DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Detroit District. (DET-DO) 300 River Place Suite 5900, Detroit, MI 48207 (313) 393-8100	10/13-15/2021; 10/18-22/2021
	FEI NUMBER 1818977

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

To: Paula Del Papa. Vice President & General Manager, Manufacturing Operations

FIRM NAME	STREET ADDRESS
PAR Sterile Products LLC	870 Parkdale Road
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Rochester, MI 48307-1740	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:

ITEM 1

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

Specifically,

a. Disinfectant Efficacy Study Protocol No. SA-2012 SUM approved 01 October 2013, conducted to qualify the disinfectants used in the aseptic manufacturing operations for Aplisol, (b) (4) , and (b) (4) have not been adequately qualified for its intended purpose. The acceptance criteria state a 3-log reduction is required for vegetative bacteria during a predetermined time, however your study results show that the organism *Pseudomonas aeruginosa* (Pa) did not achieve a 3-log reduction when used with disinfectant (b) (4) contact time. However, your study concluded that the (b) (4) data supported a (b) (4) contact time as an efficacious sanitizer on the surfaces in the manufacturing area.

b. Current written procedure PAR-ROC-SOP-00182 Rev.49 *Environmental Control Sanitation* describes the sanitization agent and the frequency used to perform cleaning and sanitization of Grade A, B & C manufacturing rooms. Your procedure, which requires (b) (4) to be used in all classified areas with a (b) (4) minimum contact time, is not supported by the findings in the disinfectant efficacy study mentioned above. The study showed that the *Pseudomonas aeruginosa* failed to meet a 3-log reduction at (b) (4) on the (b) (4) surface.

c. During a walkthrough of the manufacturing facility on 19 October 2021, a red brownish discoloration was observed in the silicone tubing which delivers (b) (4) to vials in the vial washer (asset # 12321) on Filling Line (b) (4). Line (b) (4) is used for aseptic filling of the drug product (b) (4) and Tuberculin PPD drug substance which is used in the manufacture of Aplisol drug product. The preventative maintenance frequency is (b) (4) however the task for inspection of the tubing for discoloration and roughing is not addressed in the preventative maintenance plan. The Quality Unit has not performed identification of the red-brownish discoloration and no risk assessment was performed prior to the observation made during this inspection.

ITEM 2

Written records of investigations into unexplained discrepancies do not always include the conclusions and follow-up.

Specifically,

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	(b) (6), (b) (7)(C)		10/22/2021

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DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

Reoccurring HEPA filter failures are not investigated and/or are not assigned a CAPA to prevent reoccurrence.

a. Deviations 03520, 03282, 01048, & 01045 describe the HEPA filter failures as having a full concentrated leak due to material/debris from the room being sucked into the air returns and transferred to the top side of the filters. No CAPAs were initiated to address the airflow conditions in Grade A and B which create material/debris.

b. There were 38 HEPA filter failures from January 2019 to June 2021, and 30 of the failures were in the Grade A and B areas in the sterile core of Suites (b) (4) (lines (b) (4)). An overall investigation into the failure of the HEPA filters that are within the (b) (4) expiry has not been performed.

c. Document PAR-ROC-SOP-00013 Rev. 21 effective 23 August 2021, *Test Repair and Replacement of Environmental Air and Laminar Filters* is deficient in that there is no tracking and trending of the HEPA filter failures, which are managed in the (b) (4) system but not in (b) (4) There were six HEPA filter failures in Grade A & B between December 2020 & June 2021.

ITEM 3

Hand washing facilities are not accessible.

There is an absence of a hand washing station in the visitor's gowning/changing rooms located in Building (b) (4). The area is used by visitors to gown into the controlled unclassified corridor and Grade D areas. There are no additional handing stations prior to entering the Grade D areas.

ITEM 4

Computer software used for environmental monitoring defaults to acceptance criteria.

The (b) (4) Environmental Data Collection System supplement IQ, OQ, and PQ, conducted under PAR-ROC-MVP-02114 effective 28 December 2020, is deficient in that the software defaults to a zero (0) value for colony forming units for bacteria and mold rather than defaulting to a blank entry field. The result input section which captures environmental data from Grades A, B, C, and D for contact plates, active air samples, passive air samples and personnel monitoring automatically defaults to "0" unless the technician inputs a value. An environmental monitoring result of "zero" indicates no colony forming units in the classified area.

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."