DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	7/14/2025-7/18/2025
	FEI NUMBER 3003282622

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Matthias Kuehn, Head of Europe Plant Management

FIRM NAME	STREET ADDRESS
Daiichi Sankyo Europe GmbH	Luitpoldstr. 1
CITY, STATE, ZIP CODE, COUNTRY Pfaffenhofen A.D. Ilm, Bavaria, 85276 Germany	TYPE ESTABLISHMENT INSPECTED Drug Product 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

Laboratory records do not include complete data derived from all tests, examinations and assay necessary to assure compliance with established specifications and standards.

Specifically,

A. There is no procedure that describes the appropriate use of manual integration for acquired data within the Empower chromatography system nor do manual integration events require explanation to ensure complete rationale for use. For example, during the review of the release data supporting (b) (4) mg Batch (b) (4) (b) (4) specific test samples chromatograms (and (b) (4) test sample overall within the sample set) contained manually integrated peaks with no reason provided within the audit trail, nor was there documented authorization to perform this manual integration.

   In addition, during the review of chromatographic results obtained within Empower within the project folder "uplc_0251_a_04", including results supporting the release testing of (b) (4) (b) (4) drug products, approximately (b) (4) % of the individual injections made had been manually integrated.

B. Records related to analytical testing do not include all the information related to the execution of the test. For example, test methods K-PA 0251_I_HPLC1 and K-PA 0251_I_HPLC2 are used for assay, content uniformity, and related substance determination of (b) (4)

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	Joseph A Piechocki, Investigator	X Joseph A Piechocki Investigator Signed By: JOSEPH A. PIECHOCKI JR -S Date Signed: 07-18-2025 10:42:31	7/18/2025

(b) (4) rug products for the US market. The executed laboratory records do not include complete information related to the execution of the test, which includes the following:

1. Mobile phases and solutions used for testing do not adequately document the preparations. For example, method K-PA 0251I-HPLC2 outlines preparations of (b) (4) solutions and mobile phases with specific volumes. However, the only documentation within the laboratory journal includes the reagent lot numbers.

2. Test sample and standard solutions used for assay, content uniformity, and degradation products do not document the steps used to prepare the solutions, including sonication, volumetric flasks, solutions used for dilution, and any subsequent dilutions. In addition, the content uniformity sample preparation requires (b) (4) (b) (4) (b) (4) The steps to this preparation are not documented.

OBSERVATION 2

There is a failure to thoroughly review any unexplained discrepancy and the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

Specifically,

A. Deviation 200007918 was initiated during the compression of (b) (4) (b) (4) mg Batch (b) (4) due to tablets having a tendency to stick on the (b) (4) punch while filling container (b) (4) The following deficiencies were noted:

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1. The deviation stated that the error may occur sporadically from time to time, however no definitive root cause was identified which could have caused the issue, including but not limited to a dirty punch or a material issue.
2. ~~The corrective action associated was to visually inspect containers (b) (4) which yielded an additional (b) (4) of rejected material. However, there was no heightened scrutiny of the batch to ensure that the batch did not result in any additional defective tablets after the cleaning of the tooling.~~
3. The deviation stated that this had occurred within the last 12 months, however there was no further assessment performed to determine the number of deviations where this had occurred and if any additional corrective actions needed to be implemented to prevent the repetition of the deviation.

B. OOS investigations for (b) (4) mg Batch (b) (4) (Investigation 200008934) and (b) (4) mg Batch (b) (4) (Investigation 200010548) were initiated due to one sample being outside the specification for content uniformity. The OOS investigations concluded that two tablets must have been used instead of one since the values were doubled for that specific sample. However, there was no documented interview with the analyst to corroborate this root cause determination, nor does the test sample preparation documentation have adequate documentation to support this determination. In addition, the corrective action for both OOS investigations was to retrain the specific analyst which caused the issue. However, the corrective action did not extend to the remainder of the Quality Control personnel or address the specific root cause, nor was a preventive action adequately established to address the root cause identified for having two tablets during the content uniformity to prevent reoccurrence. In addition, based on the results of the OOS, the invalid result was isolated to the individual sample. The original (b) (4) results from the content uniformity test were invalidated without scientific justification.

Observation 2A.2 was removed based on documentation within the associated deviation referenced in

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the observation.

OBSERVATION 3

Written procedures are not established and followed for the cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing or holding of a drug product.

Specifically,

Equipment, tools, and ancillary containers used in the manufacture of drug products are not adequately labeled or maintained during manufacturing or cleaning. For example, during the walkthrough of the facility on 14Jul2025, I observed the following:

1. Inspection of the (b) (4) (Room (b) (4) equipment noted an apparent (b) (4) residue observed on the exterior of the (b) (4) (confirmed during the inspection as (b) (4) from the (b) (4) apparent (b) (4) residue remaining on the (b) (4) used for (b) (4) in exterior space outside of the (b) (4) but within the (b) (4), and an apparent (b) (4) residue on the (b) (4) gasket. This equipment was documented as clean following (b) (4) mg Batch (b) (4)

2. During the inspection of the tooling used for compression operations, I observed apparent (b) (4) residue remaining within the debossing of tablet punch set #(b) (4) (for (b) (4) mg tablets), after the documentation showed that the punches were cleaned. In addition, during the inspection of tablet punch set #(b) (4) (used for (b) (4) (b) (4) mg tablets), I observed at least one punch with an apparent dent and one punch with an apparent nick.

   Furthermore, the procedure related to the maintenance, cleaning, and inspection of compression tooling does not outline the instances when an investigation would need to be

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opened for defects observed at different inspection points throughout tooling inspection processes nor is it required to define the type of defects if found prior to when tooling is removed from use.

3. During (b) (4) of (b) (4) on (b) (4) (b) (4) (Room (b) (4) (b) (4) the (b) (4) are contained within (b) (4). During the walkthrough, the (b) (4) used was not adequately labeled with its contents or identification, was not documented as clean prior to use, and was found open to the environment and not actively being used during the walkthrough.

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