DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
550 Main Street Cincinnati, OH 45202 (513)322-0700 Fax:(513)679-2772	8/31/2022-9/23/2022* FEI NUMBER 3011967886

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Ray R. Carlson, Owner/CEO	
FIRM NAME RC Outsourcing LLC	STREET ADDRESS 102 E Water St
CITY, STATE, ZIP CODE, COUNTRY Lowellville, OH 44436-1117	TYPE ESTABLISHMENT INSPECTED Outsourcing 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 OBSERVED:

OBSERVATION 1

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

Specifically,
A. Examples include but are not limited to:

1. On 08/31/22, I observed aseptic technicians (b) (6), and (b) (6) move from the ISO 7 environment to the ISO 5 a minimum of five (5) times without sanitizing hands appropriately with sterile (b) (4) (b) (4) The general practice observed was that technicians (b) (6) and (b) (6) sanitized their gloved hands with sterile (b) (4), then dried it with the sterile low-linting wipes
Also, technician (b) (6) wiped the Direct Compounding Area (DCA) which is in the ISO 5 classified area with sterile (b) (4) using the exposed sterile lint free wipes. These exposed sterile low linting wipes are located in the ISO 7 classified area. The technician used the same dirty wipes to wipe their gloved hands and immediately entered into the ISO 5 classified area to begin aseptic operations for the repackaging of (b) (4) lots (b) (4) and Lot # (b) (4) respectively.

2. i. On 08/31/2022, during the re-packaging of (b) (4) (Bevacizumab) Lot (b) (4) performed by technician (b) (6) in the LAF Hood (b) (4) (ISO 5 Classified Area), EQ ID: 2021-166295 I observed blocking first pass air with the piles of staged (b) (4) syringes and many rows of staged (b) (4) tray containing the sterile caps.

ii. Your firm's air flow visualization videos are inadequate. For example, but not limited to, your firm's

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Ucheabuchi C Chudi-Nwankwor, Investigator	X Ucheabuchi C Chudi-Nwankwor Investigator Signed By: Ucheabuchi C. Chudi-nwankwor -S Date Signed: 09-23-2022 1 :36:37	9/23/2022

smoke studies show instances where the smoke nozzle is not positioned in a manner where all aseptic manual operations occur. Therefore, your smoke studies do not allow airflow evaluation to verify if the aseptic manual operations generate air eddies/air turbulence or if unidirectional airflow recovers following the generation of air eddies/air turbulence.
In addition, your smoke studies do not allow the evaluation for unidirectional flow of your staged components or the handle attached to the HEPA grate within the direct compounding area (DCA).

3. On 08/31/2022, I observed the aseptic operator (b) (6) leaning on (b) (6) elbow inside the ISO 5 Hood DCA and touched the plunger during aseptic operations for (b) (4) (Bevacizumab) Lot (b) (4) (b) (4) re-packaging. This lot has been distributed to the public.

4. I observed your technicians (b) (6) exiting ISO 7 clean room and to ISO 8 ante room 2 times and back to ISO 7 room 2 times respectively without changing their gloves or donning new gowns and proceeded to ISO 5 Hoods for aseptic operations for the repackaging of (b) (4). When leaving the anteroom (ISO 8 Classification) and entering the cleanroom (ISO 7 Classification), your aseptic technicians appear not adequately trained to remove their sterile gloves and donn a new sterile glove in the ISO 7 classified areas.

5. On 08/31/2022, I observed the aseptic operators move vials of (b) (4), sterile caps and (b) (4) syringes in (b) (4), by their hands from ISO 8 less quality Air to ISO 7 higher quality Air without sanitizing the (b) (4) housing these materials.

B. The aseptic process simulation media fills performed to qualify technicians in aseptic operations of (b) (4) (Bevacizumab) was not adequate and do not simulate the most stressful/challenging conditions. According to your SOP P1.1.2.3, "PERSONNEL-MEASURING-MEDIA FILL, worst case scenario and real-time process for the technicians is to be followed during Media fill aseptic operations. The aseptic operators are not fully qualified to perform aseptic operations because they have incomplete media fills. You failed to adequately qualify each of the technician on their aseptic processes to simulate the most

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
550 Main Street Cincinnati, OH 45202 (513)322-0700 Fax:(513)679-2772	8/31/2022-9/23/2022* FEI NUMBER 3011967886

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Ray R. Carlson, Owner/CEO	
FIRM NAME RC Outsourcing LLC	STREET ADDRESS 102 E Water St
CITY, STATE, ZIP CODE, COUNTRY Lowellville, OH 44436-1117	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

challenge conditions.

OBSERVATION 2

Protective apparel is not worn as necessary to protect drug products from contamination.

Specifically, I observed your aseptic technicians not wearing protective goggles during aseptic operations in ISO 5 Hoods. Parts of the skin around the eyes were exposed in the ISO 5 hoods and I saw aseptic operator (b) (6) leaning on (b) (6) elbow inside the ISO 5 during aseptic operations and repackaging of (b) (4) lots # (b) (4) and Lot (b) (4)

OBSERVATION 3

Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the room and equipment to produce aseptic conditions.

Specifically,

A. Your firm's cleaning logs, from January 2022 – August 2022, do not document a contact time for the sporicidal (b) (4) used in the cleaning of your ISO 5 and ISO 7 areas. All sterile drug products, including (b) (4) and (b) (4) are repackaged in ISO 5 hoods (b) (4) located in your ISO 7 clean room.

B. Your firm use (b) (4) located in the ISO 7 area approximately 6 inches from the opening of the ISO 5 Hood. Per your firm's pharmacist, the (b) (4) is covered with a water-resistant case. This (b) (4) does not appear to be easily cleanable. You do not have a cleaning specification for the (b) (4). In addition, on 08/31/2022, I observed your aseptic operator touch the (b) (4) with their gloved hand and immediately proceed with the aseptic repackaging operations of (b) (4) lots

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
550 Main Street Cincinnati, OH 45202 (513)322-0700 Fax:(513)679-2772	8/31/2022-9/23/2022* FEI NUMBER 3011967886

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Ray R. Carlson, Owner/CEO	
FIRM NAME RC Outsourcing LLC	STREET ADDRESS 102 E Water St
CITY, STATE, ZIP CODE, COUNTRY Lowellville, OH 44436-1117	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

(b) (4) without appropriately sanitizing their hands prior to entering the ISO 5 Hood.

OBSERVATION 4

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically,

1. You do not perform environmental monitoring which includes active viable air monitoring, surface, non-viable particle and PM for each lot of repackaged (b) (4) product since the installation of ISO 5 Hoods (b) (4) on May 9th, 2022.

Your firm failed to conduct viable air sampling, during aseptic operations for each lot of repackaged (b) (4) (Bevacizumab) produced for sterile intraocular injections. I observed that you did not perform active viable air and non-viable particulate sampling at the beginning and middle while repackaging of (b) (4) lots (b) (4) and Lot (b) (4) on 08/31/2022. These lots have been released and distributed to your customers.

** THIS IS A REPEAT OBSERVATION **

2 You failed to investigate the 1 CFU recovery from your Active Air (b) (4) sample in ISO 5 Hood (b) (4) active air sample which was obtained on 01/11/2022. Per your sample media lot number (b) (4), day 6 and 7 samples yielded 1 CFU and this was not properly investigated. Your action limit is not appropriate per your Procedure which stated that (b) (4) CFU is your action limit.

OBSERVATION 5

The flow of components, drug product containers, closures, in-process materials and drug products through the building is not designed to prevent contamination.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Ucheabuchi C Chudi-Nwankwor, Investigator X Ucheabuchi C Chudi-Nwankwor Investigator Signed By: Ucheabuchi C. Chudi-nwankwor -S Date Signed: 09-23-2022 1 :36:37	9/23/2022

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
550 Main Street Cincinnati, OH 45202 (513)322-0700 Fax:(513)679-2772	8/31/2022-9/23/2022* FEI NUMBER 3011967886

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Ray R. Carlson, Owner/CEO	
FIRM NAME RC Outsourcing LLC	STREET ADDRESS 102 E Water St
CITY, STATE, ZIP CODE, COUNTRY Lowellville, OH 44436-1117	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

Specifically,

A. On 8/31/2022, I observed a gap, approximately 2", at the base of your firm's cleanroom doors (from the non-classified pre-sterilizing area into the ISO 8 anteroom and from the ISO 8 anteroom into the ISO 7 cleanroom). In addition, your firm's ISO 5 LAFH is located directly opposite the ISO 7 clean room exit door. These doors are not airlocked.

a. Negative pressure differential excursions were observed. Please refer to **OBSERVATION 7** for details.

OBSERVATION 6

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

Specifically,

A. You pool and commingle different lots of finished repackaged (b) (4) products for sterility and endotoxin testing by your Control testing Lab (b) (4) data base does not capture the individual product lots tested for repackaged (b) (4). For example, the following but not limited (b) (4) syringes lots (b) (4) were pooled together and sent to (b) (4) for sterility, endotoxin and particulate testing as Lot (b) (4) on 02/10/2022. The Certificate of Analysis (COA) did not have specifics on these (b) (4) lots tested. The COA only captured the commingled Lot number. Your QA approved the production batch records without any notation that the two (2) (b) (4) lots were commingled. The QA accepted the COA from (b) (4) failing to verify if the lot numbers were explicitly written on the COA. These 2 (b) (4) lots were released without sterility and endotoxin test results of the separate lots and distributed to your customers.

B. Your procedure, SOP P3.9.1.3,"QUALITY MANAGEMENT SYSTEM -SUPPLIER AUDIT-ALL OPERATIONS", dated Nov 16,2022 for auditing your suppliers, had specifics that your suppliers to

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
550 Main Street Cincinnati, OH 45202 (513)322-0700 Fax:(513)679-2772	8/31/2022-9/23/2022* FEI NUMBER 3011967886

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Ray R. Carlson, Owner/CEO	
FIRM NAME RC Outsourcing LLC	STREET ADDRESS 102 E Water St
CITY, STATE, ZIP CODE, COUNTRY Lowellville, OH 44436-1117	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

include third party testing laboratories (b) (4) should be audited (b) (4). You have not audited your Control testing Lab (b) (4) is responsible for the testing to release for all your (b) (4) and (b) (4) repackaged sterile products which include the sterility, endotoxin and particulate testings.

C. Your procedure, SOP P9.12.1.1,'PROCEDURE -COMPREHENSIVE TESTING-ENVIRONMENTAL-STERILE ENVIRONMENT', dated May 2,2022 for the Clean room does not require additional cleaning activities in the cleanroom areas to take place in the event there is an environmental excursion such as temperature, humidity, or pressure differential.
Your environmental monitoring identification results showed 2 (two) CFU recoveries on 05/17/2022 of an organism identified as *Staphylococcus warneri* in the (b) (4) sample of the ISO 5 classified spaces. Cleaning after this excursion was not observed on your cleaning logs after this recovery was determined on 05/17/2022.
Your firm failed to establish a procedure for cleaning activities required after a recovery in the ISO 5 hood.

OBSERVATION 7

There is a failure to thoroughly review any unexplained discrepancy whether or not the batch has been already distributed.

Specifically,

A. You did not investigate Pressure differential discrepancies in ISO 7 Clean room and the incorrect dating for the logged data between 11/15/2021 to 01/03/2022. The following lots of (b) (4), but not limited to were produced, approved, and distributed to your customers: (b) (4) (b) (4) & (b) (4)

B. In addition, your Clean room pressure log, dated 8/31/2022, shows at least 29 instances where your pressure differentials were observed to be from 0 to negative 0.11 ranging in duration from 10 min

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
550 Main Street Cincinnati, OH 45202 (513)322-0700 Fax:(513)679-2772	8/31/2022-9/23/2022* FEI NUMBER 3011967886

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Ray R. Carlson, Owner/CEO	
FIRM NAME RC Outsourcing LLC	STREET ADDRESS 102 E Water St
CITY, STATE, ZIP CODE, COUNTRY Lowellville, OH 44436-1117	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

to 30 min.

C. You failed to investigate the 1 CFU recovery from your Active Air (b) (4) sample in ISO 5 Hood (b) (4) active air sample which was obtained on 01/11/2022. Sample media lot number (b) (4) day 6 and 7 samples yielded 1 CFU and this was not properly investigated. In addition, your SOP P9.12.1.1 action limit of (b) (4) is inadequate.

OBSERVATION 8

Changes to written procedures are not drafted, reviewed and approved by the appropriate organizational unit.

Specifically, Your firm does not initiate change controls when necessary and in a timely manner. For example, according to your Quality Assurance Director, you did not initiate a change control for the installation of your new ISO 5 Hoods (b) (4) with EQ ID: 2022-179131 & 2021-166295 respectively. These hoods per your Quality Director were installed on May 8th, 2022, in the Clean Room and has been used in the packaging of (b) (4) and (b) (4) per your Production log from January to August 2022.

OBSERVATION 9

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

Specifically,

1. Pressure gauges monitoring the pressure differential of the processing rooms are not continuously or

periodically calibrated.

2. You failed to calibrate your (b) (4) Incubator (b) (4) periodically. You do not have a calibration log for the Incubator. In addition, your temperature ranges of (b) (4) for (b) (4) days per your procedure SOP P3.8.1.6, "PROCEDURE-OPERATING-TECHNOLOGY-INCUBATOR", dated Jan 11, 2022, appear inadequate for your incubation processes.

OBSERVATION 10

Your outsourcing facility has not submitted an adverse event report to FDA in accordance with the content and format requirements established through guidance or regulation under 21 CFR 310.305 as required by section 503B(b)(5).

Specifically, your firm did not submit a serious and unexpected adverse event report to FDA within 15 calendar days after first receiving information about the adverse event.
Examples include:

- FDA ICSR ID 2081606, received 2/7/2020, submitted to FDA 3/13/2020
- FDA ICSR ID 2129150, received 4/12/2022, submitted to FDA 5/25/2022
- FDA ICSR ID 2112196, received 4/15/2021, submitted to FDA 6/1/2021
- FDA ICSR ID 2112195, received 4/15/2021, submitted to FDA 6/1/2021
- FDA ICSR ID 2100701, received 10/15/2020, submitted to FDA 12/7/2020
- FDA ICSR ID 2087366, received 6/3/2020, submitted to FDA 7/14/2020
- FDA ICSR ID 2087365, received 6/3/2020, submitted to FDA 7/14/2020

***DATES OF INSPECTION**

8/31/2022(Wed), 9/01/2022(Thu), 9/06/2022(Tue), 9/08/2022(Thu), 9/12/2022(Mon), 9/13/2022(Tue), 9/16/2022(Fri), 9/23/2022(Fri)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
550 Main Street Cincinnati, OH 45202 (513)322-0700 Fax:(513)679-2772	8/31/2022-9/23/2022* FEI NUMBER 3011967886

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Ray R. Carlson, Owner/CEO

FIRM NAME	STREET ADDRESS
RC Outsourcing LLC	102 E Water St
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Lowellville, OH 44436-1117	Outsourcing Facility

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE
Ucheabuchi C Chudi-Nwankwor, Investigator

X Ucheabuchi C Chudi-Nwankwor
Investigator
Signed By: Ucheabuchi C. Chudi-nwankwor -S
Date Signed: 09-23-2022
1 :36:37

DATE ISSUED
9/23/2022

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."