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	8/4/2025-8/13/2025*
	FEI NUMBER 3005430968

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Prashant Sharma, Chief Technical Officer

FIRM NAME	STREET ADDRESS
Zydus Lifesciences Limited	Tehsil - Nalagarh
CITY, STATE, ZIP CODE, COUNTRY Baddi, Himachal Pradesh, 173205 India	TYPE ESTABLISHMENT INSPECTED Drug Products 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 OBSERVED:
QUALITY SYSTEM

OBSERVATION 1

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

Specifically, your quality unit did not to take appropriate market action for batches of US product that failed to meet the specification limit for (b) (4) Drug Substance Related Impurities (b) (4) For example:

(b) (4) out of (b) (4) batches of (b) (4) Tablets USP failed to meet the specification limit of (b) (4) ppm for (b) (4) impurities when analyzed as part of a (b) (4) risk assessment in (b) (4) A few examples are listed as follows:

Batch No.:	Product Strength	Manufacturing date	Expiry date	Age of sample when analyzed in (b) (4)	Results for (b) (4) (ppm)
(b) (4)					

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EMPLOYEE(S) SIGNATURE
Pratik S Upadhyay, Investigator - Dedicated Drug Cadre

X Pratik S Upadhyay Investigator - Dedicated Drug Cadre Signed By: PRATIK S. UPADHYAY -S Date Signed: 08-13-2025 01:11:49

DATE ISSUED
8/13/2025

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(b) (4)

The following was observed relating to (b) (4) testing failures:

a. There were no Out-of-Specification (OOS) investigation for the (b) (4) batches that failed to meet the specification limit for (b) (4) content in (b) (4) Tablets USP.

b. According to section 5.0 "Risk Assessment Conclusion" of Risk Assessment Report No.: CQ (b) (4) 0016, dated: (b) (4) your firm committed to analyze the remaining (about (b) (4)) batches within expiry of (b) (4) Tablets USP for (b) (4) impurities based on the failing test results obtained for (b) (4) batches. However, to date there was no analyses performed for any of the remaining (b) (4) batches to determine the level of (b) (4) in (b) (4) Tablets. Your Corporate Head of Quality stated the reason for not analyzing remaining (b) (4) batches of (b) (4) (b) (4) Tablets was due to potential for obtaining failing test results for the remaining (b) (4) batches against the specification limit of (b) (4) ppm.

c. Following the (b) (4) risk assessment testing, your firm then developed an increased interim limit of (b) (4) ppm which was calculated using EMA guidance and a (b) (4) treatment duration of "up to (b) (4)". Only one (1) batch (Batch Number: (b) (4) failed the (b) (4) ppm spec out of the (b) (4) batches that originally failed at (b) (4) ppm. Considering a treatment duration greater than (b) (4) as part of the interim limit calculation, which (b) (4) would have resulted in a lower interim limit of (b) (4) and thus (b) (4) additional batches failing. No justification was provided for calculating the increased interim limit and adopting this interim limit from EMA guidance.

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d. Your firm recalled only one (1) batch (Batch Number: [(b) (4)] out of the initial [(b) (4)] failing batches because it did not meet the interim limit of [(b) (4)] ppm. Your firm communicated about recalling one (1) to the FDA and claimed to have the agency permission to keep distributing batches into the US market. However, the evaluation of email communication during this inspection revealed that the FDA has neither approved your interim limit nor allowed you to keep distributing failing lots of [(b) (4)] [(b) (4)] Tablets for [(b) (4)] content into the US market.

e. Your firm suspended manufacturing of [(b) (4)] Tablets USP [(b) (4)] mg, [(b) (4)] mg, [(b) (4)] mg, [(b) (4)] mg, [(b) (4)] mg on [(b) (4)] due to continued risk associated with the formation of [(b) (4)] However, you did not analyze batches within expiry up to [(b) (4)] that were borderline to the specification limit of [(b) (4)] ppm or your interim limit of [(b) (4)] ppm.

OBSERVATION 2

Procedures describing the handling of written and oral complaints related to drug products are deficiently written or followed.

Specifically, your Quality Unit failed to thoroughly investigate adverse drug event (ADE) relating to patient death. For example,

A. On 21-Feb-2023, your firm initiated ADE No.: AE/0302/2023/0016 upon receiving complaint from a Physician regarding a male patient death in the US that was on your [(b) (4)] mg Tablets for the treatment of [(b) (4)] According to the description of ADE complaint, Physician stated over the phone call that she will email further details relating to this event to share batch number, product NDC number and so on to assist with the site investigation. However, your firm neither made sufficient attempt to know the batch number nor tried to collect the complaint sample which is required per your ADE handling procedures SOP-ZUSA-0005, Revision: 08 and 0302- SOP-QA-00036, Version: 5.0. In the absence of batch number and complaint sample, your site complaint investigation team simply closed this ADE investigation based on the available information in Annual Product Quality Report

(APQR) indicating no availability of sample and additional information to determine the root cause.

B. On 27-Jul-2021, your firm initiated ADE No.: AE/0302/2021/0055 upon receiving complaint for an unknown lot of (b) (4) Tablets (b) (4) mg USP with imprint of (b) (4) from the patient about *"feeling dizzy and product substitution"* issues. Your site complaint investigation team categorized the event as non-serious expected drug event and closed this ADE investigation on 02-Sep-2021 based on the available information in Annual Product Quality Report (APQR) indicating no availability of sample and additional information to determine the root cause. However, the same site complaint investigation team failed to determine the root cause for product substitution could potentially be due to the product mix-up for which your firm had received a separate complaint at around the same period on 03-Aug-2021 and subsequently initiated a product recall of (b) (4) Tablets (b) (4) mg USP, batch (b) (4) from the US market on (b) (4) Your product mix-up complaint investigation (ZYD-21-PC-128) revealed the mix-up of about (b) (4) tablets of (b) (4) Tablets (b) (4) mg with (b) (4) Tablets (b) (4) mg USP, batch (b) (4) during the batch packaging operation due to deficiencies in your line clearance procedure. Your firm failed to determine that inadvertent use of (b) (4) Tablets (b) (4) mg can cause dizziness as a common side effect.

OBSERVATION 3

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.

Specifically,

Reserve (Retain) samples of drug products are examined based on Acceptable Quality Level (AQL) Inspector's Rule and Inspection Manual. This practice does not consider enhanced examination when several repeated product quality complaints pertaining to tablets discoloration, broken tablets, disintegrated tablets, tablets with (b) (4) bigger tablets, foreign matters, count variability are

reported. For example,

As per your firm's SOP No.: 0302-SOP-QA-00142, Titled: "Management of Control Samples", Version: 14.0, Annexure No.: 0302-SOP-QA-00142-15, AQL calculation assumption example is as follows:

If (b) (4) batches of drug products were manufactured and sold for a given product, only (b) (4) batches will be selected for reserve (retain) sample examination on a (b) (4) basis.

This reduced examination based on selection of few batches would be ineffective in identifying the issues pertaining to physical defects and count variabilities until defected drug products reaches to the customers and gets reported through product quality complaints as it has been found during many product quality complaints. In the period of 01-Jan-2022 to 11-Aug-2025, your Quality Unit received about 237 complaints of which 125 complaints were related to physical defects and count variabilities. Out of 125 complaints 89 complaints were substantiated.

FACILITY AND EQUIPMENT SYSTEM

OBSERVATION 4

Equipment and utensils are not cleaned at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product.

Specifically,

According to your Quality Policy document number 0101-QP-CEQ00080, Titled: "Campaign Batch Manufacturing Study (Drug Product)", Approval date: 28-Sep-2023, and procedure number 0302-SOP-QA-00178, Titled: "Campaign Batch Manufacturing Study (Drug Product)", Approval date: 14-Feb-2025 states length of a campaign manufacturing shall be NMT (b) (4) batches or NMT (b) (4)

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(b) (4) However, your Quality Unit has not established campaign length for about (b) (4) (b) (4) different US drug products to determine the suitability of continuous manufacturing on the quality of drug products.

***DATES OF INSPECTION**

8/04/2025(Mon), 8/05/2025(Tue), 8/06/2025(Wed), 8/07/2025(Thu), 8/08/2025(Fri), 8/11/2025(Mon), 8/12/2025(Tue), 8/13/2025(Wed)

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