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: OPMA[(b) (4)]nspection483Responses@fda.hhs.gov	03/11/2024-03/19/2024 FEI NUMBER 3005987757
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 Mooswiesen 2,
CITY, STATE, ZIP CODE, COUNTRY 88214 Ravensburg, 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 purporting to be sterile are not established and followed. Specifically,

1. While reviewing the dynamic smoke study videos (Document 5153553, "Clean room [(b) (4)] Smoke studies - intervention") for filling line [(b) (4)] where [(b) (4)] is aseptically filled, the following deficiencies were noted:

   a. The sterile boxes containing [(b) (4)] sterilized parts for filling line assembly are placed underneath RABS [(b) (4)] on the filling line during setup. Consequently, the RABS [(b) (4)] obstruct first air during handling of the sterilized parts, including unprotected [(b) (4)] and [(b) (4)]

   b. During installation of the [(b) (4)] the RABS [(b) (4)] that previously touched the non-sterile surfaces of the filling line came in contact with the [(b) (4)]

   c. During installation, the operator held the [(b) (4)] in such a way that blocked first air over the exposed [(b) (4)]

2. The study supporting the clean hold time of up to [(b) (4)] for [(b) (4)] filling room and filling lines is inadequate. Specifically, the study (Document 50113, "Validation of the holding time of a cleaned and disinfected clean room") was conducted [(b) (4)] and the study does not include viable [(b) (4)] air monitoring of Grade A areas at

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		Bo Chi, Ph.D., Microbiologist Leiyun Boone, Ph.D., Lead Biologist Olumide Martins, Ph.D., Pharmaceutical Scientist	3/19/2024

the end of hold. No further cleaning is conducted after the clean hold, prior to the subsequent aseptic filling.

OBSERVATION 2

A procedure has not been stablished for performing identity testing on the contents of final (b) (4) of each lot after all labeling operations have been completed as required by 21 CFR 610.14. Currently, the only identity testing of (b) (4) is performed using unlabeled units and no identity testing is performed after labeling.

OBSERVATION 3

The visual inspection program for (b) (4) is deficient. Specifically,

1. According to SOP 10588 v23, "Personnel Qualification for Visual Inspection", when personnel who conduct 100% visual inspections or AQL inspections fail (b) (4) requalification, no deviation is required to evaluate the impact on the previously inspected batches.

2. The requalification of operators conducting visual inspection is inadequate. Per SOP 10588 v23, operators are retrained for a minimum of (b) (4) of (b) (4) requalification, prior to the test.

3. Standard procedures are not adequate to ensure that all samples for 100% visual inspection supplemental testing are sufficiently randomized.

OBSERVATION 4

Written procedures for (b) (4) drug product manufacturing and testing are deficient. Specifically,

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1. The master batch record for [(b) (4)] manufacturing does not require documentation of critical manufacturing steps. For example,

   a. The batch record for aseptic filling does not require documentation of critical set-up activities for the [(b) (4)] filling line, such as cleaning of the RABS [(b) (4)] prior to [(b) (4)]

   b. The batch record for the [(b) (4)] and compounding process does not require documentation of [(b) (4)] of the [(b) (4)] ports on the compounding vessel before transferring out of the laminar air flow area.

2. The stability studies for [(b) (4)] drug product do not include the establishment of scientifically sound starting times. The long-term stability starting dates are not reflective of the actual age of the batches nor are they consistent among different batches.

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