DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
550 W. Jackson Blvd., Suite 1500 Chicago, IL 60661-4716 (312)353-5863 Fax:(312)596-4187	4/30/2020-5/18/2020* FEI NUMBER 1450022

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Ricky D. McCleskey, Plant Manager

FIRM NAME	STREET ADDRESS
Fresenius Kabi USA LLC	2020 N Ruby St
CITY, STATE, ZIP CODE, COUNTRY Melrose Park, IL 60160-1112	TYPE ESTABLISHMENT INSPECTED 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:

OBSERVATION 1

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

Specifically,

On 4/21/2020 the firm updated their Master Batch Record (MBR) to change the (b) (4) tubing used during the manufacture of Ketorolac Tromethamine Injection, USP to (b) (4) tubing formulation (b) (4) ((b) (4) part #(b) (4) under change notice CN-20-02348 as a result of Investigation 685634 for particulate matter observed in several lots of Ketorolac Tromethamine Injection, USP. According to the investigation report 685634, "(b) (4) tubing is being replaced (b) (4) tubing (b) (4) ". Investigation 685634 also indicates that these particulates were also forming (b) (4) . Product Code 160101 was approved per CN-20-02348 on 04/21/2020 and the change will be verified per Protocol PR-20-00697 (approved 04/22/2020)". However, it should be noted that the firm's investigation showed that these particulates were still forming (b) (4) and the firm continues to use (b) (4) tubing in their filling process (b) (4) the Ketorolac continues to make contact with the (b) (4) tubing. The Quality Unit reviewed and approved change control CN-20-02348 and Protocol PR-20-00697 which did not include the replacement of the (b) (4) tubing (b) (4) .

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,

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Brian D Nicholson, Investigator Michele L Glendenning, Investigator	X Brian D Nicholson Investigator Signed By: Brian Nicholson -S Date Signed: 05-18-2020 14:05:47	5/18/2020

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Your firm did not perform adequate cleaning validation on Tanks (b) (4) and (b) (4) which are used in the production of multiple drug products including Lidocaine and Dexmedetomidine HCL Injection. Lidocaine was discovered as a contaminant in lots 7067815, 7069770, 7069771, 6121853 and 6122207 of Dexmedetomidine HCL when an OOT investigation identified an unknown impurity HPLC peak as Lidocaine. The unknown impurity was found in 5 of the (b) (4) lots of Dexmedetomidine produced at this site. For each affected lot of Dexmedetomidine HCL, Lidocaine was the previously manufactured product in the tanks. All affected lots of Dexmedetomidine HCL Injections were released and distributed.

OBSERVATION 3

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

Specifically,

A. Personnel Monitoring was not conducted after the aseptic connection for the (b) (4) was made. On 5/1/2020 while observing set-up operations for Methylprednisolone Sodium Succinate for Injection, USP, 40mg/vial, 3mL Lot# 7072219/6124199, I observed that a technician had performed the aseptic connection for the (b) (4) assembly. Upon completing this connection, the employee sanitized their gloves and continued with additional operations. This individual did not receive personnel monitoring for glove contact plates in filling room (b) (4) nor did they leave the room to perform glove print personnel monitoring.

B. On 5/1/2020 while observing set-up operations for Methylprednisolone Sodium Succinate for Injection, USP, 40mg/vial, 3mL Lot# 7072219/6124199, I observed that a technician was wiping down a (b) (4) hose using inappropriate aseptic technique. Firm management identified this hose as a (b) (4) hose to supply (b) (4) for (b) (4) testing. The technician attached the hose to the (b) (4) (b) (4) in the ISO 5 area.

OBSERVATION 4

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The batch production and control records are deficient in that they do not include documentation of the accomplishment of each significant step in manufacturing, processing and packing.

Specifically,

Aseptic connections are not documented on the Batch Record. Setup for filling requires that the firm connect the (b) (4) I observed this process during set-up operations for Methylprednisolone Sodium Succinate for Injection, USP, 40mg/vial, 3mL Lot# 7072219/6124199. Batch Record review of Methylprednisolone Sodium Succinate for Injection, USP, 40mg/vial, 3mL Lot# 7072219/6124199 revealed that none of the aseptic connections performed were documented on the batch record.

OBSERVATION 5

There is a failure to thoroughly review any unexplained discrepancy and the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

Specifically,

A. As of 5/13/2020 the firm has not initiated a retrospective review on the impact to additional product lines as part of the Ketorolac investigation 685634 which investigated the precipitate found in multiple lots of Ketorolac Tromethamine Injection, USP.

B. While reviewing FAR 20-1497 regarding an OOS for an impurity later identified as Lidocaine contamination in Dexmedetomidine HCL, the firm failed to extend review to other products potentially impacted by Lidocaine contamination in compounding tanks (b) (4) and (b) (4). When asked if the firm extended their review to other batches manufactured after Lidocaine the firm only provided a Carry Over Calculations Spreadsheet, which included all products manufactured in the tanks to say that their cleaning verifications were effective enough to limit the amount of cross-over in the finished products manufactured in those tanks.

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Melrose Park, IL 60160-1112	Drug Manufacturer

OBSERVATION 6

Time limits are not established when appropriate for the completion of each production phase to assure the quality of the drug product.

Specifically,

Your firm does not routinely validate the (b) (4) hold time for (b) (4) drug products prior to (b) (4) (b) (4) into the drug product. The firm manufactures numerous (b) (4) drug products such as Methylprednisolone Sodium Succinate for Injection, USP, 40 mg/vial, 3mL Lot# 7072219/6124199.

*DATES OF INSPECTION

4/30/2020(Thu), 5/01/2020(Fri), 5/12/2020(Tue), 5/13/2020(Wed), 5/18/2020(Mon)

X Michele L Glendenning
Investigator
Signed By: Michele L. Glendenning -S
Date Signed: 05-18-2020 14:06:27

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
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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."