs and used for the introduction of the stopper bags and their loading into the (b) (4) . The cart is set close to the (b) (4) (fixed) LAF and the (b) (4) doors of the LAF and the LAF cart are opened in order to do the transfer. Once the bag is transferred, with the cart still placed close to the fixed LAF and the (b) (4) doors opened, the operator cut-open the stopper bag and load it into the stopper (b) (4) within the filling-line's (b) RABs. During the smoke study the video presents the (b) (4) -stopper bag introduction into the (b) (4) (fixed) LAF and the loading of the stoppers into the (b) (4) as two separate events (not as a continuous event as it is observed during routine aseptic filling operations). The loading of the stoppers is shown as a separate recording in which when the stopper bag is cut-opened and loaded into the stopper (b) (4) , the doors of the (b) (4)

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(b) (4) (fixed) LAF are closed and the LAF cart is not set close to the (b) (4) (fixed) LAF.

b) The smoke conducted in the filtration room was conducted at rest conditions. There are no recordings taken at dynamic conditions showing the airflow patterns when the operator performs aseptic connections of the filtration system between the compounding vessel and the filtration vessel located in its LAF.

In addition,

2) During the execution of filling-line assembly procedures, the operator transfers equipment parts such as the (b) (4) stopper (b) (4) and the (b) (4) stopper bowl into the filling-line's (b) RABs. The operator transfers the stopper-(b) (4) and the stopper-bowl by grabbing the bottom (lower) area of the equipment-parts, which are not covered with the (b) (4) and/or material used for sterilization purposes.

In addition,

3) There is no assurance that the interventions simulated during media-fill runs are always representative of the interventions observed during routine aseptic filling operations (in terms of frequency and duration). The following conditions were observed during the review of routine-filling and media-fill intervention records:

a) Routine interventions (i.e., routinely executed through the (b) (4) gloves) are not documented during routine aseptic filling operations. There is no way to assess if the amount of interventions and the time duration these interventions are assigned during the execution of media fills are representative of the conditions observed during routine filling operations.

b) Current procedures for the execution of interventions (document # CPS-026-09 – "Procedure for Assembling, Operation, Cleaning, and Change Over of Vial Filling and Stoppering Machine", version # 9, effective date 11/3/19) list "major maintenance work" and "minor maintenance work" as two of the interventions that might occur during the execution of routine aseptic filling operations. However, only the minor maintenance work intervention is simulated during the media fills. Note: when simulated, the media fill intervention record does not describe what type of maintenance intervention was simulated.

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c) Interventions executed as part of environmental monitoring procedures (i.e., dynamic air sampling) are documented as a single intervention with a time range representing the beginning and end time of the air sampling procedure. Currently, dynamic-air sampling consists of at least (b) different interventions the operators have to execute at (b) different sampling locations within the filling-line's (b) RABs enclosure.

In addition,

4) Review of the intervention records generated during the execution of routine aseptic filling operations in the APA Filling and Sealing Room – Production Block (b), disclosed that:

a) Interventions such as the introduction of (b) (4) stopper bags into the (b) (4) (fixed) LAF and the loading of the stoppers into the filling-line's enclosure (b) RABs (i.e., loading of stoppers into the stopper (b) (4)) are not always documented in the intervention records.

b) While in most instances, the introduction of (b) (4) stopper bags into the (b) (4) (fixed) LAF and the loading of the stoppers into the filling-line's enclosure (b) RABs is a continuous intervention which takes approximately (b) (4) to execute, a few instances were observed in which the continuous intervention was executed in a time period of (b) to (b) (4) . There is no assurance that operators always execute the interventions with slow movements.

OBSERVATION 2

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

Specifically,

1) There is no assurance that conclusions derived on cleaning validation studies of the (b) (4) used in Production Block (b) ((b) (4) Drug Products) for the dispensing of (b) (4) APIs, compounding of bulk solutions of injectable drug products containing (b) (4) APIs, and (b) (4) for tablet products containing (b) (4)

(b) (4) APIs, are properly justified to demonstrate that the (b) (4) gloves are cleaned down to safe levels of (b) (4) drug residues. This is evidence in that:

a) The firm has not conducted studies to demonstrate that current swabbing procedures will be effective for the recovery of drug residues from (b) (4) gloves.

b) Swab samples were collected from the glove (b) (4) and from the gloves. However, there is no assurance that swab samples collected from the gloves were collected from most difficult-to-clean areas and/or worst-case locations on the gloves. The swab samples were collected from the sleeve area of the glove close to the glove (b) (4) and not from the fingers and/or palms of the gloves (i.e., areas of the gloves which get more exposed and/or in contact with (b) (4) APIs during API-dispensing, solution-compounding, and product-(b) (4) operations).

c) Current procedures for the cleaning of the (b) (4) do not include detailed and/or specific instructions on how to clean the (b) (4) gloves and/or to rinse the gloves during the execution of their cleaning procedures.

In addition,

2) Procedures for the cleaning of the (b) (4) (id # CEPR001) located in (b) (4) Room # (b) (4), and the Compounding (b) (4) (id # CEPS016 and id CEPS017) located in the Solution Preparation Room # (b) (4) of Production Block (b), do not include instructions on how to clean the (b) (4) gloves. These (b) (4) are used for the handling of (b) (4) APIs as part of the manufacturing process (i.e., compounding of (b) (4) dosage forms and injectable solutions) of (b) (4) -drug containing drug products (i.e., (b) (4) drug products).

In addition,

3) Failure to follow the procedures for the cleaning of the (b) (4) # CEPS002 in the Vial Washing and (b) (4) Room (# (b) (4)). The procedures (document # CPS-025-01 – "Procedure for Operation and Cleaning of Sterilization and (b) (4) ", version # 2, effective date 4/12/18) requires removal of broken glass pieces from the (b) (4) chamber (zone) by opening the (b) (4) . After removal of glass pieces, the (b) (4) surface of the (b) (4) belt has to be cleaned using (b) (4) . The executed cleaning procedure should be verified to assure that the entire belt (b) (4) surface was properly cleaned. However, on 11/5/19, glass pieces were observed in the upper surface of the belt in the (b) (4) zone of the (b) (4) . At that moment vial washing and (b) (4) operations for the filling of (b) (4) Injection, batch # (b) (4) had just commenced. As per the equipment use logbook, the (b) (4) had been reportedly cleaned and verified as cleaned on 11/3/19.

OBSERVATION 3

Equipment and utensils are not maintained at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product.

Specifically,

There is no assurance that equipment used in the production of USA-market (b) (4) drug products, is always properly maintained to prevent the equipment from becoming a potential source of contamination for the products processed in the equipment. The following conditions were observed during the walk-through of production areas in Production Blocks (b) ((b) (4) drug products) and (b) (general drug products):

a) Evidence of scratching / damage of (b) (4) product-contact-surfaces was observed on 11/4/19 in the following equipment located in different (b) (4) rooms in Production Block (b) : (b) (4) , and square bins (used in product

(b) (4) operations).

b) Broken / chipping gaskets were observed on 11/4/19 and on 11/6/19 in the following equipment in different production areas of Production Blocks (b) and (b): (b) (4) # DEPR200 (gasket of the (b) (4) -transfer piping system which connects the (b) (4) to the (b) (4) (b) (4) -transfer piping system – (b) (4) Area (/ Block (b); (b) (4) # CEPR002 (gasket of the equipment's loading port – (b) (4) Room / Block (b); and (b) (4) machine # CEPR004 (gasket of the unloading port – (b) (4) Room / Block (b).

c) Evidence of product-contact surface breakage / damage was observed in one corner area of the square bin with id # DEPR055 and used in (b) (4) Room (# (b) (4) in Production Block (b).

d) The glass window of the (b) (4) of Capsule Filling Machine (id # DEPR030) in Capsule Filling (b) (4) (Room # (b) (4) – Production Block (b)) was cracked in two areas. When the condition was observed the machine was being used in the filling of (b) (4) Capsules (b) (4) mg, batch # (b) (4).

OBSERVATION 4

Written procedures are not established and followed that describe the examinations to be conducted on appropriate samples of in-process materials of each batch.

Specifically,

1) Manual visual inspection procedures (document # CPS-043-09 – "Procedure for Optical (Visual) Inspection of Parenteral Drug Products", version # 9, effective date 11/9/18) were found to be deficiently written as no specific instructions are included for the inspection of (b) (4) injectable drug products. Procedures indicate that vials shall be inspected "throughout the body by (b) (4) the vials". The procedure also indicates that the vials have to be inspected "from the (b) (4) ". The procedures do not indicate if the vials have to be (b) (4) against the (b) (4) (b) (4) or against the inspector's gloved hand. Also, there are no indications for the inspection of the top area of the (b) (4) -product (b) (4). There is no assurance that AQL samples, which are inspected using the same manual visual inspection procedures, are appropriately inspected in a consistent manner.

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In addition,

2) There is no assurance that operators conducting the manual visual inspection of (b) (4) injectable drug products execute the visual inspection in a consistent manner. As observed on 11/6/19, during the visual inspection of (b) (4) Injection, batch # (b) (4), the (b) (4) operators were not consistent in their execution of the visual inspection procedure. The operators were observed:

a) Grabbing (b) (4) product vials between the fingers and thumb and doing a (b) (4) of the vials against the (b) (4) without seeing the whole circumference of the vials. In instances the vials were (b) (4) rapidly (i.e., not giving enough time for the observation of the vial).
b) Doing inspection of vials individually against the (b) (4) and not the (b) (4) of the visual inspection station.
c) Doing inspection of vials individually against the line that divides the (b) (4) and the (b) (4) of the visual inspection station.
d) Not inspecting the (b) (4) -product (b) (4) top's area.

In addition,

3) There is no assurance that the personnel in charge of the manual visual inspection of injectable drug products inspect the samples as per the conditions established during their respective certifications. While the test kit used for their certification takes approximately from (b) (4) to (b) (4) to inspect (as per inspection station logbooks), review of manual visual inspection records disclosed personnel inspecting drug product vials during inspection periods ranging from (b) (4) to (b) (4). Current visual inspection procedures (document # CPS-043-09 – "Procedure for Optical (Visual) Inspection of Parenteral Drug Products", version # 9, effective date 11/9/18) allow the operators to inspect for inspection periods of (b) (4), inspection time that has not been justified during their respective certifications.

OBSERVATION 5

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Reserve samples from representative sample lots or batches of drug products selected by acceptable statistical procedures are not examined visually at least once a year for evidence of deterioration.

Specifically,

There is no assurance that the quantity of batches selected for the annual inspection / evaluation of their reserve samples is determined by using an acceptable statistical procedure. Current procedure indicates that for each drug product the (b)(4) batch produced of (b)(4) month is selected for annual evaluation of their reserve samples, regardless the quantity of batches produced in a month. In addition, there is no assurance that the conclusions derived during the annual evaluation (i.e., visual examination) of reserve samples are properly sustained. Firm's current procedure is to visually inspect / evaluate a portion of the reserve sample (i.e., (b)(4) % of the reserve sample) from the lot (s) selected for annual inspection / evaluation. All the product units composing the reserve sample are not inspected as part of the annual evaluation of the sample.

***DATES OF INSPECTION**

11/04/2019(Mon), 11/05/2019(Tue), 11/06/2019(Wed), 11/07/2019(Thu), 11/08/2019(Fri), 11/11/2019(Mon), 11/12/2019(Tue), 11/13/2019(Wed), 11/14/2019(Thu), 11/15/2019(Fri)

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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."