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	03/19/2024-03/27/2024 FEI NUMBER 3006370533

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Mr. Arnab Pande (Vice-President & Site Head-Production)

FIRM NAME	STREET ADDRESS
Alkem Laboratories Limited	Khasra No 1544, 1553, 1558, 1559, Village Thana Tehsil Nalagarh
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Baddi, Himachal Pradesh, 173205, India	Drug 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.

The observations noted in this Form FDA-483 are not an exhaustive listing of objectionable conditions. Under the law, your firm is responsible for conducting internal self-audits to identify and correct any and all violations of the quality system requirements.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

QUALITY SYSTEM
OBSERVATION 1

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. During the preventive maintenance of Perkin Elmer UV Spectrophotometer ID #G/QC/225 connected to software and computer (UV WinLab ES 6.5.0.103 and computer ID #ABA/EQ/QC/COM/01187) on 06/28/2023, you encountered a failure for the instrument where the power supply and main board of instrument was not working. According to your service provider on 07/28/2023, the equipment could not be repaired. On 12/082023, you proposed to retire Perkin Elmer UV Spectrophotometer ID #G/QC/225 as change control PR ID #128741. Yet, you have not performed an investigation and any impact assessment on the previous generated test results from the UV Spectrophotometer before recording the instrument malfunction. You have tested (b) (4) batches of multiple products on that instrument which have been released into US market. For example,

Date of Analysis	Product Name	Batch No.	Shipped to US	Release Date
3/30/2023	(b) (4) Tablets	(b) (4)	Yes	(b) (4)
4/6/2023	Tablets		Yes	
4/13/2023	(b) (4) Tablets (b) (4) mg		Yes	

SEE REVERSE OF THIS PAGE

Nicole E. Knowlton -S Digitally signed by Nicole E. Knowlton -S Date: 2024.03.27 16:11:11 +05'30'
Yvins Dezan -S Digitally signed by Yvins Dezan -S Date: 2024.03.27 16:05:28 +05'30'

DATE ISSUED
03/27/2024

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4/20/2023	(b) (4)	Tab	(b) (4)	Yes
6/8/2023	(b) (4)	Tablets		Yes
6/9/2023		Tablets		Yes
6/21/2023		Tablets		Yes
6/21/2023		Tablets		Yes

In addition, SOP for breakdown (CQA/0210-001, *Handling of Work Requisitions through TrackWise*) is deficient and does not delineate any provisions regarding performing an investigation of the equipment breakdown. Although an impact assessment and recommendation are to be performed by the area in charge to assess the possible effects on the product, equipment, and system, it was not performed.

B. PR #59504: On 09/27/2021, you received a complaint for (b) (4) Tabs (b) (4) mg Batch # (b) (4) where the consumer reported 12 tablets of (b) (4) mg was found in a sealed bottle of (b) (4) mg (b) (4) ct bottle for Batch # (b) (4) You concluded that there are adequate controls in place at your facility during manufacturing, storage as well as packing of the batch. According to your SMEs and management team on 03/21/2024, Type A (minor) cleaning is performed for product containers (b) (4) (b) (4)

I observed you failed to follow Step #5.4.16.1.6 of SOP #CQA/0151-002 (*Handling of Investigation through TrackWise* 03/02/2020 effective date) where it states "For any kind of investigation Genchi Genbutsu (Go & See) is mandatory. Meaning of the process is to observe the problem situation first hand, personally (not to rely on the reports or others), talk to those at the sharp end (counselling) explore the contributing visible and invisible factor, analyze each factor and conclude probability." You concluded the reported complaint as unconfirmed. On 03/23/2024 during my inspectional walkthrough of Primary Packaging Room # (b) (4) I observed you encountered a power failure and you did not perform any impact assessment of the equipment and (b) (4) mg Batch # (b) (4) (US marketed product) being packaged in the room. Yet, you restarted the line and I observed 4-5 bottles from the tablet filler station going down the conveyor belt. During 2020-2024 period, you received approximately 285 marketed complaints and you have not performed Genchi Genbutsu (Go & See) for 227 of 285 (79.6%) of the marketed complaints based on the table provided by you below (not all-inclusive).

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Go and See data for Market Complaints				
Year	**No. of complaints for US market**	**Go and See (Documented)**	**Go and See (Not Documented)**	**PR ID # where Go and See not Documented (Not all- inclusive)**
2024	13 (06 complaints are under investigation)	7	0	N/A
2023	81	25	56	120167, 133403, 105751, 106093, 106687, 107287, 107383, 108154, 108369, 108655, 108975, 108976, 108978, 109210, 109500, 109554
2022	80	10	70	81752, 92337, 75710, 76245, 76355, 77819, 77847,79179, 80748, 80803, 80977, 81232, 81752, 82446, 82661, 83698, 85002, 85917, 85967, 86347, 87305, 87316, 87321, 88071
2021	55	7	48	40668, 57624, 33501, 34671, 34834, 36335, 36477, 36511, 37045, 37056, 37132, 37578, 38305, 38315, 38324, 38748, 38838, 39176, 40668, 40682, 40693, 42215, 42684, 54516
2020	56	3	53	10277, 20951, 33501, 34671, 34834, 36335, 36477, 36511, 37045, 37056, 37132, 37578, 38305, 38315, 38324, 38748, 38838, 39176, 40668, 40682, 40693, 42215, 42684
Total	**285**	**52**	**227**	**Percentage (5): 79.6%**

C. You have not taken effective measures to prevent recurrence of complaints. On 12/18/2020, you initiated complaint PR ID #31599 after receiving a complaint where Glove like part of (b) (4) material was found inside the sealed bottle of (b) (4) Capsules USP (b) (4) mg, Batch # (b) (4) Although you concluded in your investigation that the glove may get tear off during processing and might have been separated and mixed with capsules during handling of the capsules or after inspection. On 01/04/2021, you initiated CAPA #33064 to revise SOP B-PG/0033 (*Entry and Exit Procedure for Plant Personnel in Core area of General Block*) to include instructions if damaged/torn gloves are observed during any stage of manufacturing and packaging operations to report it immediately to supervisor for investigation and impact assessment. On 02/18/2021, you performed an effectiveness

check under PR #37160 for CAPA (PR ID #33064) after (b) (4) and determined the CAPA to be effective.

However, on 12/1/2022, you received another complaint under PR #101297 where the pharmacy manager reported they found a tablet which appeared to be cracked and when they looked closely, they pulled out a small piece of (b) (4) from the tablet for (b) (4) tablets (b) (4) mg, Batch # (b) (4)

D. You recorded the following recurring deviations and you have not taken effective measures to prevent their recurrences.

Deviation PR ID#	Batch #	Product	Description	Closure Date
26347	(b) (4)	(b) (4) Tablets USP (b) (4) mg (Finished)	Batch packing activity of Product (b) (4) (b) (4) Tablets USP (b) (4) mg (Batch No. (b) (4) could not be completed within the stipulated time line.	11/19/2020
28738		(b) (4) Tablets USP (b) (4) mg (FD/Stability)	Batch packing activity of product (b) (4) Tablets USP (b) (4) mg, Batch No. (b) (4) could not be completed within the stipulated hold time period.	12/15/2020
31851		(b) (4) tablets (b) (4) mg	Product (b) (4) (b) (4) tablets (b) (4) mg could not be packed within stipulated time.	12/31/2020
47164		(b) (4) Tablets USP (b) (4) mg	Missed Stability study analysis at 32 Month-25°C/60%RH time point	07/03/2021

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64474	(b) (4) (b) (4) (b) (4) gram (stability)	Initial analysis (T0) was not completed within specified time point (b) (4) (b) (4) for (b) (4) (b) (4) test by (b) (4) after receipt of samples at QC.	12/15/2021
80801	(b) (4) Tablets USP (b) (4) (b) (4) mg.	Stability study analysis was not completed within specified time point for Assay test at 18 Month-25°C/60%RH	05/20/2022

E. You have not investigated all manufacturing alarms recorded during manufacturing and packaging operations and you have not performed any assessment of their impact on products. We observed in each manufacturing suites on 03/19/2024, you posted an alarm board which classifies which ones have product impact and non-product impact. According to the Vice-President & Site Head-Production on 03/21/2024, the alarms classification and impacts were recommended by the OEM and they have not performed their own assessment. ***Repeat Observation***

OBSERVATION 2

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

A. You have not performed shipping studies of finished products shipped to US markets as required per Protocol #AB/MSP/18/007 (*Protocol for Transportation Study of Bulk/ Finished Products*, 06/13/2018 effective date) to show finished products conform to appropriate standards of identity, strength, quality, and purity. Specifically, you have manufactured and shipped the following approved .finished products into US market: (b) (4) (b) (4)

Name of the Product	Shipping Study	Mode of Shipment (b) (4)	Shipping Study Status
(b) (4)			

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(b) (4)

B. Change controls are not managed and closed within the specified timeframe. Currently, you only track the child project record identification (PR ID) for change controls in TrackWise through closures but not the parent project record identification. We observed several change controls (including those listed below, not all-inclusive) being closed beyond their target completion dates and no extensions had been requested, which is contrary to SOP # CQA/0170 (*Handling of Change Control Through TrackWise)*. According to your SMEs, your software (TrackWise) does not allow them to request extensions for the parent change control record in order to meet the target completion dates. ***Repeat Observation***

CC No./ PR ID#	Document /Product/ Material/ Equipment/ Facility	Date of Initiation	Due Date	Extension Request Date	New Due Date	Closure Date
B/CC/P/2020/0004 (PR ID #6279)	Product	1/6/2020	(b) (4)	NA	NA	4/25/2021

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			(b) (4)			
B/CC/P/2020/0012 (PR ID #6286)	Product	1/6/2020		5/1/2020	6/30/2020	Awaiting regulatory action completion
B/CC/P/2021/0048 (PR ID #34416)	Product	1/21/2021		NA	NA	9/20/2023
B/CC/P/2021/0130 (PR ID #36871)	Product	2/16/2021		NA	NA	2/8/2024
B/CC/P/2022/0115 (PR ID #73851)	Product	2/11/2022		NA	NA	12/31/2023
B/CC/P/2023/0185 (PR ID #110225)	Product	3/21/2023		NA	NA	3/14/2024

C. You have not provided training to employees in the particular operations they perform as part of their function and written procedures required by current good manufacturing practice regulations. In addition, you have not updated the training need identification for the following employees listed below (not all-inclusive) and you failed to detect and track employees that are overdue on training in the eTMS by Nichelon5 CMS (learning management software). The software does not capture the latest SOP versions for training purposes and does not notify management with overdue training.

- Associate Vice President - Quality
- Sr. Tech, Production (b) (6)
- Manager, Quality (b) (6)
- Technician, Packaging (b) (6)

D. You failed to adequately perform and assess GxP and Impact assessment for Q-Sutra computerized system/software (utilized as data acquisition software for in-process testing in manufacturing and packaging operations). According to Document #ICS-2202-149-V-01-GxP-R0 (*GxP Assessment/ Impact Assessment Document of Precise IPQA Solution, 09/06/2022 effective)*, you recorded "No" instead of "Yes" for the steps listed below which should have been recorded as "Yes" per your validation SMEs and your Associate Vice-President – Quality.

- Step (b) (4) "Is the system a process control system (e.g. PLC, SCADA, DCS, EMS) that may affect product quality and is there no independent verification of the control system performance in place?
- Step (b) (4) of Document #ICS-2202-149-V-01-GxP-R0 (*GxP Assessment/ Impact Assessment Document of Precise IPQA Solution, 09/06/2022 effective)*.

E. You failed to qualify the firm who performed the Q-Sutra software validation and they are not listed on your approved service provider list, which is contrary to SOP #CQA/0048-005 (*Handling of External Contractors/Agencies and Projects*, 08/14/2020 effective date). In addition, you failed to provide GMP training to the contractor who performed the software validation for Q-Sutra.

F. You failed to investigate and assess electronic data backup failures you encountered for all your software including HITSRV-TEST (HITPHAMS, application software for electronic batch manufacturing/packaging record) on the following dates (not all-inclusive): 02/10/2024, 02/14/2024, 03/10/2024, 05/10/2023, 06/10/2023, 07/10/2023, 07/10/2022, 08/10/2022, 09/10/2022, 10/10/2022, 11/10/2022. In addition, your procedures (B-IT/0004-005, B-IT/0009-004) for electronic data backup are deficient and do not have any provisions for investigating electronic data backup failures. According to your Manager, Corporate IT, (ID # (b) (6) on 03/26/2024 the files for electronic data backup are overwritten after (b) (4) and they do not document their (b) (4) review of the electronic data backup failures.

G. The hold time study performed under Protocol Cum Report to Generate Microbial Enumeration Test Data of (b) (4) Tablets (b) (4) mg B/P/G/22/102 was not performed by your Quality Control department it was developed and executed by your Production Development Laboratory. The testing to be performed in the study is not explicitly listed but states it is to be performed per protocol RE/Protocol/2022/0325.

The purpose of RE/Protocol/2022/0325 (b) (4) Tablets (b) (4) mg Microbial Stability Study effective 19 OCT 2022 is to assess the microbial stability of (b) (4) Tablets (b) (4) mg and the scope is limited to the stability study batches manufactured at the site.

Additionally, there is no written procedure providing instructions on how microbiology samples are to be handled in the quality control laboratory and there was no chain of custody for the (b) (4)

(b) (4) hold time study sample (AR No.: (b) (4) that was collected 11 NOV 2022 and delivered to the microbiology laboratory on 14 NOV 2022.

Hold Time Study B/P/G/22/102 was performed to support the (b) (4) hold time of the (b) (4) Tablets (b) (4) mg (b) (4) and was submitted in support of Drug Application (b) (4)

FACILIITES AND EQUIPMENT SYSTEM
OBSERVATION 3
Separate or defined areas to prevent contamination or mix-ups are deficient regarding the manufacturing and processing operations. Specifically,

A. Movement of personnel and gowning process are not defined and/or adequately assessed in the manufacturing and processing area to prevent contamination during manufacturing of (b) (4) products. We observed on 03/19/2024 during our inspectional walkthrough of (b) (4) (Room # (b) (4) that we must completely remove our gown from inside the room and keep the gloves before exiting the room to the clean corridor. (b) (4) Room # (b) (4) is utilized as one of the rooms for (b) (4) products (i.e. (b) (4) Tablets, US marketed product).

B. Personnel from QC are allowed to go to (b) (4)-Block (utilized for manufacturing and packaging of (b) (4) products shipped to U.S market); (b) (4)-Block personnel are allowed to go to QC; (b) (4) Block personnel are allowed to go to QC, but QC personnel are not allowed to go (b) (4) Block.

OBSERVATION 4
Buildings used in the manufacturing, processing, packing, and holding of a drug product are not maintained in a good state of repair. Specifically,

A. We observed during our inspectional walkthrough of (b) (4) Block on 03/19/2024 that washing and toilet facilities in Room # (b) (4) and men's washroom in (b) (4) Block gowning area lack hot water for production personnel to wash their hands as required before gowning.

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B. The walls inside (b) (4) (Room # (b) (4) located by (b) (4) ID #GA/53) and (b) (4) system (ID # (b) (4) were observed cracked and chipped; Cracked ceiling and leakage stain were observed above the opening of (b) (4) ID #GA/11 in (b) (4) (Room # (b) (4) Peeling paint observed on top of the opening of (b) (4) (ID # (b) (4) located in Room # (b) (4). The firm was manufacturing (b) (4) Tabs USP (b) (4) mg Batch # (b) (4) (US marketed product).

OBSERVATION 5

Equipment and utensils are not cleaned, maintained, and sanitized at appropriate intervals to prevent contamination of the products. Specifically,

A. You have not defined and labeled hardest to clean or "hot spots" areas in your primary packaging cleaning SOPs and equipment where tablets or capsules (packaged for the U.S. market) might be hidden during cleaning operations to prevent product mix-ups / foreign products.

B. Presence of excessive powder was observed inside the (b) (4) bowl, ID #GA/56), in-process container (ID #GA/744), (b) (4) (ID #GA/715), (b) (4) (ID #GA/05) located in (b) (4) (Room # (b) (4) after performing a Type A cleaning on 03/19/2024 for (b) (4) (b) (4) Tabs USP (b) (4) mg Batch # (b) (4) in (b) (4) Block. The Type A cleaning record was reviewed by your Production and approved by your QA personnel on 03/19/2024.

C. Presence of tools (scissors and Philip screw driver) and eight (8) (b) (4) tablets coded (b) (4) were observed underneath the (b) (4) balance (ID #GD/06) on 03/19/2024 in (b) (4) (Room # (b) (4) while the firm was running (b) (4) Tablets (b) (4) mg Batch # (b) (4) for the US market. However, the firm could not tell us to which batch they belong to since they only perform a Type A cleaning (b) (4) batches campaign cleaning for Type B).

D. Dispensing Room # (b) (4) of HEPA Filter has numerous holes and open gaps, light switch is taped with clear tape, the floor in the dispensing area is cracked in several areas (behind the scale and opposite area), plastic is peeling off (b) (4) balance, and missing a (b) (4) at the entrance of the dispensing room. The dispensing room is utilized to dispense APIs going to manufacturing operations at the firm.

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E. No documentation was available to justify why no recovery study was performed on the (b) (4) inner surface of the (b) (4) of Counting and Filling Machine ID (GE/380) during cleaning validation for (b) (4) Tablets (b) (4) mg (Drug Application (b) (4)

OBSERVATION 6

Appropriate controls governing computer acquired data and/or related systems have not been established to assure that changes and access to computerized software for laboratory control system or other systems is instituted/accessed only by authorized personnel. In addition, you cannot assure data generated from your manufacturing and laboratory equipment/instruments are true and accurate.

Specifically, your quality system cannot adequately ensure the accuracy and integrity of data to support the safety, effectiveness, and quality of the finished products manufactured at your firm. Your personnel are not knowledgeable of the implemented data acquisition software at your firm.

A. HMI alarms and audit trails for manufacturing and packaging operations are not backed up and are automatically erased by the system after (b) (4) per your Manager IT (b) (6) In addition, a review of these alarms and audit trails are not performed and documented. In addition, the firm implemented the electronic batch records and I observed they are not familiar with the software.

B. According to Section 2.9 of OQ #ICS-2202-149-V-01-OQ-RO 12/21/2022 (*Operational Qualification Document of Precises IPQA Solution*) for Q-Sutra validation "If the actual results are not expected, the actual results shall be recorded as observed, and also the tester shall mark as "Fail" in the "Pass/Fail" column. Then the tester shall follow the procedure described, in the deviation management."

- We observed you recorded several failures during the execution of the OQ in Step 3.3 (Verification of Security Level). However, you reported them as "Pass" instead of "Fail" and stated in the document "refer to discrepancy form". Yet, you approved the discrepancy and corrective action form on 12/26/2022 and stated in the discrepancy form "CS shall be revised and approved before post approval of this document." You then proceeded to PQ and later released the software on 02/15/2023 for use. Q-Sutra is being utilized as the data acquisition software for in-process control for weighing balance, (b) (4) test in manufacturing operations.

- You also executed several scripts for PQ (Data Table of Functional Configuration) without having/collecting the protocol instructions from your software engineer who performed the software validation. You initiated discrepancy and corrective actions for "Pause and Restart, Instrument Approve, Report View, Initial Mode Report, In-Process Report Verification, IPOOS Run Mode Approval, MDT (Verification)).

C. The HMI data from (b) (4) GA/396 used to manufacture the (b) (4) mg (b) (4) Exhibit batche (b) (4) which were submitted in support of Drug Application (b) (4) was not backed up. Your Process Development Assistant General Manager (b) (6) stated the memory will only hold (b) (4) batches.

Additionally, (b) (4) GA/396 is intended to be used in commercial production of (b) (4) (b) (4) mg (b) (4) as noted in Master Batch Record B/BMR/NGEJ01/0001-001 effective 14 MAR 2023.

MATERIAL SYSTEM
OBSERVATION 7
There was a failure to handle and store **drug product containers** at all times in a manner to prevent contamination. Specifically,

A. We observed on 03/23/2024 during our inspectional walkthrough of (b) (4) Block Raw Material (API) Room # (b) (4) that you are comingling (b) (4) APIs (e.g. (b) (4) USP Batch # (b) (4) USP (b) (4) Batch # (b) (4) with (b) (4) APIs (e.g. (b) (4) USP Batch # (b) (4) However, you have not performed any risk-assessment showing there is no impact for comingling these APIs.

B. According to the storage conditions recommended by the manufacturer of the following APIs as observed on 03/23/2024 in the (b) (4) Block API Warehouse, you have not demonstrated through documentation how you are meeting the storage conditions and the shelf-life of these APIs. You failed to (b) (4) the following materials with (b) (4) as required per Form-VI of SOP B-WH/0020-039 (Dispensing of Raw Material): (b) (4) (not all-inclusive).

In addition, your sampling and dispensing controls for these APIs are not captured in your eLogbook.

- (b) (4) API Batch # (b) (4) label states "Store (b) (4) (b) (4) 25^0 C)".
- (b) (4) USP Batch # (b) (4) label states "Store (b) (4) (b) (4) 25^0 C".
- (b) (4) API Batch # (b) (4) label states "Store (b) (4) (b) (4) Temperature (b) (4) 25^0 C".

C. You have not established and demonstrated through your temperature mapping for (b) (4) Block API Warehouse regarding the maximum height API containers can be stored on the racks. We observed API containers were double-stacked and close to touching the ceiling on Rack # (b) (4) and (b) (4) in (b) (4) Block on 03/23/2024. However, Report #AB/MSR/23/018-07 (*Temperature Mapping Report of Raw Material Store (API) (Room No.* (b) (4), performed on 08/04/2023 to 08/11/2023 period revealed no double-stacking of API on the top shelf of Rack # (b) (4) which is the same level of probe placement.

PRODUCTION SYSTEM
OBSERVATION 8

Control procedures are not established which [**monitor the output**] [**validate the performance**] of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product. Specifically,

You have not established or failed to follow instructions in your electronic batch records (HITPHAMS application software) when manufacturing and packaging products (b) (4) regarding what actions must be taken by production personnel (operators/technicians and supervisor) before starting the manufacturing and packaging operations and for performing in-process checks. In addition, we observed the following on 03/23/2024 in Room # (b) (4) (Primary Packaging Room) during the packaging of (b) (4) Tablets (b) (4) mg Batch # (b) (4) (US marketed product):

a) The HMI displayed (b) (4) TABS (b) (4) mg" as the product being packaged in the primary room after observing a power failure while in the room. Your operator restarted the line after the power resumed and did not even check if the information displayed in the HMI was accurate. In addition,

it is not included as one of the parameters for checking prior to starting the line according to electronic batch packaging record #B/eBPR/NT1327/0001-003 (b) (4) (b) (4) Tablets USP (b) (4) mg).

b) The HMI is not connected to uninterrupted power supply (UPS) and is automatically reset to a product according to the Vice-President & Site Head-Production and Production Supervisor.

c) Line personnel did not perform any checks on the line and equipment to ensure all equipment is working as intended, and removing any bottles which were being filled under the filler during the power failure.

d) When performing in-process checks in primary packaging, the operator/technician must leave the primary room to perform the in-process checks and taking the only laptop in the primary room to record the reading in HITPHAMS (application software for electronic batch manufacturing/packaging record). This process is not captured in the eBPR. We further observed the operator left the room at 12:56pm and returned approximately at 1:09pm. However, there are no other means in the room for documenting any other activities that may need to be recorded in the electronic batch records contemporaneously.

e) The operator collected filled tablet bottles before capping to perform the (b) (4) weight check (using the (b) (4) counter for tablets and capsules) and left them (approximately (b) (4) tablets) into the collected jar underneath the instrument. According to your Production Supervisor for (b) (4) Block) Room # (b) (4) the operator/technician is to collect the filled bottles before capping, perform the weight check, and place them back immediately into the (b) (4) This practice is not described and/or followed. I observed the jar collecting the in-process samples contained at least (b) (4) tablets of (b) (4) Tablets (b) (4) mg Batch # (b) (4).

f) Rejected bins/areas on the equipment for packaging operations are not identified and controlled to prevent their use in manufacturing or processing operations for which they are unsuitable. Several rejected bottles of (b) (4) Tablets (b) (4) mg Batch # (b) (4) were observed in unlabeled and unlocked bins on the packaging line (e.g. in capper, across from HMI bin) in (b) (4) Block Room # (b) (4) except for the (b) (4) bin.

LABORATORY CONTROL SYSTEM
OBSERVATION 9

Laboratory controls do not include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, test procedures designed to assure that components, drug product containers,

closures, in-process materials, labeling, drug products conform to appropriate standards of identity, strength, quality and purity. Specifically,

A. [redacted] USP API Batch # [redacted] (observed in location # [redacted] in Warehouse # [redacted] on 03/19/2024) was last retested on 01/06/2023 and was due for retest in 365 days. However, it has not been retested according to the established retest frequency and no deviation has been processed. According to your Assistant Manager QC (ID # [redacted] on 03/19/2024, they have too many samples to retest.

B. On 03/21/2024, we observed stability samples for [redacted] Batch # [redacted] inside a cabinet located in the QC sample receiving room [redacted] block), which was received on 03/21/2024. The area is not being monitored for temperature and relative humidity. According to SOP #B-QC/0010-019 (*Handling of Analytical Samples*), the sample is to be immediately transferred to QC laboratory after receiving and verifying the sample.

C. On 03/21/2024, we observed an analyst in the QC laboratory performing preparation of test solution for [redacted] Tablets [redacted] mg Batch # [redacted] (9-month stability study 25^0 C/60 RH) where he was [redacted] weighing, performing calculations without referring to STP #RE/FPSTP/2020/0297 001, and failed to document each steps in the analytical worksheet (Stability Study). In addition, analytical results are not documented on the analytical worksheet until they are reviewed by the reviewer as observed in QC [redacted] Room.

D. The microbiology worksheets do not document the incubation start and end times for media/samples in all steps required testing. For example,

i. The Microbial Limit Testing performed on [redacted] Tablets Batch [redacted] on long term stability conditions at time point 35 months requires incubation of the [redacted] Medium at 30-35°C for [redacted] and incubation at 30-35°C for [redacted] The documented dates are [redacted] There is no indication the incubation time met the first [redacted] requirement.

ii. The Test for Specified Microorganism performed on [redacted] sampling point SPQ/[redacted] sample [redacted] requires the inoculated

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov	03/19/2024-03/27/2024
	FEI NUMBER 3006370533

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Mr. Arnab Pande (Vice-President & Site Head-Production)	
FIRM NAME Alkem Laboratories Limited	STREET ADDRESS Khasra No 1544, 1553, 1558, 1559, Village Thana Tehsil Nalagarh
CITY, STATE, ZIP CODE, COUNTRY Baddi, Himachal Pradesh, 173205, India	TYPE ESTABLISHMENT INSPECTED Drug Manufacturer

(b) (4) Medium to be incubated at 30-35°C for (b) (4) The worksheet indicates the analysis was performed 22 MAR 2024 and the observation was verified on 23 MAR 2024. There is no indication the incubation time met the (b) (4) requirement.

OBSERVATION 10

Reserve samples from representative sample lots or batches of drug products selected by acceptable statistical procedures are not examined visually at least once a year for evidence of deterioration.

No annual visual examination has been performed for the (b) (4) control samples in bottles identified by your firm as currently on the US market. Firm personnel stated they started collecting (b) (4) observation sample for each batch in February 2024 and will conduct the first review of those samples in one year. Examples of the products in the control sample room are (b) (4) Tablets USP (b) (4) (b) (4) mg, (b) (4) Tablets USP (b) (4) mg, (b) (4) Capsules USP (b) (4) (b) (4) mg, and (b) (4) Tablets USP (b) (4) mg.

***DATES OF INSPECTION**

03/19/2024 (Tue), 03/20/2024 (Wed), 03/21/2024 (Thu), 03/22/2024 (Fri), 03/23/2024 (Sat), 03/26/2024 (Tue), 03/27/2024 (Wed).

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 judgment, 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."