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	8/3/2022-8/12/2022*
	FEI NUMBER 3002807979

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Sunil Yadav, Site Head

FIRM NAME	STREET ADDRESS
Sun Pharmaceutical Industries Limited	Unit 1 Plot A-41, Sez Industrial Area, Phase Viii A
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Mohali, Punjab, 160071 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.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

There is a failure to thoroughly review any unexplained discrepancy whether or not the batch has been already distributed.

1. Disclosure 2020-01 was received January 22, 2020, and alleged backdating was occurring by QA and QC personnel. The Investigation into disclosure 2020-01 confirmed instances of backdating, but was not thorough to evaluate the scope of backdating of records in the QA and QC departments.

    a. The investigation did not include interviews of all QA reviewers alleged to have been aware of backdating of GMP records or thoroughly evaluate allegations that QA reviewers were asked not to document observations in order to avoid Lab Events or Deviations, to ensure timely release of products.

    b. The investigation confirmed backdating by employees that had denied participating in backdating during their interviews. The investigation did not include a thorough review of other work performed by these employees.

    c. A two-day corporate quality audit to assess the backdating risk identified examples of non-contemporaneous recording in GMP documents, but did not include specific actions that would further identify whether backdating was still occurring or the extent of previous

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backdating.

d. Additional QC employees were not interviewed when evaluating the scope of the backdating in the QC laboratory.

2. Disclosure 2020-3 was received June 21, 2020, from a former employee and alleged many back dating cases in the QC laboratory. The disclosure provided documents as well as identifying a current employee that was involved in backdating. The reporter did not respond to requests for additional information and the disclosure was closed without any investigation.

   The associated disclosure report does not thoroughly justify why there was not enough information to initiate an investigation. At the time of the disclosure there were similar open investigations for disclosure 2020-1 related to backdating in QA and QC and investigation #549840 for counterfeit signatures in batch production records.

3. OOS investigation 571594 confirmed cross contamination of (b) (4) in the product (b) (4) Tablet (b) (4) mg batches (b) (4) through analytical testing. The investigation identified shared use equipment as the likely root cause, but no specific source of the contamination. The investigation led to the recall of batch (b) (4) however batches (b) (4) were released to the market because the detected cross contamination was below the specification for unknown impurities. The investigation could not determine if cross contamination was uniformly distributed throughout the batch.

OBSERVATION 2
Established sampling plans, test procedures and laboratory control mechanisms are not documented at the time of performance.

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1.Building access records showed an employee responsible for collecting (b) (4) samples did not enter the buildings where the samples were documented to have been collected or that the employee was in a different building at the time the sample was documented to have been collected. For example:

a.On June 2, 2022, (b) (4) samples were documented to have been collected in the production block building for points (b) (4) Building access records show the employee documented to have collected the samples used their badge to access the Documentation Cell at (b) (4) in the quality block, a different building. Additionally, the badge access records show no entrance or exit from the changing room or (b) (4) required for entrance and exit of the production block manufacturing area where (b) (4) are located.

The badge access records also show the employee entered the service floor of the production block building at (b) (4) and exited the service floor at (b) (4) During this time period, the sampling records document point (b) (4) was sampled at (b) (4) and point (b) (4) was sampled at (b) (4) . (b) (4) are located in the quality block, a different building.

b.On January 7, 2021, (b) (4) sample for (b) (4) was documented to have been collected at 11:03 on the service floor in the production block. Badge access records show the employee documented to have collected the sample leaving the microbiology laboratory at 11:03 in the quality block, a different building. Additionally, the badge access records show no entrance or exit from the service floor where (b) (4) is located.

The sampling records also show the employee collecting a (b) (4) sample from (b) (4)

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(12:32) and (b) (4) (12:37) inside of the production block. Badge access records show the employee leaving the microbiology laboratory at 12:34 and entering the quality dining area at 12:36, both of which are in the quality block, a different building. Additionally, the badge access records show no entrance or exit from the changing room or (b) (4) required for entrance and exit of the production block manufacturing area where (b) (4) and (b) (4) are located.

c. On January 29, 2021, (b) (4) sample for (b) (4) was documented to have been collected at 12:37 inside the manufacturing area in the production block. Badge access records show the employee documented to have collected the sample entering the quality dining room at 12:35 in the quality block, a different building.

The sampling records show the employee collecting a (b) (4) sample from (b) (4) at 13:02 on the service floor of the production block. Badge access records show the employee leaving a changing room in the quality block, a different building, at 13:03.

d. On August 9, 2021, (b) (4) sample for (b) (4) was documented to have been collected at 12:37 inside the production block. Badge access records show the employee documented to have collected the sample entering the quality dining room at 12:39 in the quality block, a different building. Additionally, the badge access records show no entrance or exit from the changing room or (b) (4) required for entrance and exit of the production block manufacturing area where the employee had collected (b) (4) samples.

e. On October 22, 2021, (b) (4) samples were collected from points (b) (4) and (b) (4) from the service floor in the production block. Badge access records show no entrance or exit from the service floor where these points are located for the employee documented to have collected the samples.

f. On November 17, 2021, (b) (4) samples were collected from points (b) (4) inside the manufacturing area in the production block. Badge access records show no entrance or exit from the changing room or (b) (4) required for entrance and exit of the production block manufacturing for the employee documented to have collected the samples.

2. Entries were not made into GMP records contemporaneously.

a. On August 3, 2022, the logbook for incubator MQAWIC06 did not have an end of incubation date, time, and signature for (b) (4) samples collected on July 27, 2022, which had been removed from the incubator and read on August 1, 2022, or (b) (4) samples collected on July 28, 2022, which had been removed from the incubator and read on August 2, 2022.

b. On August 3, 2022, the (b) (4) logbook 001 had an incomplete entry missing the source of the isolate, date, and analyst signature for the use of the instrument for isolate IHI033-22 analyzed on July 29, 2022.

OBSERVATION 3

Written procedures are not drafted, reviewed and approved by the appropriate organizational units and reviewed and approved by the quality control unit.

1. Review of APQRs of (b) (4) revealed that based on the calculated process capability (Cpk) for dissolution attributes, the manufacturing process is not capable of consistently manufacturing products that meet the dissolution specifications.

2.CAPA 1207288 proposed to address the dissolution OOS trend for (b) (4) with changes to the amount of (b) (4) utilized during the (b) (4) process and increase (b) (4) time. Review of records associated with the CAPA revealed that there is no adequate plan designed to evaluate the effectiveness of these changes. In addition, review of in-process data for (b) (4) of (b) (4) revealed that the process is skewing towards the higher (b) (4) limit, and this information was not considered during the recommendation for corrective actions.

3.Review of APQRs for the year 2020-2021 of (b) (4) as well as SOP 000807 revealed that data from in-process controls quality attributes are not evaluated during the yearly evaluation of process performance capability.

4.During compression at tablet press MPDRCM03 of (b) (4) mg tablets, batch # (b) (4) executed on August 3, 2022, we observed that the reject level for the process was set up using average compression force from 2018 instead of using the values obtained during set up for the batch currently being manufactured. The rejection limit is susceptible to change based on the compression force that is observed during equipment setup for each batch that is manufactured.

OBSERVATION 4

Laboratory records are deficient in that they do not include a complete record of all data obtained during testing.

When an analyst processing chromatography data determines the existing processing method is not appropriate or chooses to use a different processing method for samples within the same sample set during impurities analysis, the original chromatogram is not saved. The analyst can integrate the chromatogram and see the results within the software, but does not save the result. To change the processing method the analyst must document that the integration was inappropriate and get approval on

Form000505. But the original chromatogram is not saved to justify the changes to the processing method were necessary.

OBSERVATION 5

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.

1. Procedures to ensure accurate and consistent integration of chromatographic peaks have not been established. The analysts can choose the integration algorithm and manually enter timed integration events into the processing methods. Procedures have not been established to ensure the appropriate and consistent use of these timed integration events.

2. In-housed prepared (b) (4) microbiology media plates used for testing (b) (4) samples collected July 29, 2022, showed indications of desiccation on August 4, 2022, prior to the end of incubation. This included cracking of the media and media pulling away from the edges of the plate on eight of the (b) (4) plates.

3. Procedures have not been established to ensure the potential source of microorganisms identified from the environmental monitoring program are evaluated. For example, *Enterococcus faecium*, an organism that may be associated with fecal contamination, was identified in Compression Room (b) (4) in 2021 and Dispensing Room (b) (4) in 2020. It is included in the isolate library and colonies with similar morphology do not require any additional identification.

OBSERVATION 6

Written procedures are not followed for the testing of components.

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Procedure SOP000858 "Reduced Testing Procedure" requires confirmed OOS results to be considered in determining whether reduced testing should be approved. Report MP-R/AS/1008 was used to justify reduced testing for the API (b) (4) The report stated it would not consider a previous batch that was rejected for a particle size distribution OOS.

After approval of reduced testing, subsequent investigations, including 911981, 1004103, 1008080, and 1026612 into dissolution failures that resulted in rejected batches of finished (b) (4) Tablets identified the particle size of the API was critical and attributed more fines in API lots as a root cause. The approved reduced testing for particle size distribution in (b) (4) API was not reevaluated as described in procedure SOP000858.

***DATES OF INSPECTION**

8/03/2022(Wed), 8/04/2022(Thu), 8/05/2022(Fri), 8/08/2022(Mon), 8/09/2022(Tue), 8/10/2022(Wed), 8/12/2022(Fri)

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