DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
ORA OPQO HQ, Room #2032 12420 Parklawn Drive, Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	09/04/2023-09/08/2023
	FEI NUMBER 3011139911
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED Mr. Zhang Ge, Chairman	
TO: FIRM NAME Sichuan Deebio Pharmaceutical Co. Ltd.	STREET ADDRESS 15 She, Gaocao Village, Xiaohan Town
CITY, STATE, ZIP CODE, COUNTRY Guanghan, Sichuan, 618304 China	TYPE ESTABLISHMENT INSPECTED Active Pharmaceutical Ingredient 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 WE OBSERVED:

OBSERVATION 1

Laboratory records are not completed contemporaneously and do not include complete data derived from all tests to assure compliance with established specifications and standards. Specifically,

A. During our visit to your QC microbiology laboratory, we observed that microbiology TAMC test results for QC microbiology work bench ((b) (4) plates) and bio safety cabinet ((b) (4) plates), (b) (4) water samples from Workshop (b) (4) ((b) (4) plates, sample points (b) (4) (b) (4) USP drug substance production for US Market), and (b) (4) samples from Workshop (b) (4) ((b) (4) plates, sample points (b) (4) (domestic and non US international market production), and Workshop (b) (4) ((b) (4) plates, sample points (b) (4)) (domestic and non US international market production) purported to be read by your QC team leader, had not been recorded per your firm's SOP no. MA0057-04, titled 'Data reliability management procedures', effective date 07/01/2021. Specifically, upon entering the microbiology laboratory on 09/04/2023 at approximately 11:40 am, we observed approximately (b) (4) plates in the waste bin which had been (b) (4) Per your QC team leader, she stated that she had read these plates earlier in the morning around 10:00 am, and the test worksheet with recorded results was downstairs with a QA personnel. Your QC team leader than proceeded to provide misleading information, stating that she did not read the results as she had stated doing so when we first arrived in the laboratory, and shortly after this, stated that she did read the results and signed the test data worksheet which was somewhere on the (b) (4) floor with QA personnel, only to finally admit that she did in fact read the plates, however, was not telling the truth about recording the results on respective data worksheets, and no worksheet existed. When we asked the analyst how she remembered the results of all (b) (4) plates, she stated that it was in her "mind" and proceeded to provide at least (b) (4) plate results varying from 18 to 23 CFU from

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (*Print or Type*)	DATE ISSUED
	Arsen Karapetyan Anders W Evenson	Arsen Karapetyan, Investigator, DDC Anders W. Evenson, Investigator	09/08/2023

"memory". Your firm's investigation was not able to replicate any of these 12 values that your analyst provided to us in person. We left the laboratory around 1:40 pm, having initially arrived around 11:40 am. As a result of providing misleading information with respect to these samples, your firm delayed our inspection.

B. During our review of (b) (4) USP drug substance test item 'Limit of (b) (4) (b) (4) ' performed with SevenExcellence software on your Multiparameter analyzer equipment ID No. J01-0310A, we observed no available electronic test data for process validation batches (b) (4) (b) (4) which were subsequently shipped for the US Market after QA approval. Per your firm, the electronic data had been lost due to potential inadequate data backup procedures. Next, when we requested the related physical analytical batch records, we observed no printouts attached with the test worksheets reviewed by QC and QA for batch approval and release for batches (b) (4) Per your firm, at the time of performing these tests, the printer was not connected, and no such printout exists for any test performed prior to June 2022. There is no evidence of (b) (4) esting performed for these process validation batches, which have been shipped to the US Market.

C. During my review of electronic test data for test item 'Limit of (b) (4) with specification as 'limit of ≤ (b) (4) %', our review found that when undesirable results are encountered during analysis of (b) (4) USP drug substance, samples are re-tested until desirable results are achieved. The original test results for batch no. (b) (4) (forced degradation) and batch no. (b) (4) (accelerated 2-month stability study) were both OOS. These results were not reported, and no laboratory investigation was initiated per your firm's OOS procedure. For Example, sample for batch no. (b) (4) was tested on 11/01/2021 at around (b) (4) pm with result as (b) (4) %. This result was not reported, and no OOS investigation was initiated. Shortly after on the same day, around (b) (4) pm, a second test was performed with result of (b) (4) %, which was within specification and reported.

OBSERVATION 2

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
ORA OPQO HQ, Room #2032 12420 Parklawn Drive, Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	09/04/2023-09/08/2023 FEI NUMBER 3011139911

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED	
Mr. Zhang Ge, Chairman	
TO: FIRM NAME Sichuan Deebio Pharmaceutical Co. Ltd.	STREET ADDRESS 15 She, Gaocao Village, Xiaohan Town
CITY, STATE, ZIP CODE, COUNTRY Guanghan, Sichuan, 618304 China	TYPE ESTABLISHMENT INSPECTED Active Pharmaceutical Ingredient Manufacturer

The quality control unit lacks responsibility to approve all procedures, specifications, or test methods impacting on identity, strength, and purity of drug substances. Specifically,

A. Your firm's test method validation for Residual Solvent test by GC for (b) (4) content for (b) (4) USP drug substance is inadequate. During your method validation, your firm failed to identify two additional peaks observed in the sample solution chromatogram. Per your firm, after this deficiency was identified through a customer audit performed on or around 03/24/2022, after which your firm contracted a third-party laboratory who identified the (b) (4) additional peaks as (b) (4) (b) (4) As of the current inspection, your firm has not initiated an investigation with respect to this event, nor has it performed any laboratory or manufacturing studies to determine the source of the (b) (4)

B. Your firm has not performed an impurity profile to study the identified and unidentified impurities which may be present in your (b) (4) USP drug substance and consequently does not perform impurity testing for released drug substance.

C. Supervisory oversight over the laboratory electronic systems and data is deficient. For example, there is no procedure in the QC Laboratory which describes the requirements/conditions under which the manual integration of chromatograms generated by the HPLC, and GC systems can be performed.

OBSERVATION 3

Your firm failed to establish adequate written procedures for production and process controls designed to assure that the drug substance have the identity, strength, purity, and quality that they are purported or represented to possess. Specifically,

A. Process validation studies executed to assure intended drug substance quality is achieved are inadequately designed and executed. For example, process validation performed for (b) (4) USP drug substance fails to contain scientific justifications for the establishment of the following: blend

	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (*Print or Type*)	DATE ISSUED
SEE REVERSE OF THIS PAGE		Arsen Karapetyan, Investigator, DDC Anders W. Evenson, Investigator	09/08/2023

uniformity sample size and frequency, %RSD established for intra batch variability, airflow pressure, blending time, and lack of in-process sampling. During the inspection, we reviewed customer complaint no. TS-2023002, dated 04/13/2023, for inadequate (b) (4) of the (b) (4) USP drug substance for process validation/commercial batch numbers (b) (4) (b) (4), where the customer obtained OOS results after sampling from the top, middle, and bottom of the drums. As stated, theses batches were also used for your process validation studies.

B. Your firm's practice of mixing more than (b) (4) drug substance with (b) (4) to get the (b) (4) USP drug substance has not been evaluated for its potential impact on the variation of (b) (4) assay content. During our review we observed that five (5) out of (b) (4) process validation batches to each contain at least (b) (4) sublots blended with (b) (4) to make (b) (4) finished lot. Per your firm, in most cases the firm used (b) (4) lot to produce (b) (4) finished API lot, however, has the option to blend (b) (4) sub-lots per the validation study.

C. No studies have been performed on the effect of the manufacturing processes, such as (b) (4) parameters, with respect to microbiological and degradant control in the (b) (4) USP drug substance which considers the validated procedure during normal manufacturing operations using the (b) (4) equipment for (b) (4) operations.

OBSERVATION 4

Written records of investigation into unexplained discrepancies and the failure of a batch or any of its components to meet specification do not always include the conclusions and follow-up. Specifically,

A. Your firm received Complaint No. TS-2023002 reporting out-of-specification (b) (4) (b) (4) levels of '(b) (4) USP (b) (4) ' from batches (b) (4) (b) (4) sampled at the top, middle, and bottom of (b) (4) drums, and your firm received Complaint No. TS-2023003 reporting out-of-specification (b) (4) and microorganism limits of

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
ORA OPQO HQ, Room #2032 12420 Parklawn Drive, Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	09/04/2023-09/08/2023 FEI NUMBER 3011139911

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED
Mr. Zhang Ge, Chairman

TO: FIRM NAME	STREET ADDRESS
Sichuan Deebio Pharmaceutical Co. Ltd.	15 She, Gaocao Village, Xiaohan Town
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Guanghan, Sichuan, 618304 China	Active Pharmaceutical Ingredient Manufacturer

(b) (4) USP for batch (b) (4) Your firm's investigations did not extend to other batches manufactured before and after batches (b) (4) and your firm did not adequately document investigation into critical pieces of manufacturing equipment nor critical manufacturing process steps. Per your firm's quality control team leader for investigation into Complaint No. TS-2023002, your firm conducted sampling with a handheld scoop at the top, middle, and bottom of remaining (b) (4) USP drums from batch (b) (4) retesting. Your firm's investigation was deficient because it did not adequately develop and describe the sampling methods used for (b) (4) retesting of batch (b) (4) Additionally, your firm did not document nor carry out corrective and preventive actions following these complaint investigations.

B. Deficiencies identified within your quality unit operations by your firm based on a customer audit performed on or around 03/24/2022, including, but not limited to, loss of electronic data, unreported test results, inadequate documentation of investigations and CAPA's were not adequately documented in your Quality System per your deviation, CAPA, change control, and OOS procedures. For Example, with respect to electronic and paper data loss in your SevenExcellence software for Multiparameter analyzer equipment ID No. J01-0310A used for test item 'Limit of (b) (4) a data integrity risk assessment with CAPA's was performed for your customer, however no official investigation, deviation, or CAPA was initiated per your procedures in order to have the ability to track, trend, and document these deficiencies.

OBSERVATION 5

Written procedures are not established nor followed for the cleaning and maintenance of equipment, including utensils used in the manufacturing, processing, packing, or holding of a drug product. Specifically,

A. Your firm failed to develop a validated cleaning and testing method for the (b) (4) (b) (4) (equipment S13-005) and other pieces of critical manufacturing equipment that confirm your firm's ability to detect and remove (b) (4) and other residual solvents on manufacturing equipment used in the production of (b) (4) USP. Your firm's reasoning for not

	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (*Print or Type*)	DATE ISSUED
SEE REVERSE OF THIS PAGE	AK AWE	Arsen Karapetyan, Investigator, DDC Anders W. Evenson, Investigator	09/08/2023

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
ORA OPQO HQ, Room #2032 12420 Parklawn Drive, Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	09/04/2023-09/08/2023 FEI NUMBER 3011139911

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED	
Mr. Zhang Ge, Chairman	
TO: FIRM NAME Sichuan Deebio Pharmaceutical Co. Ltd.	STREET ADDRESS 15 She, Gaocao Village, Xiaohan Town
CITY, STATE, ZIP CODE, COUNTRY Guanghan, Sichuan, 618304 China	TYPE ESTABLISHMENT INSPECTED Active Pharmaceutical Ingredient Manufacturer

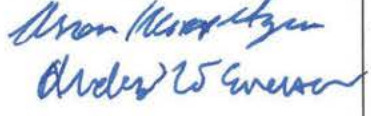
evaluating (b) (4) and other residual solvents on manufacturing equipment used in the production of (b) (4) USP is not supported with documented scientific justification.

B. On pages 13 and 17 of your firm's cleaning record FP 0612-02 that documented cleaning operations of the (b) (4) (equipment S13-005), your firm did not adequately accomplish nor review the (b) (4) (b) (4) of the (b) (4) (b) (4) for (b) (4) per the (b) (4) cleaning procedure (WP0306-03) after production of (b) (4) USP batches (b) (4) (b) (4) Additionally, your firm's deviation (Deviation No.: PC-2023309-002) opened on 2023.09.04 for these discrepancies did not adequately document investigations into cleaning record deviations for other critical pieces of manufacturing equipment used in the manufacturing of (b) (4) USP.

OBSERVATION 6

Control procedures are not established which validate the performance of distribution processes that may be responsible for causing variability in the characteristics of the drug substance. Specifically, your firm ships (b) (4) USP drug substance with temperature storage specifications of (b) (4) to (b) (4) degrees Celsius for temperature, and (b) (4) % RH. There is no official validation study regarding the shipping container and components used which provide assurance that the (b) (4) USP drug substance in transit stays within its specified range for the duration of the shipment.

***DATES OF INSPECTION**
09/04/23 (Mon), 09/05/23 (Tue), 09/06/23 (Wed), 09/07/23 (Thu) and 09/08/23 (Fri)

	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (*Print or Type*)	DATE ISSUED
SEE REVERSE OF THIS PAGE		Arsen Karapetyan, Investigator, DDC Anders W. Evenson, Investigator	09/08/2023