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 Fax:(973)331-4969 ORAPHARM1_RESPONSES@fda.hhs.gov	5/23/2022-6/8/2022* FEI NUMBER 3022897129

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Michael J. Moore, Senior Director Compounding Operations

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

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 the system for monitoring environmental conditions.

Specifically:

1. Your airborne particulate monitoring program for aseptic operations is not designed and conducted to provide meaningful data to support the quality of your drug products intended to be sterile. You do not monitor airborne particulates to ISO 5 air classifications throughout aseptic operations and the orientation of the particle counter (b) (4) is not directed into the flow of air during monitoring. For example:

   a. On 05/24/2022 during the aseptic filling of Ketamine HCL 50 mg per ml Injection, NDC (b) (4), Lot No.: (b) (4) in cleanroom 142-6 within ISO 5 (b) (4) Laminar Flow Hood No.: (b) (4), we observed that airborne particulate monitoring was performed (b) (4) for approximately (b) (4) during the operation. You do not provide scientific justification for the frequency and duration of airborne particulate monitoring performed during aseptic operations in the critical zone of the ISO 5 (b) (4) Laminar Flow Hood.

   b. On 05/24/2022 during the aseptic filling of Ketamine HCL 50 mg per ml Injection, NDC (b) (4), Lot No.: (b) (4) in cleanroom 142-6 within ISO 5 (b) (4) Laminar Flow Hood No.: (b) (4) we observed that the orientation of the particle counter (b) (4) (b) (4) was not directed into the flow of air during monitoring. The particle counter was positioned nearly (b) (4) in the (b) (4) laminar flow hood where

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Edmund F Mrak, Investigator Samir C Gala, Investigator Jay B Shah, Investigator X Edmund F Mrak Investigator Signed By: Edmund F. Mrak Jr -S Date Signed: 06-08-2022 11:58:28	6/8/2022

the airflow is expected to be (b) (4) as delivered from the HEPA filter in the back of the hood. You do not provide scientific justification for the observed orientation of the particle counter (b) (4).

c. Requirements written in your procedure SOPDTN15162, Routine Non-Viable particle count procedure, Effective 02/28/2022, specify an airborne particulate monitoring frequency of (b) (4) for (b) (4) during (b) (4) aseptic compounding and filling operation to include pooling, subassembly, and syringe or IV Bag filling. You do not provide scientific justification for this frequency and duration of airborne particulate monitoring performed during aseptic operations in the critical zone of the ISO 5 (b) (4) Laminar Flow Hood.

2. On 05/24/2022 during the aseptic filling of Ketamine HCL 50 mg per ml Injection, NDC (b) (4), Lot No.: (b) (4) in cleanroom 142-6 within ISO 5 (b) (4) Laminar Flow Hood No.: (b) (4), we observed that the passive airborne viable monitoring (settling plate) location was adjacent to the HEPA filter face in the back of the hood. You do not provide scientific justification for the observed monitoring location. Your procedure SOPDTN15121, Microbiological Environmental Monitoring of Compounding Department, Effective 02/28/2022, describes the passive airborne viable monitoring (settling plate) location as "Inside LFH, back of the workbench".

OBSERVATION 2

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

Specifically:

You have not evaluated the airflow pattern in all your ISO 5 (b) (4) Laminar Flow Hoods under (b) (4) conditions simulating (b) (4) aseptic operation performed in each hood during sterile-to-sterile

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compounding and aseptic filling of your drug products intended to be sterile.
Inspectional evaluation of your ISO 5 area airflow pattern studies; Document No.: (b) (4), Risk Assessment Regarding the Equivalency of the LFH through the process of (b) (4) smoke studies, Approved Date: 05/26/2022; and List of Commercial Batches Compounded related with hood smoke studies in (b) (4), revealed that (b) (4) products/lots were produced during the period 02/22/2022 to the present through aseptic operations performed in ISO 5 (b) (4) Laminar Flow Hoods for which there was no direct (b) (4) airflow pattern evaluation. For example: Fentanyl Citrate 50 mcg/ml (100 mcg per 2 ml) in 0.9% Sodium Chloride Injection, NDC (b) (4), Lot No.: (b) (4), Expiry: 07/15/2022, was produced in cleanroom suite 142-7 and filled in ISO 5 (b) (4) Laminar Flow Hood No.: (b) (4) which was not directly assessed in an airflow pattern study for the aseptic syringe filling operation.

Furthermore, your (b) (4) airflow pattern studies performed in ISO 5 (b) (4) Laminar Flow Hoods did not consider the condition when the cleanroom suite (housing the ISO 5 Hoods) (b) (4) (b) (4) during aseptic operations.

OBSERVATION 3
An adequate number of batches of each drug product are not tested to determine an appropriate expiration date.

Specifically:
1. Your drug product stability program for commercial drug products labeled with a (b) (4) (b) (4) does not include data from direct testing of those products produced in your facility. To date you have not placed any drug products/lots produced in your facility on a stability testing program. Your stability program and current (b) (4) for all drug products is based on data derived from testing of stability products/lots produced for this purpose in other facilities.

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2. Your drug product stability program for commercial drug products labeled with a (b) (4) (b) (4) does not include testing of container closure integrity at or beyond the labeled (b) (4) For example: your Report# (b) (4), Compounding Development and Stability Report for 50µg/mL Fentanyl Citrate Injection (PF) for the Dayton Outsourcing Facility does not include container closure integrity testing results for a timepoint at or beyond the labeled (b) (4).

***DATES OF INSPECTION**

5/23/2022(Mon), 5/24/2022(Tue), 5/25/2022(Wed), 5/26/2022(Thu), 5/27/2022(Fri), 6/08/2022(Wed)

X Samir C Gala
Investigator
Signed By: 2002953776
Date Signed: 06-08-2022 11:59:15

X Jay B Shah
Investigator
Signed By: 2003178113
Date Signed: 06-08-2022 11:59:53

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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."