DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Director, Division of Inspections and Surveillance FDA / CBER / Office of Compliance and Biologics Quality 10903 New Hampshire Avenue (W071-5128) TEL: 240-402-9159 Silver Spring, MD 20993-0002 CBER483responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	11/10-18/2022 FEI NUMBER 3009153654

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. George Lam, Site Head, Global Manufacturing and Supply

FIRM NAME	STREET ADDRESS
Takeda Manufacturing Singapore Pte. Ltd.	2a Woodlands Industrial Park D, Street 2
CITY, STATE AND ZIP CODE	**TYPE OF ESTABLISHMENT INSPECTED**
Singapore, Singapore 737779	Licensed Biological 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. Written records of investigations into unexplained discrepancies do not always include all the appropriate conclusions and follow-up. Specifically,

a) Deviation (Event) Record PR ID: 2287615, dated 27Sep2021, reported a Negative Trend for (b) (4) Recovery for Suite (b) (4) Purification, Cold Room (b) (4) (ISO (b) (4) Grade (b) (4) from (b) (4) This excursion/ negative trend was classified as equivalent to an alert limit, a root cause was not identified, immediate correction was not performed, an additional investigation was not initiated, and a Corrective Action/Preventive Action (CAPA) was not initiated.

b) Deviation (Event) Record PR ID: 2386776, dated 12Nov2021, reported a Negative Trend Observed for (b) (4) (b) (4) Recovery in the Buffer Preparation Area (ISO (b) (4) Grade (b) (4) Room (b) (4) from (b) (4) This excursion/negative trend was classified as equivalent to an alert limit, a root cause was not identified, immediate correction was not performed, an additional investigation was not initiated, and a Corrective Action/Preventive Action (CAPA) was not initiated.

c) Deviation (Event) Record PR ID: 2610047, dated 07March2022, reported that the (b) (4) for (b) (4) (b) (4) batches (b) (4) to (b) (4) was atypical. The immediate action performed on (b) (4) by the Automation engineer was to change the (b) (4) from (b) (4) to (b) (4) for impacted (b) (4) (b) (4) and (b) (4) prior to SOQ Batch (b) (4) CAPA PR ID: 2790469, dated 01Aug2022, reported a change control to revise the (b) (4) (b) (4) recipe ADV_SOQ_PACKING to correct the (b) (4) (b) (4) value from (b) (4) to (b) (4) The lack of an Effectiveness Check (EC) was not sufficiently justified. CAPA 2790469 concluded that An Effective Check (EC) was not required as the issue will not recur with the implementation of the recipe modification.

2. The responsibilities and procedures applicable to the quality control unit were not fully followed. Training on Good Documentation Practices (GDP) and data integrity practices per the applicable version of SOP

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (*Print or Type*)	DATE ISSUED
	/s/	Prabhu P. Raju, Investigator Zuben Sauna, Ph.D., CBER Biologist	11/18/2022

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Singapore, Singapore 737779	Licensed Biological Manufacturer

PROC-0001058, "Global SOP, Good Electronic Data Management Practices", dated 17Oct2022, was not adequate in preventing the following events. For example,

a) Deviation (Event) Record PR ID: 2133649, dated 07Jul2021, reported that a Security Audit Trail was not printed and reviewed after completion of a (b) (4)

b) Deviation (Event) Record PR ID: 1729701, dated 18Nov2020, reported on completion of Endotoxin Run 17121920-20201116-001, performed using (b) (4) that the test file was found missing from the "Completed Assays" in the software database.

c) Deviation (Event) Record PR ID: 1731338, dated 19Nov2020, reported loss of electronic data of Environmental Monitoring (EM) Non-Viable Particle (NVP) Sample Result.

d) Deviation (Event) Record PR ID: 2404519, dated 17Nov2021, reported the electronic measurement data file not saved to designated folder on the (b) (4) automated cell counter (b) (4) and could not be found.

e) Deviation (Event) Record PR ID: 2589274, dated 24Feb2022, reported a (b) (4) value in the electronic file for Replicate (b) (4) (post (b) (4) sample) for the (b) (4) measurement of Bioreactor (b) (4) which is different from the value shown in the printed hardcopy.

f) Deviation (Event) Record PR ID: 2174377, dated 29Jul2021, reported Process Control System (PCS) temperature trending loss for cold room (b) (4) for (b) (4) The calibration associate engineer disconnected the temperature sensor in cold room (b) (4) instead of control room (b) (4) which was scheduled for initial calibration.

/s/

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	/s/	Prabhu P. Raju, Investigator Zuben Sauna, Ph.D., CBER Biologist	11/18/2022

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."