DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
CDER Division of Inspectional Assessment; Attn. Mahesh Ramanadham, Director E-MAIL: Mahesh.Ramanadham@fda.hhs.gov White Oak Building 51, Room 4328 PHONE +1-301-796-3272 Industry Information: www.fda.gov/oc/industry	23 - 27 April 2018, 30 April - 1 May 2018
	FEI NUMBER 3005949964

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Melvin R. Hawkins, General Manager

FIRM NAME	STREET ADDRESS
Cook Pharmica LLC	1300 S. Patterson Drive
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Bloomington, IN 47403	Drug Substance Manufacturing 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 (I) (WE) OBSERVED:

Observation 1. There is an unacceptably high number of mold recoveries in the classified rooms used for manufacture of (b) (4) bulk drug substance. Specifically, mold recoveries in ISO-8 classified rooms ranged from 6 to 46 during 2017, and one mold was recovered in the ISO-7 manufacturing area during 2017. The mold recoveries have been trending upward since 2015.

Observation 2. Written procedures to prevent contamination of (b) (4) drug substance are not followed. Specifically, deviation PR 104369 was opened due to a bioburden excursion of the (b) (4) of (b) (4) lot (b) (4) on 12 July 2014. 190 CFU/mL were recovered (action limit: ≤ (b) (4) CFU/mL). The root cause investigation showed that equipment (b) (4) -160-01) was improperly setup: the (b) (4) connector was incorrectly (b) (4) during (b) (4) resulting in an ineffective cleaning cycle.

Observation 3. There is a lack of quality oversight in the review of records and procedures followed in drug substance manufacture. Specifically, after deviation PR 176620 (due to a bioburden excursion of the (b) (4) (b) (4) on 2 March 2017) was opened, an unacceptably high level of bioburden (b) (4) CFU/100 mL) was detected on 1 May 2017 (LIMS sample #974194), on the same process equipment (X-165-01) used to manufacture (b) (4) drug substance. The result (LIMS sample #974194) did not automatically trigger a root cause investigation because the associated bioburden limit was "report result."

Observation 4. Corrective actions do not include implementation of adequate procedures to prevent similar deviations from recurring. Specifically, deviations PR 188727 and PR 189163 were opened because (b) (4) µm (b) (4) (b) (4) filter, Item Master (IM) number 403350 (lot (b) (4)), failed to pass the (b) (4) integrity test. The root cause was determined to be a defect in the filter's manufacturing process. The filter vendor implemented corrective actions to the filter manufacturing process in August 2017. The corrective actions implemented after deviations PR 188727 and PR 189163 did not include establishing appropriate procedures to prevent use of defective filters in the (b) (4) manufacturing process.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (*Print or Type*)	DATE ISSUED
	Nicholas L. Paulin	Scott R. Nichols, PhD., Microbiologist; Nicholas L. Paulin, Consumer Safety Officer; Cristina Ausin-Moreno, PhD., Senior Staff Fellow; Yanming An, PhD., Chemist	05/01/2018

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Observation 5. Sufficient controls to prevent unauthorized changes to data stored on your firm's HPLC and GC computer systems are inadequate. Specifically, on 25 April 2018, a Senior Scientist demonstrated that the time zone setting could be changed and saved on the HPLC and GC systems. No requirement of administrative privileges was required to change the time zone of your firm's (b)(4) HPLCs and (b)(4) GC system, thereby allowing for the alteration of real-time records and data collection.

SRN 1 MAY 2018

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