

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT OFFICE ADDRESS AND PHONE NUMBER FDA/CBER/OCBQ/DMPQ 10903 New Hampshire Avenue, Silver Spring, MD 20993 Attention: Carolyn Renshaw, Building 71 Room 4042 Telephone: 240.402.7343 Industry Information: www.fda.gov/oc/industry	DATE(S) OF INSPECTION March 13 to 17, 2023 and March 20 to 21, 2023
	FEI NUMBER 3016855360

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Dr. Karl Leitner, General Manager

FIRM NAME Octapharma Produktionsgesellschaft Deutschland mbH.	STREET ADDRESS Wolfgang-Marguerre-Allee 1,
CITY, STATE AND ZIP CODE Springe, Lower Saxony, Germany, 31832	TYPE OF ESTABLISHMENT INSPECTED Drug substance 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. Failure to establish a batch release protocol to include testing on the critical (b) (4) products including (b) (4) and (b) (4). Specifically, There is no yield and/or identity and bioburden tested to ensure the quality of the released batches.

2. Procedures for deviations and corrective and preventive actions are not adequately established or implemented. Specifically,

A. Deviations are not closed in a timely manner. For example, Procedure A_SOP_054_018, effective 20FEB2023, "Deviation, CAPA, and Task Handling" requires that deviations be closed within (b) (4) days. In the year 2022, approximately 50% of deviations were not closed within this timeframe, with seventeen percent open up to (b) (4) days, eleven percent open up to (b) (4) days, and twenty three percent open over (b) (4) days.

B. The late closure or extension of deviations from written production and process control procedures are not always adequately justified. The same reason, i.e., late completion of the deviations has no negative impact on product quality, was repeatedly used for extension of the deviations including but not limited to:

- a. Deviation 169048 (b) (4) Overrun of temperature during (b) (4) measurement (b) (4) date opened 06JUL2022.
- b. Deviation 167652 (b) (4) Exceeding the (b) (4) temperature, date opened 09JUN2022.
- c. Deviation 169447 (b) (4) Use of wrong batch protocols for the (b) (4) date opened 13JUL2022.
- d. Deviation 163933 (b) (4) Total duration (b) (4) exceeded, date opened 06APR2022.
- e. Deviation 164077 (b) (4) Falling below the (b) (4) of the (b) (4) (b) (4) date opened 08APR2022.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE   	EMPLOYEE(S) NAME AND TITLE (Print or Type) Laura Fontan, Lead Inspector CBER/OCBQ/DMPQ Zainab Mansaray-Storms, CSO CBER/OCBQ/ DMPQ, Yonggang Wang, Biologist CBER/OTAT/ DPPT/PDB	DATE ISSUED March 21, 2023
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C. Corrective actions are not opened immediately or executed in a timely manner, allowing similar deviations to repeat numerous times. Specifically, including but not limited to the following:

- a. Deviation 179130, opened 31JAN2023, for (b) (4) area that exceeded the total viable count (TVC) surface limit, includes thirty-nine (39) related deviations, all opened as early as 17MAR2022. No immediate cleaning actions were taken and corrective actions were not opened until February and March 2023.
- b. Eight deviations were opened for exceeding the (b) (4) TVC limit at (b) (4) (b) (4), which is used for (b) (4) product contact equipment. Four deviations were opened between 02DEC2021 and 25MAR2022 and four more deviations were opened between 21OCT2022 and 06FEB2023. Corrective actions were not opened until 21OCT2022, 17Feb2023 and 14MAR2023.

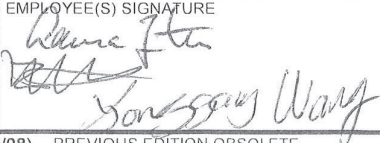
D. There is no documentation of preventative correction actions and corrective action effectiveness checks as defined in Procedure A_SOP_054_018, effective 20FEB2023, "Deviation, CAPA, and Task Handling".

3. Manufacturing areas are deficient regarding the system for monitoring environmental conditions. Specifically,

- A. The environmental monitoring frequency of Grade (b) (4) manufacturing areas where open processing is performed is not adequately justified. For example, in Grade (b) (4) areas (b) (4) air particulates are monitored (b) (4) (b) (4) and viable air, surfaces and floors are monitored (b) (4) (b) (4).
- B. Maximum number of people allowed in Grade (b) (4) manufacturing areas is not determined.

4. Manufacturing procedure is not always supported by the validated process and not documented in the batch record, Specifically,

After (b) (4) of (b) (4) and (b) (4) the (b) (4) is disassembled and the remaining (b) (4) in the (b) (4) and (b) (4) is (b) (4). The procedure is not validated prior to use and the operation is not documented in the executed batch records.

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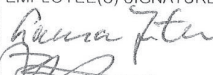
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Octapharma Produktionsgesellschaft Deutschland mbH.	Wolfgang-Marguerre-Allee 1,
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Springe, Lower Saxony, Germany, 31832	Drug substance manufacturer

5. Cleaning validation program is inadequate. Specifically,

Manual cleaning for small parts used in (b) (4) and (b) (4) (b) (4) does not include operator training qualification testing to ensure the cleaning is performed consistently and successfully by each operator. In addition, there is no routine monitoring of the manual cleaning performed by operations personnel to verify that cleaning acceptance criteria are continued to be met over time.

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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."