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	11/28/2022-12/2/2022
	FEI NUMBER 3005709762

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Riichi Hatakeyama, Head of Kawagoe Quality Assurance Department

FIRM NAME	STREET ADDRESS
Bushu Pharmaceuticals Ltd.	Takeno 1, Oazatakeno
CITY, STATE, ZIP CODE, COUNTRY Kawagoe, Saitama, 350-0801 Japan	TYPE ESTABLISHMENT INSPECTED Manufacturer of Drug Products

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:
QUALITY SYSTEM

OBSERVATION 1

The responsibilities and procedures applicable to the quality control unit are not in writing and fully followed.

Specifically,

1. Complaint records completed for investigations conducted on site as described in procedure 141.0-QA, Procedure for Quality Information /Complaints Control, are not fully documented or include evidence to justify actions reported. The procedure includes the evaluation of retention samples but activities conducted for this inspection are not fully described (e.g.: quantity inspected, inspection steps, timeliness of the investigation). Complaints reporting Lack of Efficacy do not include analytical testing, only visual inspection on retention samples (e.g.: (b) (4) Tabs (b) (4) mg CHK2003-004 /2003-005, Lack of Effect).

2. Deviation reports completed on site as described in procedure 1B7.0QA (Deviation Control Procedure) are not always fully documented to support conclusions or no further actions. Deviation report DVK210238, issued on 16Dec2021 for failed disintegration test in process (IPC) for (b) (4) mg Lot (b) (4) and (b) (4) identified that results outside specification of NMT (b) min ((b) (4), (b) (4) respectively). After the evaluation and impact assessment disclosed no product impact, no additional actions were implemented and both batch lots were released for

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EMPLOYEE(S) SIGNATURE
MRA MunizN, Consumer Safety Officer

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12/2/2022

further processing with the failed IPC test. The suspect OOS result were attributed to the (b) (4) (b) (4) lot used. However, other batches manufactured with the same suspect lot were tested with acceptable results after the deviation was raised and no further actions were implemented.

3. QC Laboratory Investigation records completed as described in procedure 512.0-QC, Procedure for handling of Test Deviations, do not always include evidence for events reported or to support conclusions (Lab investigations: QCA-021-057, QCC-19-157, QCC-22-120).

LABORATORY CONTROLS

OBSERVATION 2

Established test procedures and laboratory control mechanisms are not followed and documented at the time of performance.

Specifically,

a. Paper records issued during sample analysis completed at the QC (b) (4) Lab (ex. (b) (4)) can be partially completed prior to being sent via Fax to a non-controlled area for completion of information without clear identification of individuals entering information/date. A clear distinction of who completed the information before and after the pages are transmitted is not documented (documents are sent via Fax, original records stay in controlled areas).

b. Sample containers received at the QC Laboratory as per SOP# 510.3QC, Specimen Record Operation, are not inspected to confirm the reported sample quantity being transferred. The

sample container does not include this information and is never verified as testing operations are conducted; only a paper reconciliation is done when all tests per sample are completed.

c. Document for "Specifications and Test Methods Document for Intermediate Product (IS-623,40-00-10)" does not indicate the test method used for in-process controls (IPC) reported by the QC Lab for tablets thickness/hardness in (b) (4) Tablets (b) (4) mg. The batch record does not include a reference to the method used, only the instrument used.

d. Paper logbooks created to include verification activities on Micro lab equipment (incubators) are not fully controlled with a unique and traceable identification number, include hand-written page numbers without a strong binding seal, total page number is only written on first/last page, when issued as described in applicable Procedure 52C.1-QC, Procedures for Test Inspection Records.
Similar logbooks were also observed in use for production equipment at Manufacturing Building (b) (4) (including manufacturing activities for (b) (4), (b) (4)).

EQUIPMENT & FACILITIES

OBSERVATION 3
The separate or defined areas and control systems necessary to prevent contamination or mix-ups are deficient.

Specifically,

1. Records of abnormal events reported for Manufacturing Building (b) (4) ((b) (4)) are not fully documented to describe event and actions or justification when a formal Deviation is not issued, when completed as per SOP 411.3-PH (Handling and Control of Environmental

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Monitoring Systems for Pharmaceuticals). The procedure requires that any abnormality (Temperature/Humidity) be documented in Form 2 and action is to be documented with Form1 but review of a sample of records associated to Manufacturing Building (b) (4) disclosed that events are not fully described and the action Form1 was not completed.

2. Facility Cleaning records completed on site as per SOP 423.1PP (Procedure for cleaning and inspection of warehouse areas) are not complete according to instructions described on the procedure. For example, warehouse areas for the High-Rac material storage (floor level observed with poor lighting) are to be inspected and clean but reported as "vacuumed" which is not part of the cleaning procedure.

3. Warehouse areas are not permanently identified to ensure material stored is segregated. A similar practice was observed in staging areas at the Packaging Building.

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