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	8/27/2018-8/31/2018
	FEI NUMBER 3002809586

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Pradipta Swain, Vice President Operations

FIRM NAME	STREET ADDRESS
Sun Pharmaceutical Industries Ltd.	Halol - Baroda Highway
CITY, STATE, ZIP CODE, COUNTRY Halol, Gujarat, 389350 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:
LABORATORY SYSTEM

OBSERVATION 1

Laboratory controls do not include the establishment of scientifically sound and appropriate test procedures designed to assure that drug products conform to appropriate standards of identity, strength, quality and purity.

For example, electronic data for (b) (4) mg exhibit batch (b) (4) for 0-month stability shows: dissolution at buffer stage L1 was conducted on 9/26/15 with results for the sampling time point at 5 hours, to have a minimum of (b) (4) % release, a maximum of (b) (4) % release and a mean of 47% release. The stability report STB4332 15 for the same batch and time point shows you conducted an L2 test. Based on the data contained in the report, the L2 was conducted with results to have a minimum of (b) (4) % release, maximum of (b) (4) % release and a mean of 66% release. The chromatograms are reflective of variability between the L1 and L2 stages. Similar variability was seen for (b) (4), (b) (4) and (b) (4) for L1 and L2 results for time 0-month for accelerated and intermediate stability repeat studies. You were unable to provide scientific justification for this variability.

OBSERVATION 2

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

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	Angela E Glenn, Investigator Sarah Ibrahim, FDA Center Employee or Employee of Other Federal Agencies	X Sarah Ibrahim FDA Center Employee or Employee of Other Federal Agencies Signed By 2001591303 Date Signed 08-31-2018 16:45:49	8/31/2018

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To date, no testing for burkholderia cepacia has been performed on 11 of the 12 products identified as having high (b) (4) content. On 3/14/17, you established Raw Material Specification Report WT001-BCC to test (b) (4) utilized as a raw material in the manufacture of drug products for the presence of burkholderia cepacia complex. On 5/1/18, you identified 12 finished drug products as having a high (b) (4) content. To date, you have initiated testing for burkholderia cepacia on (b) (4) utilized to produce one product - (b) (4) gel (b) (4) %.

OBSERVATION 3

The written stability program for drug products does not include sample size based on statistical criteria for each attribute examined to assure valid estimates of stability.

Specifically, on 8/28/18, we observed unused stability samples stored inside a styrofoam cooler, on top of a stool, located inside stability chamber QCC-380, 25 degrees 60% relative humidity. Your Senior General Manager, Quality Non-Sterile Manufacturing, stated these were extra samples remaining from a completed stability study for (b) (4) product coded as Protocol of (b) (4) tablets, (b) (4) mg strength and they were being held in response to a request from the research and development site under protocol number SP1550 in case additional testing is required.

PRODUCTION SYSTEM

OBSERVATION 4

There are no written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess.

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Specifically, there is no line clearance required during intervention activities performed by production operators. On 8/30/18 we observed capsule filling of batch (b) (4) of (b) (4) (b) (4) capsules USP (b) (4) mg being performed on capsule filling equipment HC-084. For no less than one hour and ten minutes, we observed the equipment to be intermittently operational. During this time, we observed production staff perform no less than three manual interventions in an attempt to clear a recurring critical alarm. In between these attempts, we observed capsules moving from the filling equipment, through the in-line check weight device and into the accepted capsule bag. We observed one operator performing interventions inside the (b) (4) access barrier (RABS) while wearing the protective goggles on top of his head rather than in an appropriate manner and observed use of a (b) (4) to remove (b) (4) and capsules from inside the filling equipment. After approximately one hour, the production staff requested assistance from the engineering department. Your Head of Operations, (b) (4) Solid Dosage, and your Senior General Manager, Quality Non-Sterile Manufacturing, stated that if the capsules pass the weight check, they are not rejected. Additionally, they stated there is no line clearance required during intervention activities performed by production operators. The same alarm occurred during production of the same lot on the (b) (4).

Filling machine HC-084 was also utilized to produce a characterization batch of (b) (4) mg (b) (4) on (b) (4) and is one of the filling machines intended to be utilized during commercial production of the (b) (4) mg products.

QUALITY SYSTEM

OBSERVATION 5

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Written procedures are not for the cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing or holding of a drug product.

Specifically,

A) You performed equipment cleaning verification activities for a specific number of batches after you identified (b) (4) as a high risk product. During the cleaning verification you did not perform analyses for the detergent residues nor did you perform bio-burden testing. Your Deputy General Manager Quality Assurance stated that you are no longer performing sampling and testing for equipment utilized in the manufacture of (b) (4) drug products and are awaiting commercialization before completing cleaning validation activities.

B)Your Vice President Operations stated that you did not conduct cleaning validation activities for the (b) (4) used inside the capsule filling equipment to remove capsules and (b) (4) and consequently ensure no risk of cross contamination between drug products.

OBSERVATION 6

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

Specifically, your Head of Operations, (b) (4) Solid Dosage and your Senior General Manager, Quality Non-Sterile Manufacturing stated that you do not have procedures in place which require across batch trending of critical alarms raised during production activities, such as those which occurred on capsule filling equipment ID HC-084 during filling of batch (b) (4) of (b) (4) (b) (4) capsules USP (b) (4) mg on (b) (4) and again while we were observing on 8/30/18.

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