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 ORAPHARMInternational483responses@fda.hhs.gov	11/20/2024-11/22/2024 FEI NUMBER 3010031951

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Kyungah Kim, Executive Vice President, Development Division Leader

FIRM NAME	STREET ADDRESS
Samsung Bioepis Co. Ltd.	76, Songdogyoyuk-ro, Yeonsu-gu,
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Incheon 21987, Korea, Republic of (South)	Testing Laboratory

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 WE OBSERVED:

OBSERVATION 1

Procedures describing the handling of written and oral complaints related to drug products are not written and/or followed.

Specifically,

A. Your complaint handling procedure, SOP-GxP-CML-00944 Version 13.0 Product Quality Complaints Management (Effective date 8/23/2024) does not have a timeline for initial assessment for the market complaints. Your Senior Manager Quality Assurance 1 (b) (6) stated that initial assessment is generally done within (b) (4)

One 1/9/2024, you recorded Complaint # PC-016468 for Particulate in two vials of (b) (4) (b) (4) mg Vial Lot No's (b) (4) (Mfg. date 6/20/2023, Expiry date (b) (4) and (b) (4) (Mfg. date 8/14/2023, Expiry date (b) (4) According to your procedure, criticality classification for particulate matter in drug product is High/Class 1 that requires to complete the investigation within (b) (4) You did not complete the Initial Assessment until (b) (4) after (b) (4) of recording the complaint. You did not launch an investigation and based on the field report (initial assessment), you decided particulate matter in the drug product was because of coring and classified the complaint as Medium. On (b) (4) after (b) (4) you requested for

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Rajiv R. Srivastava -S Digitally signed by Rajiv R. Srivastava -S Date: 2024.11.22 16:47:58 +09'00'	Rajiv R Srivastava, CSO	11/22/2024

extension and finally closed the complaint on 4/3/2024.

B. One 7/18/2024 you recorded Complaint # PC-017796 for a "spot, like an ink mark" (Particulate) inside a vial of (b) (4) mg Vial Lot No's (b) (4) (Mfg. date 3/5/2024, Expiry date (b) (4) According to your procedure, criticality classification for particulate matter in drug product is High/Class 1 that requires to complete the investigation within (b) (4) You did not complete the Initial Assessment until (b) (4) after (b) (4) of recording the complaint. Based on the field report (initial assessment), you classified it as Particulate. You received the sample and based on the visual inspection, you decided that there was no particle in the liquid solution but a spot with black color was found at the bottom of the vial which was non-removable and located on the outer surface of the vial. You further stated that the defect size was measured as approximately (b) (4) to (b) (4) mm, which is less than the minimum criteria (b) (4) mm) that is classified as a defect. Based on your investigation, you assessed the complaint as 'non-confirmed". The investigation was closed on 11/19/2024 but the complaint is till open as of 11/22/2024.

C. One 11/3/2023 you recorded Complaint # PC-016044 Particulate inside a vial of (b) (4) mg Vial Lot No's (b) (4) (Mfg. date 5/22/2023, Expiry date (b) (4) According to your procedure, criticality classification for particulate matter in drug product is High/Class 1 that requires to complete the investigation within (b) (4) You did not complete the Initial Assessment until (b) (4) after (b) (4) of recording the complaint. Based on the field report (initial assessment), you decided particulate matter in the drug product was because of coring and classified the complaint as Medium and did not conduct any investigation.

D. One 5/21/2024, you received a customer complaint that stated, "***the (b) (4) stopper at the top of the vial disconnected and fell through***". On the same day, 5/21/2024, you recorded this Complaint # PC-017396 wrongly as Particulate inside a vial of (b) (4) mg Vial Lot No's (b) (4) (Mfg. date 2/7/2024, Expiry date (b) (4) According to your procedure, criticality classification for particulate matter in drug product is High/Class 1 that requires to complete the investigation within (b) (4) You did not complete the Initial Assessment until (b) (4) after (b) (4) of recording the complaint. Based on the field report (initial assessment), you decided

particulate matter in the drug product was because of coring and classified the complaint as Medium. You visually checked the defective vial and concluded that "***no anomalies identified that would increase risk related to the claimed product***". Your investigation does not include any test of the Particulate to confirm the nature of the particulate. No root cause was identified, and the complaint was assessed as "Non-confirmed".

E. Between January 2023 and November 15, 2024, you received 335 market complaints for (b) (4) mg (b) (4) **Table 1** summarizes some of the complaints that are related to defective device. You did not conduct any formal investigation to find the root cause. Your Senior Manager Quality Assurance 1 (b) (6) stated that the reported defects were within the firm's Acceptance Quality Level (AQL) and alert level as set by the firm's complaint handling procedure, SOP-GxP-CML-00944 Version 13.0. In your procedure, you set the AQL that is reflective to critical defects and the alert level is based on the historical data.

Table 1. Selected market complaints for (b) (4) for defective device

Type of defect	Number of complaints
Activation failure	52
Injection failure	84
Leakage-before injection-from the needle	27
Stalling	14
Unidentified device malfunction	10

F. On 7/9/2024, you recorded Complaint # PC-017757 for Device Malfunction/Injection Failure for (b) (4) mg (b) (4) Lot No. (b) (4) (Mfg. date 10/31/2023 Expiry date (b) (4) The complaint report was generated by your Quality Assurance Manager (b) (6) who also did the Initial Assessment (b) (4) after recording the complaint) and criticality classification of the complaint as "Medium". Without any investigation, your Quality Assurance Manager (b) (6) closed the complaint on 9/6/2024. On 9/6/2024, your Quality Assurance Manager

(b) (6) also endorsed/approve the report.

G. You use a Complaint Intake form to record the market complaint. This form is not reviewed and approved by your quality department. You conduct your initial assessment and categorize risk level of complaint (Critical, Medium, Low) based on the data collected on the Complaint Intake form.

OBSERVATION 2

Responsibilities and procedures for quality units are not in writing and/or followed to ensure a need for Biological Product Deviation Report (BPDR) are adequately assessed and reported for the distributed products that are implicated with product quality issues.

Specifically,

The Quality Agreement Between (b) (4) and Samsung Bioepis – (b) (4) (Effective date (b) (4) does not define the roles and responsibility for determining the need for filing Biological Product Deviation Report (BPDR). According to the QA, you are responsible for handling and investigating all quality related products complaints from the market (Market Complaint) but determining a need for submitting BPDR is not defined in the Quality Agreement.