DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10903 New Hampshire Ave,Bldg 51,Rm 4225 Silver Springs, MD 20993 (301)796-3334 Fax:(301)847-8738	7/11/2016-7/19/2016* FEI NUMBER 3002806288

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Yves Buelens , General Manager

FIRM NAME	STREET ADDRESS
Kaysersberg Pharmaceuticals SAS	23 Avenue Georges Ferrenbach
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Kaysersberg, 68240France	Drug 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 OBSERVED:

OBSERVATION 1

Written records of investigations into unexplained discrepancies do not always include the conclusions and follow-up.

A root cause and corrective/preventative actions have not been pursued for two batches that failed testing for environmental viable air at the (b) (4) location while filling batches on (b) (4) machine (b) (4) Deviation investigation # 13305 was opened in January 2015, finding that (b) (4) (b) (4) batch # (b) (4) failed to meet viable air specifications, detecting (b) (4) cfu of yeast. Similarly, Deviation investigation # 13442 was opened in Fe(b) (4)uary 2015, finding that (b) (4) batch # (b) (4) failed to meet viable air specifications, detecting (b) (4) cfu of mold. These two batches were released to the US market, as (b) (4) procedures require two environmental failures of a batch before quarantine is required, per SOP document KBPROC-00263.

A root cause and corrective/preventative actions have not been pursued for three (b) (4) is used as an ingredient for (b) (4) manufacturing, for cleaning process equipment and as (b) (4) for (b) (4) used in sanitization/sterilization) samples that failed testing for microbial specifications. Deviation investigation # 13833 was opened in April 2015, finding that (b) (4) failed to meet specifications, detecting (b) (4) cfu and (b) (4) cfu at (b) (4) sampling locations. Similarly, Deviation investigation # 14135 was opened in June 2015, finding that (b) (4) failed to meet specifications, detecting (b) (4) cfu at (b) (4) sampling location. In all instances resampling was conducted, with acceptance of resampling results, when there was no scientific basis for invalidating initial OOS results, as procedures (SOP KBPROC-00370) allow additional sampling and analysis and permit only the reporting of new values from additional analysis that meet specifications. Thus, procedures tolerate acceptance of retested material in favor of passing retest results from additional sampling without a scientific basis for

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invalidating the original OOS results and without pursuing root cause and corrective/preventative actions in the production of (b) (4)

OBSERVATION 2

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

Viable air and particulate monitoring are not regularly conducted in the Grade A areas of the (b) (4) (b) (4) to show that environmental conditions conform to requirements. There are (b) (4) (b) (4) that are used to aseptically fill (b) (4) (b) (4) was tested once for Viable air and particulates in 2009, but (b) (4) have no record of monitoring, nor is there a schedule for any regular verification that these (b) (4) filling machines are operating in Grade A conditions as intended.

OBSERVATION 3

There is a lack of written procedures describing in sufficient detail the methods, equipment and materials to be used for sanitation.

Procedures for sanitization do not always reflect contact times that were determined in your "Report of Qualification of the Efficacy of Disinfectants on Surfaces of the Manufacturing Facility According to Requirements of USP <1072>." For example, when using the the sporicide (b) (4) procedures (SOP-KBPROC-00083) specify to apply for (b) (4) then spray with (b) (4) and wipe. The efficacy report indicates that it may take up to (b) (4) of contact time with (b) (4) to deactivate certain tested species.

OBSERVATION 4

Written procedures for cleaning and maintenance fail to include description in sufficient detail of methods, equipment and materials used and parameters relevant to the operation.

Cleaning validation documents process parameters for cleaning (b) (4) from (b) (4) equipment) to include a (b) (4) cleaning cycle with (b) (4)

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(b) (4) But during actual cleaning operations, only pressure and time are recorded as accomplished, which does not fully assure a validated cleaning result.

OBSERVATION 5
Routine calibration of mechanical equipment is not performed according to a written program designed to assure proper performance.

Calibration of (b) (4) speeds (rpm) for processing tanks used to make (b) (4) is not always conducted following a scheduled program, such as for the (b) (4) # 3, C 40, and C 26 tanks.

OBSERVATION 6
Written production and process control procedures are not documented at the time of performance.

Although (b) (4) times are documented during the manufacturing of (b) (4), (b) (4) speeds for formulation, which are critical process parameters, are not recorded in batch records during production.

OBSERVATION 7
Control procedures are not established which monitor the output and validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product.

For (b) (4) manufacturing (used as an ingredient in drug production and used for cleaning), operating ranges for process parameters are not fully established, such as determining acceptable levels of pressures and flow during routine production, in order to sufficiently validate and control this manufacturing process. For example, appropriate ranges (upper and lower limits) for the monitoring of flow/pressure for retention time and proper filtering and manufacturing have not been fully established for processing (b) (4) through the (b) (4) filter (only a delta P is observed, no pressure or flow is recorded), (b) (4) is recorded, but no flow/pressure), (b) (4) (only a delta P is observed, no pressure or flow is recorded), (b) (4) (no monitoring of pressure/flow), (b) (4) filter (only a delta P

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is observed, no pressure or flow is recorded); the (b) (4) has no monitoring of flow, the (b) (4) has a flow listed as >(b) (4) with no upper limit, and the (b) (4) has no monitoring of pressure/flow.

OBSERVATION 8

Laboratory controls do not include the establishment of scientifically sound and appropriate test procedures designed to assure that in-process materials conform to appropriate standards of identity, strength, quality and purity.

Microbial analysis of (b) (4) (SOP-KBPROC-00370) utilizes only a (b) (4) ml portion via (b) (4) (b) (4) method. Larger sample portion quantities, e.g., (b) (4) ml, are not (b) (4) following your firm's analytical method, in order to gain assurance that colony counts detected are statistically representative, especially when results are low to undetectable using (b) (4) ml volumes.

*DATES OF INSPECTION

7/11/2016(Mon),7/12/2016(Tue),7/13/2016(Wed),7/15/2016(Fri),7/18/2016(Mon),7/19/2016(Tue)

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