DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
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NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Wolfgang Weikmann, Senior Vice President Quality

FIRM NAME	STREET ADDRESS
Vetter Pharma-Fertigung GmbH & Co. KG	Schuetzenstrasse 87, 99-101
CITY, STATE, ZIP CODE, COUNTRY Ravensburg, Upper Swabia, 88212, Germany	TYPE ESTABLISHMENT INSPECTED Drug Product Manufacturer

cThis 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.

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DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

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

A) After Clean Room (b) (4) Installation Sequence Part (b) (4) (SOP 21580) is complete, the (b) (4) fill line is decontaminated with (b) (4) The RABS (b) (4) are used as sterile tools in aseptic processing. For instance, the installation of sterilized (b) (4) by operators is performed by holding the (b) (4) with RABS (b) (4) (b) (4) and securing them in place (Step (b) (4) SOP 21580). It was observed that the RABS (b) (4) that holds the (b) (4) come in contact with a nearby white plastic cable at (b) (4) (also shown in Smoke study 3_3_2_33, 4:45). In addition, operators use RABS (b) (4) to make difficult to manipulate (b) (4) sterile connections to the sterile (b) (4) and (b) (4) (b) (4) tank (b) (4) SOP 21580). The RABS (b) (4) (b) (4) that (b) (4) the (b) (4) is also used for (b) (4) of the (b) (4) sterile connections to the (b) (4) (b) (4) Step (b) (4) SOP 21580, also shown in Smoke study 3_3_2_29).

B) Smoke studies to support interventions for vial removal on the (b) (4) on fill line (b) (4) per SOP 10090 do not demonstrate good aseptic technique. For instance, the smoke study 3.3.3.8 shows the RABS (b) (4) hover over the (b) (4) blocking unidirectional air flow onto container closures that are subsequently used for filling in drug product operations

C) Not all (b) (4) that are installed and used in (b) (4) manufacturing are swabbed in post-production environmental monitoring as governed by SOP 20618. The manufacturing process requires at least (b) (4) but potentially (b) (4) of (b) (4) replacements during

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
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production due to setup and line stoppages. Currently, only the (b) (4) (b) (4) in total) are swabbed for the presence of microbial contamination per (b) (4)

OBSERVATION 2

Quality Assurance is inadequate. Specifically,

A) Quality Assurance did not generate a report at the conclusion of PPQ (batches (b) (4) (b) (4) that stated a clear conclusion as to whether the data indicates the process met the conditions established in the protocol and whether the process is considered to be in a state of control. Two of the three PPQ lots exceeded the allowable major defect rate (> (b) (4)%) for (b) (4) in the (b) (4) during (b) (4) visual inspection. The root cause of the defect was attributed to encrustation on the (b) (4) Your firm then implemented an amendment to the PPQ protocol to manufacture (b) (4) additional batches (b) (4) with CAPAs to overcome the (b) (4) procedure (CAPA PR849744), CAPAs to Line Stoppages (CAPA PR849744), and CAPAs to remove (b) (4) (CAPA PR848749). The (b) (4) supplemental PPQ (b) (4) batch (b) (4) of the amendment had a defect rate of (b) (4)% for (b) (4) An additional CAPA was implemented after (b) (4) (CAPA PR866283) for (b) (4) (b) (4) batches were successfully completed and the PPQ report stating that the process met the conditions of the protocol using information from all (b) (4) PQ batches was approved by Quality Assurance.