DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
FDA 158-15 Liberty Ave Jamaica, NY 11433 718 340 7000 Fax: 718-662-5661 Industry Information: www.fda.gov/oc/industry	3/21/2017 - 3/30/2017
	FEI NUMBER 3001833549

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Anthony M. Pavell, Plant Manager

FIRM NAME	STREET ADDRESS
Fresenius Kabi USA, LLC	3159 Staley Road
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Grand Island, NY 14072	Drug Product Manufacturer

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DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

OBSERVATION 1

Regarding procedures designed to prevent microbiological contamination of drug products purporting to be sterile:
a. A trend of pre-filtration bioburden out-of-specification results was identified, starting in September 2013, primarily involving Ralstonia picketti and other Gram-negative rods, in samples taken in the (b) (4) (b) (4) and continued with the most recent OOS result obtained on 1/24/17, despite corrective measures taken to identify and rid the source of the bioburden. Those batches calculated to have a total bulk solution bioburden load that was less than the bacterial filter retention (BFR) capability for the sterilizing filter were determined to be "acceptable". For example,

1. pre-filtration bioburden result for (b) (4) sterilized Calcium Gluconate Injection, USP, batch #7053762, was (b) (4) on 1/24/17; test limit is (b) (4) Ralstonia pickettii was recovered from the OOS sample. Batch disposition was "acceptable".

2. pre-filtration bioburden result for (b) (4) sterilized Sodium Chloride Injection, batch 7051728, was (b) (4) on 8/2/16; test limit is (b) (4) Ralstonia pickettii was recovered from the OOS sample. Batch disposition was "acceptable".

3. pre-filtration bioburden result for (b) (4) sterilized Calcium Gluconate Injection, USP, batch #7052332, was (b) (4) on 9/7/16; test limit is (b) (4) Ralstonia pickettii and Sphingomonas species were recovered from the OOS sample. Batch disposition was "acceptable".

4. pre-filtration bioburden result for (b) (4) sterilized Heparin Sodium Injection (preservative-free), batch 7051161, was (b) (4) on 6/27/16; test limit is (b) (4) Ralstonia pickettii was recovered from the OOS sample. Batch disposition was "reject".

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE *(Print or Type)*	DATE ISSUED
		Helen B. Ricalde, Investigator Mindy Chou, Investigator Erika E. Englund, Chemist	March 30, 2017

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5. pre-filtration bioburden result for (b) (4) sterilized Heparin Sodium Injection (preservative-free), batch 7051570, was (b) (4) on 7/26/16; test limit is (b) (4) Pseudomonas japonica, Sphingomonas sanguinis, Pyllobacterium myrsinacearum, were recovered from the OOS sample. Batch disposition was "reject".

b. The sterilization process for 13mm stoppers Part (b) (4) includes (b) (4) (b) (4) stoppers. The stoppers are then placed into (b) (4) (b) (4) which are loaded into (b) (4) which has a (b) (4) Once sterilized, the stoppers can (b) (4) (b) (4) This stopper code is used for drug products including (b) (4) (b) (4) This sequence of treatments and handling is also used for sterilization of stoppers (b) (4) used for (b) (4) sterilized drug products. This process for stopper sterilization is deficient as follows:

1. The (b) (4) hold time is based on validation studies performed in March 1994 on a sterilizer that is no longer at the site, in which bioburden and endotoxin was performed by testing (b) (4) for each of these tests; (b) (4) runs were performed. There is no rationale that testing of (b) (4) is representative of the maximum load of sterilizer currently in use.

2. Requalification studies of the sterilizer use (b) (4) but test only (b) (4) There is no rationale that (b) (4) is representative of the maximum load.

OBERVATION 2

Aseptic processing and/or (b) (4) sterilization filling lines are deficient regarding the system for monitoring environmental conditions:

a. (b) (4) containing sterilized stoppers and WFI are brought into the ISO 5 ((b) (4) sterilization filling lines (b) (4)) and Class A (aseptic processing filling lines (b) (4)), and drained of WFI adjacent to the stopper hopper in the ISO 5 and adjacent to (b) (4) in lines (b) (4)

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b. Environmental monitoring is deficient as there is (b) (4) surface monitoring in Fill Room (b) (4) at the vial infeed into (b) (4) and at the location where (b) (4) are drained of WFI in Class A. HBM 3/30/17

c. Water was observed on the floor in the ISO5 area of (b) (4) sterilization line (b) (4) during filling operations

HBM 3/30/17

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