DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
USFDA/CBER/OCBQ 10903 New Hampshire Avenue (WO71-5128) Silver Spring, MD 20993 Tel.: (240) 402-9159 Industry Information: www.fda.gov/oc/industry	10/23/17-11/02/17
	FEI NUMBER 3005987757

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Wolfgang Weikmann, Senior Vice President Quality

FIRM NAME	STREET ADDRESS
Vetter Pharma-Fertigung GmbH & Co. KG	Mooswiesen 2
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
88214 Ravensburg, Germany	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 (I) (WE) OBSERVED:

1. Procedures designed to prevent microbial contamination of drug products purporting to be sterile are inadequate. Specifically,

A. On October 25, 2017 during observation of the aseptic (b) (4) process for (b) (4) batch (b) (4), specifically for personnel monitoring, the Operator sanitized their hands, performed personnel monitoring for two other operators and then touched contact plates as part of the exiting procedure for a cleanroom. The behavior exhibited by the Operator having sanitized gloved hands prior to touching the contact plates is not a true representation of the activities performed in the Grade (b) (4) cleanroom area during dynamic conditions. This Operator's activities during dynamic conditions include the placement and removal of (b) (4) ((b) (4) (b) (4)) from the Grade (b) (4) area into the (b) (4).

B. An Operator performing personnel monitoring was observed plating the (b) (4) instead of the (b) (4).

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

A. Deviation (b) (4) was written due to cleaning re-qualification failures of the (b) (4) and (b) (4) used in the (b) (4) processes for (b) (4). Both pieces of equipment were found with visual residues after cleaning. With regard to the (b) (4) cleaning re-qualification failure, the root cause was most likely traced back to the dirty holding time ((b) (4)) that was evaluated during the re-qualification. During routine manufacturing a maximum dirty hold time of (b) (4) is allowed. The re-qualification was re-performed also with a (b) (4) dirty hold time of (b) (4). The second re-qualification passed, however there is no written explanation as to how the conflicting re-qualification results will be handled.

B. As reported in the Quarterly reports dated 1. Quartal 2017 dated May 2017; 2. Quartal 2017 dated July 2017; 2.

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	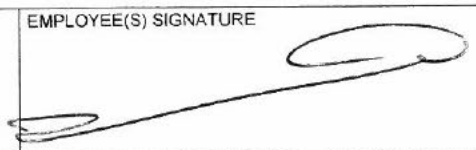	Mihaly S. Ligmond, CSO Simone E. Pitts, CSO	11/02/2017

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Quartal 2016 dated July 2016 and 4. Quartal 2016 dated February 2017, microorganisms categorized as gram negative rods of water origin; aerobic spore-formers; other gram negative rods that are not of water origin; gram positive rods; yeast; micrococcus and staphylococcus organisms are routinely recovered from the (b) (4) (b) (4) analytical test. The (b) (4) is a (b) (4) maintained at (b) (4), and is (b) (4) on a (b) (4) basis. No corrective and or preventative actions have been implemented to eradicate the organisms. (b) (4)

Additionally, the following investigation reports identify the objectionable organisms recovered from the (b) (4) System:

i. Deviation Report (b) (4) dated April 24, 2017 was initiated as an excursion of the specified limit for (b) (4) (b) (4) ((b) (4)) with results for locations (b) (4) (b) (4) which are (b) (4) sampling points for (b) (4) (b) (4). (b) (4) is the (b) (4) area for the CBER licensed product (b) (4). The organism was classified as a microorganism of water and the most probable root cause is human error during sampling. The organisms were identified as Sphingomonas panni, Sphingomonas ginsenosidimultans, Methylobacyeriem extorquens primarily. As per the deviation report there was no product or regulatory impact as this was a single event and no CAPA measures were deemed necessary.

ii. Deviation Report (b) (4) dated April 17, 2016 was initiated as an excursion of the specified limit for (b) (4) (b) (4) ((b) (4)) with results for locations (b) (4) (overgrown), (b) (4) (overgrown) which are (b) (4) sampling points for (b) (4) (b) (4). (b) (4) is the (b) (4) area for the CBER licensed product (b) (4). The organism was classified as a microorganism of water and the most probable root cause is human error during sampling. The organisms were identified as Novosphingobium capsulatum, Microbacterium laevaniformans and Sphingopyris alaskensis for (b) (4) Sphingopyris alaskensis, Pigmentiphaga and Sphingomonas ginsenosidimultans for (b) (4) and for (b) (4) the organisms were identified as Microbacterium laevaniformans, Novosphingobiul capsulatum and Acidovorax delefieldii. As per the deviation report there was no product or regulatory impact as this was a single event and no CAPA measures were deemed necessary.

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		Mihaly S. Ligmond, CSO Simone E. Pitts, CSO	11/02/2017

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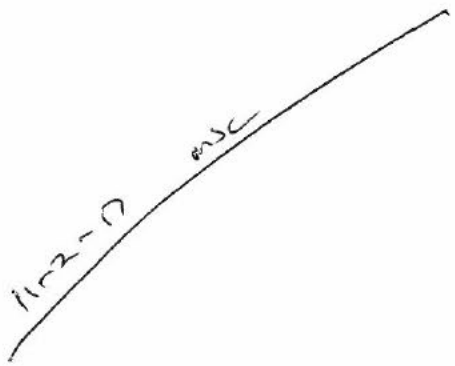
iii. Deviation Report (b) (4) dated September 04, 2016 was initiated as an excursion of the specified limit for (b) (4) ((b) (4)) with results for locations (b) (4) which are (b) (4) sampling points for (b) (4) areas for (b) (4) (b) (4) is the (b) (4) area for the CBER licensed product (b) (4). The organism was classified as a microorganism of water and the most probable root cause is a contamination of the affected sampling valve. The organisms were identified as Sphingmonas panni, Methylobacterium extorquens, Brevundimonas for sample point (b) (4) and Sphingmonas panni, Sphingmonas terrae and Sphingmonas species for sample point (b) (4). As per the deviation report there was no product or regulatory impact as this was a single event and no CAPA measures were deemed necessary.

3. Each lot of components is not withheld from use until the lot has been sampled, tested, examined, and released by the quality control unit. Specifically,

SOP Doc. No. (b) (4) Version 18 English title "Inspection of Incoming Goods and Release of Starting Materials" allows (in certain circumstances) for the release of starting materials before the usage decision has been made.

4. Access to the storage area for labels and labeling materials is not limited to authorized personnel. Specifically,

Non-Vetter personnel who deliver drinking water supplies have access to Building (b) (4) Room (b) (4) where labeling materials are stored on a short term basis.



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	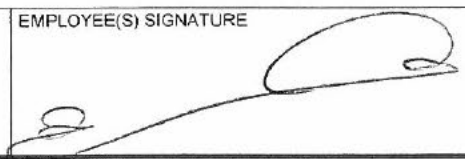	Mihaly S. Ligmond, CSO Simone E. Pitts, CSO	11/02/2017

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 judgement, 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."