DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10 Waterview Blvd., 3rd Floor Parsippany, NJ 07054 (973)331-4900 ORAPHARM1_RESPONSES@fda.hhs.gov	6/10/2024-6/25/2024* FEI NUMBER 3022897129

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Tanis J. Flinkman, Sr. Director, Compounding Operations, PIC

FIRM NAME	STREET ADDRESS
Hikma Injectables USA Inc	36 Stults Rd
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Dayton, NJ 08810-1540	Outsourcer

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

Aseptic processing areas are deficient regarding air supply that is filtered through high-efficiency particulate air filters under positive pressure.

Specifically:

The design and configuration of (b) (4) syringe filling lines (b) (4), and (b) (4) and associated enclosures do not maintain first pass HEPA-filtered laminar flow air over all critical areas to include open syringes and tamper evident syringe caps handled within the ISO 5 classified filling enclosures.

1. The following video recordings of airflow visualization studies conducted in each of the (b) (4) syringe filling lines (b) (4), and (b) (4) demonstrate objectionable airflow patterns including turbulence and upward circulating air adjacent to and above open syringes and tamper evident syringe caps in the ISO 5 classified loading zone. This airflow condition was accepted and approved by your firm management without corrective actions:

   - (b) (4) syringe filling line (b) (4) Videos identified as:
     (b) (4) Loading (b) (4) Room (b) (4)
     (b) (4) Loading (b) (4) Room (b) (4)

   - (b) (4) syringe filling line (b) (4), Videos identified as:

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Edmund F Mrak, Investigator Ogechi C Nna, Investigator Luxuly Abraham, Investigator X Edmund F Mrak Investigator Signed By: Edmund F. Mrak Jr -S Date Signed: 06-25-2024 14:47:18	6/25/2024

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(b) (4) Room# (b) (4)
(b) (4) Room# (b) (4)

- (b) (4) syringe filling line (b) (4), Video identified as: (b) (4) Loading (b) (4) Room (b) (4)

2. The divider/safety guard between the loading and filling/capping sides of (b) (4) syringe filling lines (b) (4), and (b) (4) obstructs first pass HEPA filtered air over open syringes and tamper evident syringe caps carried on the load dials from the loading to the filling/capping zones within the ISO 5 classified enclosure.

(b) (4) syringe filling lines (b) (4), and (b) (4) are used to fill drug products intended to be sterile including Phenylephrine HCL 1 mg per 10 ml (100 mcg/ml) in 0.9% Sodium Chloride Injection.

OBSERVATION 2

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

Specifically:

1. You do not perform active air sampling for airborne viable monitoring in the ISO 5 classified syringe filling and capping zone of your (b) (4) syringe filling lines (b) (4), and (b) (4) during syringe filling operations for drug products including Phenylephrine HCL 1 mg per 10 ml (100 mcg/ml) in 0.9% Sodium Chloride Injection, Lot #

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(b) (4) Compounders reach with their gloved hands and gowned arms into the ISO 5 filling/capping zone within the filling lines enclosures to make drug product flow path aseptic connections and to perform filling operations interventions such as removing a cap stuck in the capping fixture.

2. You do not monitor total airborne particulate in the ISO 5 classified syringe and cap loading zone of your (b) (4) syringe filling lines (b) (4), and (b) (4) during syringe filling operations for drug products including Phenylephrine HCL 1 mg per 10 ml (100 mcg/ml) in 0.9% Sodium Chloride Injection, Lot # (b) (4). Compounders reach with their gloved hands and gowned arms into the ISO 5 loading zone within the filling lines enclosures to manually introduce syringes to the syringe loading dial and caps to the cap loading dial during syringe filling operations.

3. You have not identified all critical sites of your (b) (4) syringe filling lines (b) (4) and (b) (4) for (b) (4) filling surface monitoring for microbiology testing after syringe filling operations for drug products including Phenylephrine HCL 1 mg per 10 ml (100 mcg/ml) in 0.9% Sodium Chloride Injection, Lot (b) (4). For example, you have not identified all critical surfaces of your (b) (4) syringe filling lines for (b) (4) filling monitoring including but not limited to the following:

   a. The fill connector of the tubing set which is required to be maintained sterile throughout filling operations.

   b. The (b) (4) transfer tooling (b) (4)) which is not sterilized and is in contact with the outer periphery of tamper evident syringe caps above and in close proximity to the female cap insert which is a product contact surface and is required to be maintained sterile as part of the container closure system.

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OBSERVATION 3

Samples taken of drug products for determination of conformance to written specifications are not representative.

Specifically:

You do not ensure that compounded finished drug product samples for quality control testing and disposition of the lot are representative of each sub-assembly when a sub-assembly batch process is followed in compounding and filling operations. Your procedure, SOPDTN15106, Finished product sampling procedure, specifies that "Sampling should be done from the (b) (4) of the lot (if applicable) to retrieve a composite sample." For example:

1. Phenylephrine HCL 1 mg per 10 ml (100 mcg/ml) in 0.9% Sodium Chloride Injection Lot # (b) (4) was compounded as (b) (4) and filled into syringe primary packaging on (b) (4) syringe filling line (b) (4) According to the master batch record, quality control sample collection for microbiology consisted of (b) (4) samples for sterility testing and (b) samples for endotoxin testing; quality control sample collection for chemistry testing consisted of (b) (4) samples for ID/Potency, (b) (4) for Appearance, pH, and (b) (4) samples for Sub-Visible Particles. There is no record of the sample distribution to demonstrate that samples tested are representative of each sub-assembly of the lot.

2. Diltiazem HCL 125 mg per 125 ml (1 mg/ml) in 0.9% Sodium Chloride Injection Lot # (b) (4) was compounded as (b) (4) and (b) (4) filled in IV Bags. According to the master batch record, quality control sample collection for microbiology consisted of (b) (4) samples for sterility testing and (b) (4) samples for endotoxin testing; quality control sample collection for chemistry testing consisted of (b) (4) for ID/Potency, (b) (4) for Appearance, pH, and (b) (4) for Sub-

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Visible Particles. There is no record of the sample distribution to demonstrate that samples tested are representative of each sub-assembly of the lot.

OBSERVATION 4

Laboratory controls do not include the establishment of scientifically sound and appropriate test procedures designed to assure that drug products conform to appropriate standards of identity, strength, quality and purity.

Specifically:

You do not fully follow your written procedure SOPDTN15087, Growth Promotion Test, to confirm the ability of a new batch of media to support growth of a predetermined selection of representative microorganisms to include environmental isolates. Performance of growth media including those used for drug product sterility testing, environmental monitoring, and aseptic process simulation is not demonstrated through use of select "(b) (4)" in growth promotion testing in accordance with your procedure SOPDTN15087, Growth Promotion Test.

***DATES OF INSPECTION**

6/10/2024(Mon), 6/11/2024(Tue), 6/12/2024(Wed), 6/13/2024(Thu), 6/14/2024(Fri), 6/25/2024(Tue)

X Ogechi C Nna
Investigator
Signed By: 2004008930
Date Signed: 06-25-2024 14:47:58

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."