COPY

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
FDA/CBER/OCBQ/DMPQ 10903 New Hampshire Avenue, Silver Spring, MD 20993 Attention: Jay Eltermann, Building 71, Room 6038 Telephone: (240) 402-9168	19 – 22 June 2017
	FEI NUMBER 978403

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Doug Chambers, Site Head

FIRM NAME	STREET ADDRESS
SAFC Pharma Carlsbad	6211 El Camino Real
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Carlsbad, CA 92009	Biologics 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 equipment and supplies used to work on or exposed to potentially pathogenic agents is not kept separate from the equipment and supplies used in product manufacturing as necessary to prevent cross contamination. Specifically,

A. You have not dedicated equipment or facilities for (b) (4) manufacturing.

B. On 20 JUN 2017 we observed consumables, taken from production, in the quarantine cage located in the (b) (4) with "Released" status stickers.

OBSERVATION 2

Procedures designed to prevent microbiological contamination of (b) (4) products purporting to be sterile are not established, written, or followed. Specifically,

A. Active non-viable and viable particulate sampling is not performed during aseptic processing ((b) (4) (b) (4)) in BSC (b) (4) (Grade (b) (4)) in Room (b) (4)

B. Cleaning of Biological Safety Cabinets (BSCs) as outlined in (b) (4) "Operation, Cleaning, and Maintenance of the Biological Safety Cabinets" is inadequate in that:

i. The cleaning method for BSCs is not validated to confirm the absence of carryover in the event of a spill or other exposure of product.

ii. The cleaning solutions and method specified in your procedure ((b) (4) were not used during our observation of the cleaning of Biological Safety Cabinet BSC (b) (4) on 20 JUN 2017. Operators used (b) (4) (which was not specified in the written cleaning procedure) to clean the BSC on this date.

iii. Your procedures for cleaning are ambiguous and do not allow for consistent execution. For example, (b) (4) "Operation, Cleaning, and Maintenance of the Biological Safety Cabinets" states "Use of (b) (4) is mandatory in cleaning the BSC" and "If using (b) (4) (b) (4) ".

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE *(Print or Type)*	DATE ISSUED
		CDR Donald Ertel, Lead Investigator Michael Havert, Ph.D., Biologist Arie C. Menachem, Investigator Jakob Reiser, Ph.D., Research Biologist Wei Wang, Ph.D., Microbiologist	06/22/2017

C. Risk Assessment RA032 "Environmental Monitoring Sampling Sites" does not include a rationale for EM sampling locations within Class (b) (4) environments during production of (b) (4) (b) (4)

D. During production activities on 20 JUN 2017 we observed the following departures from Aseptic Processing Technique during the (b) (4) steps in BSC (b) (4) and during (b) (4) operations in BSC (b) (4) :

i. While your BSC operators don sterile sleeves to protect the integrity of product we observed several cases where operators' gowns entered the BSC

ii. Your operators do not consistently maintain their hands in an upright position; we observed that operators rested their hands on the BSC working surface

iii. We observed that (b) (4) containing (b) (4) entered BSC (b) (4) without being sanitized prior to entry.

E. You employ contractors to clean your BSCs; you no longer perform personnel monitoring of these contractors upon exiting the BSCs despite significant recoveries from these personnel uncovered during your (b) (4) environmental monitoring trend report.

F. As part your Environmental Monitoring Trending Program, you do not consider the implications of recoveries of spore forming vs. non-spore forming microorganisms in your (b) (4) trend reports.

OBSERVATION 3

Written procedures are not approved by the appropriate organizational units. Specifically,

A. In SOP, (b) (4) , Version 5.0, (b) (4) specific procedures for (b) (4) are not established.

B. SOP, (b) (4) Version 7.0, Preventative Maintenance (PM) Program, does not provide instructions for the assessment of equipment that is overdue for PM or calibration.

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OBSERVATION 4

Container closure systems do not provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the (b) (4) product.

Specifically, you label (b) (4) containing (b) (4) with (b) (4) during (b) (4) steps. Your procedure instructs operators to (b) (4) (b) (4) prior to placing (b) (4) into the BSC. This (b) (4) is then (b) (4) You have not established the compatibility between (b) (4) and (b) (4)

OBSERVATION 5

Routine calibration of equipment is not performed according to a written program designed to assure proper performance.

Specifically, probes used to monitor your Liquid Nitrogen Dewars for temperature and LN2 excursions are not regularly calibrated. You use these Dewars to (b) (4)

OBSERVATION 6

Establishment of the reliability of the component supplier's report of analyses is deficient in that the test results are not appropriately validated at appropriate intervals.

Specifically, you do not periodically validate your suppliers' certificates of analysis for components or consumables used during (b) (4)

6/22/17

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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 judgement, 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."