DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
CDER/OPQ/OPMA/Division of Biotechnology Manufacturing 10903 New Hampshire Avenue; White Oak Building 51, Room 2269 Silver Spring, MD 20993 Email: OPMABLAInspection483Responses@fda.hhs.gov	04/16/2024-04/24/2024 FEI NUMBER 3002808846

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Wolfgang Weikmann, Senior Vice President Quality	
FIRM NAME Vetter Pharma-Fertigung GmbH & Co. KG	STREET ADDRESS Eisenbahnstr. 2-4
CITY, STATE, ZIP CODE, COUNTRY 88085 Langenargen, Germany	TYPE ESTABLISHMENT INSPECTED Sterile Drug Product 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

Procedures designed to prevent microbiological contamination of drug product (DP) purporting to be sterile are not established and followed. Specifically,

A. There is no assurance that (b) (4) DP (b) (4) are maintained sterile after (b) (4) and prior to aseptic filling. Specifically, th (b) (4) re temporarily stored on a non-sterilized (b) (4) rack in clean room (b) (4) RABS after (b) (4) The rack is wiped w (b) (4) disinfectant after each batch and disinfected with (b) (4) (b) (4) by (b) (4) every (b) (4)

B. Multiple deviations have been initiated from December 2020 to 2024 due to (b) (4) not conforming the manufacturer specification(s) before recalibration. For example, for cleanroom (b) (4) (b) (4) ecalibration results for (b) (4) in 2022, 2023, and 2024 respectively, did not conform to the specifications fo (b) (4) size calibration, or size resolution (deviations 757638, 828507, 905985, respectively). Among these (b) (4) (b) (4) observed during the 2022, 2023, and 2024 recalibrations, respectively, belong to cleanrooms (b) (4) where (b) (4) DP is aseptically filled. In addition, there is no assurance that (b) (4) deviation 757638) and (b) (4) (deviation 828507) have no product impact because the count rate efficiency at (b) (4) µm could not be determined for both during recalibration.

C. The dynamic smoke study videos (Documents "Room and process overview for flow visualization for Clean room (b) (4) and Clean room (b) (4) or filling line (b) (4) and (b) (4) where (b) (4) DP is aseptically filled, showed that RABS (b) (4) previously touching non-sterile surfaces of the filling line came in contact with direct and indirect product-contact equipment. For example,

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE *(Print or Type)*	DATE ISSUED
	Bo Chi -S Digitally signed by Bo Chi -S Date: 2024.04.24 08:07:39 -04'00' Andrea Franco -S Digitally signed by Andrea Franco -S Date: 2024.04.24 08:12:08 -04'00'	Bo Chi, Ph.D., Microbiologist Andrea Franco, Ph.D., Pharmaceutical Scientist	4/24/2024

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
CDER/OPQ/OPMA/Division of Biotechnology Manufacturing 10903 New Hampshire Avenue; White Oak Building 51, Room 2269 Silver Spring, MD 20993 Email: OPMABLAInspection483Responses@fda.hhs.gov	04/16/2024-04/24/2024
	FEI NUMBER 3002808846
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED Wolfgang Weikmann, Senior Vice President Quality	
FIRM NAME Vetter Pharma-Fertigung GmbH & Co. KG	STREET ADDRESS Eisenbahnstr. 2-4
CITY, STATE, ZIP CODE, COUNTRY 88085 Langenargen, Germany	TYPE ESTABLISHMENT INSPECTED Sterile Drug Product Manufacturer

1. During the (b) (4) between the (b) (4) and the (b) (4) on the filling line using a (b) (4) an operator was observed touching the sterile-product contact gasket inside th (b) (4) with a RABS (b) (4) There is no SOP describing details of this extensive aseptic manipulation (b) (4) f the (b) (4) According to Vetter QA management, operators are allowed to touch the (b) (4) gasket with RAB (b) (4) during the (b) (4) assembly process.
2. An operator was observed stretching RABS (b) (4) and blocking Grade A laminar air over the (b) (4) on the filling line when putting on RAB (b) (4) near the (b) (4)
3. During (b) (4) replacement, the RAB (b) (4) touched the end of the (b) (4) that is used to connect the (b) (4) with the (b) (4) on the filling line.
4. During (b) (4) eplacement, an operator was observed holding th (b) (4) near the (b) (4) with RABS (b) (4)

D. During aseptic filling operations for (b) (4) DP Batch# (b) (4) in filling room (b) (4) on (b) (4) (b) (4) RABS (b) (4) previously touching non-sterile surfaces of the filling line was observed coming in ct with direct and indirect product-contact equipment:
   1. During installation of the (b) (4) for the (b) (4) an operator was observed holding the (b) (4) near the (b) (4) with the RABS (b) (4)
   2. During environmental monitoring operations, an operator was observed stretching RABS (b) (4) over the (b) (4) containing sterile (b) (4) parts and blocking Grade A laminar air over the (b) (4) parts.

E. The (b) (4) of the (b) (4) requires extensive manipulation, and therefore is unsuitable for the aseptic filling operations of (b) (4) P manufacturing.

OBSERVATION 2

The visual inspection program for (b) (4) is deficient and was not able to remove defects, resulting in multiple 100% visual inspections failing the major defect acceptance criterion. Specifically, (b) (4) linical batch (b) (4) (deviation PR 745461) failed 100% visual inspection and AQL due to the p (b) (4) dirt/abrasion and foreign particle at (b) (4) The 100% visual inspection was repeated two additional times. The cumulative stopper defect rates for the (b) (4) 100% visual inspections were

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
CDER/OPQ/OPMA/Division of Biotechnology Manufacturing 10903 New Hampshire Avenue; White Oak Building 51, Room 2269 Silver Spring, MD 20993 Email: OPMABLAInspection483Responses@fda.hhs.gov	04/16/2024-04/24/2024
	FEI NUMBER 3002808846
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED Wolfgang Weikmann, Senior Vice President Quality	
FIRM NAME Vetter Pharma-Fertigung GmbH & Co. KG	STREET ADDRESS Eisenbahnstr. 2-4
CITY, STATE, ZIP CODE, COUNTRY 88085 Langenargen, Germany	TYPE ESTABLISHMENT INSPECTED Sterile Drug Product Manufacturer

(b) (4) respectively, which exceeded the acceptance criterion for the major defects. A (b) (4) 100% visual inspection focusing on (b) (4) defects was subsequently conducted and resulted in an (b) (4) % defect rate, which is above the acceptance n of ≤ (b) (4) .

OBSERVATION 3

Environmental monitoring of aseptic processing areas following critical Grade A filling operations is deficient. Specifically,

A. (b) (4) monitoring is deficient. For example, on April 16, 2024 and April 17, 2024, during filling line setup and filling activities in clean room (b) (4) RABS (b) (4) (e.g., (b) (4) were used (b) (4) the same (b) (4) used with (b) (4) of the operators). During environmental monitoring of the RABS, the noted (b) (4) that were used (b) (4) were not monitored (b) (4) (b) (4)

B. The environmental surface monitoring program does not include the door handles of (b) (4) (b) (4) which are used by the operator to open and close the (b) (4)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE *(Print or Type)*	DATE ISSUED
	Bo Chi -S Digitally signed by Bo Chi -S Date: 2024.04.24 08:08:49 -04'00' Andrea Franco -S Digitally signed by Andrea Franco -S Date: 2024.04.24 08:13:23 -04'00'	Bo Chi, Ph.D., Microbiologist Andrea Franco, Ph.D., Pharmaceutical Scientist	4/24/2024