**DEPARTMENT OF HEALTH AND HUMAN SERVICES**
FOOD AND DRUG ADMINISTRATION

Use this check box to generate the required 483 statement on page 1 for medical device observations. ☐

| DISTRICT OFFICE ADDRESS AND PHONE NUMBER | DATE(S) OF INSPECTION |
|---|---|
| 12420 Parklawn, Drive, Room 2032<br>Rockville, MD 20857<br>CDER-OC-OMQ-International483Response@fda.hhs.gov<br>Industry Information: www.fda.gov/oc/industry | 05/26-31/2025 |
| | FEI NUMBER<br>3003821360 |

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Pradeep Chakravarty, Head - Global Quality

| FIRM NAME | STREET ADDRESS |
|---|---|
| Alembic Pharmaceuticals Limited (Units I and II) | API Division - Unit I, Village Panelav, P.O. Tajpura, |
| CITY, STATE AND ZIP CODE | TYPE OF ESTABLISHMENT INSPECTED |
| Tal. Halol, Panchmahal Dist. – 389350, Gujarat, India | API 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 (I) (WE) OBSERVED:

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## QUALITY SYSTEM

### OBSERVATION 1

Laboratory investigations were not conducted timely based on an identifiable trend or thoroughly to determine the root cause.

Specifically,

**A.** An investigation into (b) (4) API (DMF: (b) (4), stability batch number: (b) (4) for the Related Compound (b) (4) was not performed until the impurity was OOS at the 12M timeframe even though the impurity was approximately doubling through the first 6 months and borderline OOS. The OOT procedure, C/QA/SOP/0187, Titled: "Handling of Out of Trend (OOT) Test Results", Effective date: 28-Nov-2024, Annexure X (Trend Analysis for Stability Testing) only requires an OOT investigation if there is a difference in value (b) (4) between stability testing points and does not consider proactively investigating an identifiable trend.

**Table 1**

| Batch Number | Stability Time point | | | | |
|---|---|---|---|---|---|
| | Initia 1 | 3 month | 6 month | 9 month | 12 month |
| (b) (4) | (b) (4) % | (b) (4) % | (b) (4) % | (b) (4) % | (b) (4) % |

**B.** (b) (4) API (DMF: (b) (4), batch number: (b) (4) failed to meet specification limit for Related Compound (b) (4) impurity at 12 month, 18 month and 36 month long term (25°C±2°C/60%RH±5% RH) stability time points. The following OOS investigations were performed:

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| TO: Mr. Pradeep Chakravarty, Head - Global Quality | |
| FIRM NAME<br>Alembic Pharmaceuticals Limited (Units I and II) | STREET ADDRESS<br>API Division - Unit I, Village Panelav, P.O. Tajpura, |
| CITY, STATE AND ZIP CODE<br>Tal. Halol, Panchmahal Dist. – 389350, Gujarat, India | TYPE OF ESTABLISHMENT INSPECTED<br>API Manufacturer |

- OOS No.: OOS/A1/22/0053, Reported date: 11-May-2022, Stability time point: 12M, Result: (b) (4)%, Limit: NMT (b) (4)%
- OOS No.: OOS/A1/22/0150, Reported date: 10-Nov-2022, Stability time point: 18M, Result: (b) (4)%, Limit: NMT (b) (4)%
- OOS No.: OOS/A1/24/0054, Reported date: 13-May-2024, Stability time point: 36M, Result: (b) (4)%, Limit: NMT (b) (4)%

These OOS investigations concluded that the root cause was based on improper stability sample (b) (4) packing i.e. not (b) (4) with (b) (4) after (b) (4) sample (b) (4) prior to packing leading to oxidative degradation of their stability samples. However, the consistent upward trend of Related Compound (b) (4) impurity from Initial to 9 month stability time points (**Table 1**) confirmed quality issues with (b) (4) API, batch number: (b) (4) In addition, your laboratory investigation checklist (Phase-I (b)) reported no issues with sample integrity and its storage and handling. Re-measurement (re-injection and re-vial) results confirmed the original (OOS) test results during each of these investigations. However, your firm performed retest analyses in triplicate using additional (b) (4) (new sample) which showed passing test results at 12 month and 18 month time points. Your firm provided no justification for differences in the test results of original and retest analyses considering the stability samples were packaged in (b) (4) at the same time following the same practices of not (b) (4) each (b) (4) with (b) (4) by the same QA Executive.

Further, your firm provided no justification for not conducting side-by-side comparative analyses on the same sample set sequence to demonstrate that slight variations in chromatographic conditions, diluent, mobile phase, etc. may not have led to variation in the test results.

## LABORATORY CONTROL SYSTEM

### OBSERVATION 2

Laboratory control does not include establishment of scientifically sound and appropriate test procedures and specifications designed to assure quality of drug substances.

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| Tal. Halol, Panchmahal Dist. – 389350, Gujarat, India | API Manufacturer |

Specifically,

Analytical test procedures used to perform stability testing on APIs for the US market are not adequately validated as stability indicating. For over (b) (4) products there is incomplete data on degradant products and pathways as the Related Substances by HPLC and Assay by HPLC test methods did not meet the validation protocol degradation acceptance limits of (b) (4) to (b) (4) % for at least (b) (4) conditions. For many of these products the degradation level achieved was 0%.

Some examples include:

| Sr. No. | Product Name | DMF No. | Acid Degradation | Base Degradation | Oxidation | Thermal Degradation | Photo Stability | Humidity |
|---|---|---|---|---|---|---|---|---|
| (b) (4) | | | | | | | | |

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| Sr. No. | Product Name | DMF No. | Acid Degradation | Base Degradation | Oxidation | Thermal Degradation | Photo Stability | Humidity |
|---|---|---|---|---|---|---|---|---|
| (b) (4) | | | | | | | | |

**FACILITY AND EQUIPMENT SYSTEM**

**OBSERVATION 3**

Equipment is not cleaned and maintained to prevent contamination that would alter the safety, identity, strength, quality and purity of the drug product.

Specifically,

On 26-May-2025, I observed non-dedicated production equipment used to manufacture US products in API Uni (b) (4) Plant (b) (4) in a state of disrepair, and it contained residual powdery materials while in the clean status. For example,

1. (b) (4) ID: (b) (4) 013 contained a very thin layer of white powdery residues in some sections post (b) (4) filter in the direction of high velocity air (b) (4) cfm) towards (b) (4) bowl while this equipment was tagged in "Ready for use" status upon product changeover cleaning post manufacturing of (b) (4) API USP, Batch Number: (b) (4) There is no additional filter post (b) (4) filter to prevent residual powdery materials from getting blown towards the (b) (4) bowl and contaminating the product. This equipment was tagged in "Ready for use" status upon product changeover cleaning post manufacturing of (b) (4) API USP, Batch Number: (b) (4) when these issues were observed. These issues were identified to management at the initiation of this inspection on 26-May-2025 but the equipment continued to be used

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without cleaning for the next (b) (4) to manufacture (b) (4) API, Batch Numbers: (b) (4)

2. (b) (4) ID: (b) (4) 047 was observed encrusted in parts with white to off-white powdery materials on the side walls of (b) (4) along with black color (b) (4) was missing, peeled-off, and loosely hanging on many areas of this equipment that comes directly and indirectly in contact with the product under manufacturing. Additionally, there were dent marks, rough surfaces, and corrosion formation in some areas which may interfere with cleaning of (b) (4) 047. This equipment was tagged in "Ready for use" status upon product changeover cleaning when these issues were observed.

   Further, this equipment underwent (b) (4) preventative maintenance on 06-May-2025 i.e. about 20 days prior to the start of this inspection, however, the severity of damage to (b) (4) was underreported as a minor issue and there were no mention of issues relating to dent marks, corrosion, and rough surfaces in the preventative maintenance report.

3. (b) (4) ID: (b) (4) 012 was observed encrusted with and color residues in product contact areas. Additionally, had numerous dent and scratch marks through the product hold areas which may interfere with equipment cleaning. This equipment was tagged in "Ready for use" status upon product changeover cleaning post (b) (4) API USP, Batch Number: (b) (4) manufacturing when these issues were observed.

## QUALITY SYSTEM

### OBSERVATION 4

Lack of Quality Unit oversight on document control and review.

Specifically,

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Your Quality Unit lacked adequate oversight on employees' practices of documenting GMP activities on uncontrolled papers. For example,

On 26-May-2025, I observed torn pieces of uncontrolled papers along with a few intact pieces containing handwritten information in black color ink pen relating to equipment cleaning, maintenance, and QC testing activities. According to your procedure C/QA/SOP/0018, Titled: "Good Documentation Practices", Effective date: 26-Apr-2025, section: 4.1.3 black color indelible ink is used for documentation of GMP activities. These papers were found disposed inside the main scrapyard of your API Unit (b) (4) facility. The evaluation of one of the torn pieces revealed that your operator communicated issues relating to heavy leakage through (b) (4) valve of (b) (4) 150 while this equipment was in use at intermediate stage for (b) (4) batch number (b) (4) There was no incident logged, no impact assessment done, and there was no mention of this issue occurred anywhere in the batch manufacturing record and (b) (4) usage logbook.

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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 judgement, 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."