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	5/29/2024-6/12/2024* FEI NUMBER 2220525

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Omar F. Alkhrisat, General Manager

FIRM NAME	STREET ADDRESS
Hikma Pharmaceuticals USA Inc.	2 Esterbrook Ln
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Cherry Hill, NJ 08003-4002	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

Procedures designed to prevent objectionable microorganisms in drug products not required to be sterile are not established and followed.

Specifically, your air visualization "smoke" studies, *TestProtCHH15017 Protocol to Perform Smoke Profile in Room 115* and *TestProtCHH15372 Protocol to Perform Smoke Study In Room 115 for Machine Adjustments* utilized by your firm to qualify your controlled environment revealed deficiencies.

For example:

A. In your protocol, *TestProtCHH15017* operations under dynamic conditions were not included such as but not limited to, the changing of the settle plates (occurs (b) (4)), refilling the (b) (4) with stoppers during filling operations and clearing a jam from the (b) (4) unit. These are operations that are part of your filling process as observed on 05/29/2024 of the filling of Fentanyl 10mcg/250ML lot (b) (4) . In addition, in the video titled *Dynamic Machine Filling Station* (b) (4) the "smoke" used to show the operation of the (b) (4) filler difficult to fully visualize.

B. In your protocols, *TestProtCHH15372* and *TestProtCHH15017,* the length of the studies, and volume of smoke utilized are not sufficient to visualize the flow of air within the filling unit. Further, the camera angles in all the studies do not provide a full view of the unit and the movement of air from the top of the unit to the bottom under dynamic conditions.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Christina K Theodorou, Investigator Yoriann Cabrera Bartolomei, Investigator Christian F Gomez Lugo, Investigator Azeezat M Lawal, Investigator	X Chris tina K Theodorou Investigator Signed By: Chris tina K. Theodorou -S Date Signed: 06-12-2024 10:31:19	6/12/2024

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OBSERVATION 2

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, your firm's co-validated method transfer, *ReportCHH15181 Method Transfer Report for SOPCHH15817 (TM D227) Determination of Fentanyl in Fentanyl Citrate in 0.9% Sodium Chloride Injection IV Bags* omits established characteristics for conducting a method validation, such as but not limited to, Accuracy and instrument comparability. Your firm also provided *Memo: FDA Discussion - Co-Validation of the Analytical Procedure for Fentanyl Citrate Injection Assay,* dated June 6, 2024, to support your co-validation. *TM D227 Determination of Fentanyl in Fentanyl Citrate in 0.9% Sodium Chloride Injection IV Bags* was validated by your contracted testing laboratory on their premises and your co-validation was conducted in your Research and Development laboratory. The rationale to support not including characteristics of a method validation other than precision are not discussed in either document.

OBSERVATION 3

The responsibilities and procedures applicable to the quality control unit are not fully followed.

Specifically, your firm did not follow the instructions outlined in your procedure, *SOPCHH15028 Manufacturing Investigation Report (MIR) System*. According to section 7.4.2.4 of SOPCHH15028, "*when performing an investigation, if a review of previous lot data, stability and retain samples, customer complaints, Annual Product Reviews, and other identifiable data is performed, this documentation of reviews should be included in the investigation*". However, the documentation of the following deviations QE-021941, QE-018568, and QE-007589 did not include the results and data of the

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additional samples taken to support the impact and risk assessment of the investigation.

***DATES OF INSPECTION**

5/29/2024(Wed), 5/30/2024(Thu), 5/31/2024(Fri), 6/03/2024(Mon), 6/04/2024(Tue), 6/05/2024(Wed), 6/06/2024(Thu), 6/07/2024(Fri), 6/12/2024(Wed)

X Yoriann Cabrera Bartolomei
Investigator
Signed By: Yoriann M. Cabrera Bartolomei -S
Date Signed: 06-12-2024 10:46:09

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE

Christina K Theodorou, Investigator
Yoriann Cabrera Bartolomei, Investigator
Christian F Gomez Lugo, Investigator
Azeezat M Lawal, Investigator

X Chris Ina K Theodorou
Investigator
Signed By: Chris Ina K. Theodorou -S
Date Signed: 06-12-2024 10:31:19

DATE ISSUED
6/12/2024

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."