DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10903 New Hampshire Ave,Bldg 51,Rm 4225 Silver Springs, MD 20993 (301)796-3334 Fax:(301)847-8738	3/21/2016-3/25/2016
	FEI NUMBER 3004956904

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Ravindra K. Pandey , Senior Vice President Formulation - Manufacturing

FIRM NAME	STREET ADDRESS
Alembic Pharmaceuticals Limited	Formulation Unit I, Village Panelav, Tajpura, Near Baska, Taluka, Halol
CITY, STATE, ZIP CODE, COUNTRY Dist. Panchmahal, Vadodara, Gujarat, 389 350 ,India	TYPE ESTABLISHMENT INSPECTED 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.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

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

Specifically,
For blister packaging machines (b) (4), the change to include a piece of (b) (4) prepared on-site into the (b) (4) the pill and capsule (b) (4) and (b) (4), to prevent vibration and pill ejection from the (b) (4), was not done in accordance with the established change control procedure, to include review, evaluation, and approval by quality assurance. On 22 March 2016, the packaging of (b) (4) mg tablet (batch (b) (4)), (b) (4) mg capsules (batch (b) (4)), and (b) (4) mg capsules (batch (b) (4)) was observed for (b) (4) different packaging lines. On packaging machine (b) (4), capsules of (b) (4) mg were observed vibrating in a (b) (4) the (b) (4) and the (b) (4), with several capsules being slowly forced upward and falling onto the machine (Photo Taken). Blister packaging lines (b) (4) were in operation, but the vibration was mitigated using a piece of (b) (4) placed in the (b) (4) to mitigate vibration. While the equipment was designed to include a piece of (b) (4) to dampen vibrations in the (b) (4) described, it is unclear whether the new material is of similar design and quality to ensure that it does not lead to contamination of the packaged material with foreign material. Moreover, the change from the manufacturers supplied component, to that which was cut and prepared on-site, was not done per the change control procedure, and was not evaluated by quality assurance for its potential impact on product quality.

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EMPLOYEE(S) SIGNATURE
Erika V Butler, Investigator
Jason K Morgan, Generic Drug User Fee Amendments (GDUFA)
Zhaoyang Meng, FDA Center Employee or Employee of Other Federal Agencies

3/25/2016
X Erika V Butler
Erika V Butler
Investigator
Signed by: Erika V. Butler -S

DATE ISSUED
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OBSERVATION 2

Written production and process control procedures are not documented at the time of performance.

Specifically,
During the inspection of blister packaging, in Blister Pack room (b) (4) (b) (4) mg capsules batch (b) (4) was in the process of set up. It was observed on the batch packaging record that the operator had completed the (b) (4) Challenge Test by initialing the "Done by" column. This was verified with the "Checked by" column being initialed and dated. However, it was observed on the blister pack line the (b) (4) Challenge test was still in progress and was stated as such by the operator. Your firm is not documenting records contemporaneously as activities are completed.

OBSERVATION 3

Procedures designed to prevent objectionable microorganisms in drug products not required to be sterile are not established , written and followed.

For example,

1) On 22 March 2016, for plates under incubation, air bubbles were observed between the (b) (4) and (b) (4) used to perform (b) (4) filtration and microbiological enumeration of (b) (4) samples; the test procedure, APL/RT0122, for (b) (4) testing is inadequate in that does not contain sufficient detail to ensure the absence of air bubbles between the (b) (4) and (b) (4) prior to incubation. (b) (4) is used during the production of non-sterile drugs and for cleaning of manufacturing equipment. There is no data to support the accuracy and sensitivity of this test method when air bubbles are present between the filtration (b) (4) and the (b) (4) during incubation.

2) The written procedure for environmental monitoring and swab sampling, ALP/QC/SOP098, fails

to include the use of (b) (4) for the total combined yeast and mold test, which is specified for cleaning validation studies performed for non-dedicated drug manufacturing equipment.

3) On 23 March 2016, a leak was observed from a pipe connecting the (b) (4) liter (b) (4) storage tank for distribution and use for production and cleaning operations. The leak was identified as originating from the (b) (4) clamp connecting the use-point distribution pipe to the (b) (4) tank. There were no controls in place to prevent the potential ingress of objectionable microorganisms into the (b) (4) tank from this leak if (b) (4) pressure changes were to occur, and microbiological control systems such as (b) (4) (b) (4) are all upstream of this connection. (b) (4) from the (b) (4) liter tank is distributed through the continuous loop, and is used during the production of non-sterile drugs and for cleaning of manufacturing equipment.

OBSERVATION 4

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,

1) Deviation Investigation #ALP/QA/DC6020 failed to address other drug products that may have been affected by the (b) (4) breach coming from the (b) (4) and entering the (b) (4) (PD/09/(b) (4) 02) through the duct pipe. (b) (4) tablets (b) (4) mg trial batch (b) (4) was being (b) (4) at the time. The (b) (4) gasket of the (b) (4) line was found damaged and was leaking from the service area, which is the floor (b) (4) the (b) (4) area. The (b) (4) was traveling down the duct work into the (b) (4). Your firm did not assess batches prior to the (b) (4) breach to assure there was no product impact.

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2) Deviation Investigation # ALP/QA/DC5175 reported metal detection in (b) (4) tablets (b) (4) mg batch (b) (4) (Lot rejected). The probable root cause was attributed to a damaged screw on the compression machine which was mishandled with incorrect tools to cause abrasions on the screw. Your firm failed to document re-training on disassembly procedures for the operators identified as a preventative action measure to prevent or mitigate future re-occurrence of the deviation.

3) Tablet and capsule filled bottles that are initially rejected at the (b) (4) checkweigher after filling, labeling, sealing, and capping are re-passed through the checkweigher without investigation into the cause of the initial rejection. If the rejected bottles pass the second pass-through, they are accepted. On 21 March 2016, a bottling operation was observed on the (b) (4) equipment (PD/67/(b) (4) 04) in room (b) (4) wherein an operator removed a bottle that had been rejected from the (b) (4) checkweigher and re-passed it through the checkweigher without investigating the cause of the initial rejection. The procedure describing rejected bottle handling, ALP/PR/SOP243, does not include instructions for investigations into rejected bottles failing at the (b) (4) checkweigher. Since 20 February 2015, there have been 20 market quality complaints regarding bottles which were missing pills or tablets.

3/25/2016

X Jason K Morgan
Jason K Morgan
Generic Drug User Fee Amendments (GDUFA)
Signed by: Jason K. Morgan -S

3/25/2016

X Zhaoyang Meng
Zhaoyang Meng
FDA Center Employee or Employee of Other F...
Signed by: Zhaoyang Meng -S

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	Erika V Butler, Investigator Jason K Morgan, Generic Drug User Fee Amendments (GDUFA) Zhaoyang Meng, FDA Center Employee or Employee of Other Federal Agencies 3/25/2016 X Erika V Butler Erika V Butler Investigator Signed by: Erika V. Butler -S	3/25/2016