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	12/4/2023-12/15/2023* FEI NUMBER 3004561553

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Reem Malki, Chief Quality Officer

FIRM NAME	STREET ADDRESS
Sun Pharmaceutical Industries Limited	Survey No. 1012
CITY, STATE, ZIP CODE, COUNTRY Dadra, Dadra & Nagar Haveli and Daman, 396191 India	TYPE ESTABLISHMENT INSPECTED Finished Drug Products Manufacturer - OSD

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

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, your laboratory investigations pertaining to Out of Specification (OOS) investigations are not thoroughly investigated to determine the root cause(s) for long-term (25°C/60%RH) stability samples failures for the drug products sold into the US market. For example,

A) Your OOS Investigation PR ID #724426 was not thoroughly investigated for Product: (b) (4) (b) (4) and (b) (4) Tablets (b) mg/(b) mg, Batch Number: (b) (4), date of initiation: 26-Oct-2020, Issue: *"Dissolution by HPLC test results was found not meeting S1 stage criteria due to a significantly lower result in vessel 1 of dissolution apparatus (ID: GQC/IN.307) the dissolution test will not comply in S2 and S3 stage criteria"*. Your firm filed an initial Field Alert on 28-Oct-2023 to the FDA for obtaining OOS test result at 18-month stability stage and based on your preliminary investigation. The dissolution test result at S1 stage are as follows:

Dissolution Vessel	1	2	3	4	5	6
(b) (4)	**30%**	(b) (4) %	(b) (4) %	(b) (4) %	(b) (4) %	(b) (4) %
(b) (4)	**18%**	(b) (4) %	(b) (4) %	(b) (4) %	(b) (4) %	(b) (4) %

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE
Pratik S Upadhyay, Investigator

X Pratik S Upadhyay Investigator Signed By: Pratik S. Upadhyay -S Date Signed: 12-15-2023 08:20:09

DATE ISSUED
12/15/2023

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	12/4/2023-12/15/2023*
	FEI NUMBER 3004561553

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Reem Malki, Chief Quality Officer	
FIRM NAME Sun Pharmaceutical Industries Limited	STREET ADDRESS Survey No. 1012
CITY, STATE, ZIP CODE, COUNTRY Dadra, Dadra & Nagar Haveli and Daman, 396191 India	TYPE ESTABLISHMENT INSPECTED Finished Drug Products Manufacturer - OSD

Given the value obtained in vessel 1, dissolution will also automatically fail in S2 and S3 stage. The preliminary investigation conducted by your Quality Unit ruled-out the possibilities of analyst error, solution preparation error, dissolution parameter error. The result of reanalysis from the same solution and refilled solution was found comparable to the initial test result for vessel 1 of the failing batch and a marker batch (one of another batch that was analyzed in the same sample set sequence) which confirmed that there was no solution preparation, vial filling and instrument error. Your firm concluded the root cause (detached dissolution basket in vessel 1) based on the two (2) QC Analysts interviews of the events, but these same employees also admitted in the interview that the Dissolution Parameter Checklist (4 pages document) was simply filled-out without verifying the actual dissolution parameters while the testing was conducted and the document was signed and dated under Performed by (by QC Analyst - (b) (6)) and Reviewed by (QC Senior Analyst - (b) (6)) sections. I observed the following issues:

1. Your Quality Unit restricted the evaluation of two (2) QC Analyst's (initialed (b) (6) and (b) (6)) practices of falsifying the Dissolution Parameter Checklist to the failing Batch Number: (b) (4) only and did not extend the investigation to the other three (3) stability batches (IDs: (b) (6) (AR Number: STB/C/20/1570), and (b) (4) (AR Numbers: STB/C/20/1556 and STB/C/20/1555)) at 9-month long term and intermediate conditions) that were also analyzed by these two (2) QC Analysts on the same day (24-Oct-2020) in the (b) (4) since the results of the three (3) batches met the specification limit. Further, your Quality Unit failed to investigate the impact of these two (2) QC Analyst's practices on the integrity of data of previously analyzed materials and drug products.
2. Your Quality Unit provided no scientific justification supported with documented evidence for the QC Analyst's failure to report a missing basket on the shaft of vessel 1 upon completion of dissolution and when the basket shafts were lifted upward for cleaning purposes.
3. According to your QC Head, a QC Junior Technician conducts equipment cleaning, however no training was provided to these Technicians to report unusual observation while taking the

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Pratik S Upadhyay, Investigator	X Pratik S Upadhyay Investigator Signed By: Pratik S. Upadhyay -S Date Signed: 12-15-2023 08:20:09	12/15/2023

equipment for cleaning.

4. The hypothesis study conducted by your firm to rule-out the possibility of dissolution basket dropping from the shaft in vessel 1 (resulting in 30% for (b) (4) and 18% for (b) (4)) remained inconclusive considering the result obtained for this activity was less than (b) (4) % for both the actives. Your firm closed the OOS investigation and FAR based on the likelihood that the basket fell off from the shaft without scientifically demonstrating it through hypothesis studies. The repeat analysis conducted by the second analyst gave a passing dissolution result at S1 stage based on which the investigation was closed.

(b) (4) and (b) (4) Tablets (b) mg/(b) mg, Batch Number: (b) (4) was manufactured on Mar-2019, released to the US on 20-May-2019 and as a stability batch represented total (b) (4) (excluding (b) (4) stability batch (b) (4)) batches made during year 2019.

B) Your OOS investigations pertaining to Related Substance by HPLC test method were not thoroughly investigated. For example,

OOS Investigation PR ID: 1502090, Date of initiation: 09-Jun-2023, Product: (b) (4) and (b) (4) Tablets (b) mg/(b) (4) mg, Batch No.: (b) (4), Stability Period: 12 month (Long Term stability), Issue: Any unknown impurity at RRT about (b) (4) (RT (b) (4)) (w.r.t (b) (4)) was (b) (4) %. Limit: (b) (4) % for Relates substance by HPLC test of (b) (4) (Method-II). This OOS investigation was categorized as Not-confirmed.

Your Quality Unit did not find any obvious error during the preliminary investigation and no assignable root cause was identified at Phase 1a and 1b investigations along with the Phase 2 investigations. Your firm concluded the investigation based on probable root cause of sample solution preparation error with respect to improper rinsing of volumetric flask or sample handling. Your firm did not rule-out the

possibilities of an unknown peak at RRT about (b) (4) (RT (b) (4)) (w.r.t (b) (4)) potentially coming from improper rinsing of glassware by looking into the products tested around the same time period in the areas of QC laboratory where the OOS batch test sample solution was prepared by conducting a simulation study to identify the source of unknown peak.

As such the unknown impurity at RRT about (b) (4) was present at BLQ level at the 9-month long term stability timepoint (13-Jan-2023) in the subject batch ((b) (4)), which suggests the impurity at the 12-month time point was not from dirty glassware and instead related to product degradation. This unknown peak was also present in the other two (2) batches (9-month long term stability) at BLQ level that were analyzed in the same sample set sequence along with the subject OOS batch number (b) (4) (12-month long term stability), further suggesting that this peak is related to the product and not an outside contamination source such as dirty glassware.

FACILITY AND EQUIPMENT SYSTEM

OBSERVATION 2

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

Specifically,

A. On 04-Dec-2023, I observed about 450 mL of (b) (4) "stagnant liquid" partially covered in sections with (b) (4) layers inside the Air Purification Unit (APU) in between the (b) (4) µ filter and the (b) (4) of Processing Area (b) (4) ID: GPN/EQ/285. Your firm stated the accumulation of stagnant liquid may have occurred after the last preventative maintenance of 13-Oct-2023 due to leakage of water from the (b) (4) located inside (b) (4) close to the APU. This area gets verified for cleanliness during the (b) (4) preventative maintenance. There is a potential for the growth of microorganism in the stagnant liquid in the area where the temperature is (b) (4) °C to (b) (4) °C while

is use for (b) (4) and at around (b) (4) °C while not in use.

The filtered air from the (b) (4) µ filter flows through the section containing stagnant water at a high velocity ((b) (4) m/sec ((b) (4))) into the (b) (4) Unit and the (b) (4). There is a potential for microorganisms, yeast and mold growth in this stagnant liquid that could potentially contaminate via the high velocity air the material under (b) (4) in (b) (4) ID: GPN/EQ/285.

Per my request on 04-Dec-2023, your firm collected a sample of this stagnant liquid for microbial and chemical analyses. The microbial analyses revealed TNTC (Too Numerous To Count) microbial, yeast and mold colonies. There is a potential for microorganisms, yeast and mold grown in this stagnant liquid to get carried with the high velocity air through the (b) (4) in to the (b) (4) ID: GPN/EQ/285 and potentially contaminate the product while it is used for manufacturing drug products.

The chemical analyses by LC-MS showed the presence of (b) (4) API along with numerous large areas of peaks pertaining to (b) (4) and (b) (4) impurities. There have been about (b) (4) different drug products manufactured since the manufacturing of product containing (b) (4) API (last manufactured on 16-Sep-2023) using (b) (4) ID: GPN/EQ/285.

Based on these observed chemical and microbial test results, there is a potential for contamination of (b) (4) drug products that are manufactured using this non-dedicated (b) (4) ID: GPN/EQ/285 for the US market.

B. On 04-Dec-2023, I observed a hole and rough around the (b) (4) located inside the body of (b) (4) ID: GPN/EQ/285. I also observed light yellowish color sealant that was used to cover gaps surrounding the (b) (4) was missing sealant and small pieces of (b) (4) on the hole. There is a potential for these missing pieces may have mixed into the products manufactured using this non-dedicated (b) (4). Further, there is a potential for the deposition of powdery materials to get accumulated

inside the holes and rough surfaces which may not get removed during the manual Type B (product changeover) cleaning of this equipment. According to your procedure (SOP No.: SOP009109, Version No.: 10.0), there is no swab sample collected and tested for chemical and microbial testing from these areas of (b) (4) ID: GPN/EQ/285.

QUALITY UNIT

OBSERVATION 3

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

Specifically,

A) There is a lack of Quality Unit oversight on the issuance, handling, retrieval and reconciliation of GMP documents that are used in the manufacturing of drug products at your site. This lack of oversight violates the firm's QA SOP 018075 for GMP form issuance. For example,

1) Controlled documents related to the following departments can be printed from the Electronic Document Management System (EDMS) without any oversight of the Quality Unit. These documents are used to record original GMP information. For example, but not limited to:

QC forms such as Form 060789: Request Form for Re-processing, Form: 039593: Dissolution analysis checklist, Form: 011918: Auto sampler validation record for model EDT-08LX, Form: 034262: HPLC Chromatogram Checklist, Form 011907: U.V. Vis Spectrophotometer graph checklist

Production forms such as Form 011406: Equipment Cleaning Record of (b) (4) Compression Machine, Form 040690: Equipment Cleaning Record of (b) (4),

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	12/4/2023-12/15/2023*
	FEI NUMBER 3004561553

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Reem Malki, Chief Quality Officer

FIRM NAME	STREET ADDRESS
Sun Pharmaceutical Industries Limited	Survey No. 1012
CITY, STATE, ZIP CODE, COUNTRY Dadra, Dadra & Nagar Haveli and Daman, 396191 India	TYPE ESTABLISHMENT INSPECTED Finished Drug Products Manufacturer - OSD

Form 011459: Cleaning and Operation of (b) (4) and (b) (4) compression machine, Form 042113: Line Clearance checklist for Product to Product Changeover

RM warehouse forms such as Form 012373: Performance check of Barcode scanner/RF Gun, Form 012468: Cleaning Record of Cold Storage Cabinet, Form 012472: Cleaning Record of (b) (4) booth

Packaging forms such as Form 011450: Challenge Test for Tablets Inspection machine, Form 041188: Equipment Cleaning Record Tablet Inspection Machine (Product to Product)

The Head of Quality Unit of your firm stated that there is no controlled copy issuance log maintained by the firm for the issuance and retrieval of GMP documents. In addition, the Quality Unit has given an access to employees across the site to all documents on EDMS, which allows employees of other departments to print controlled documents unrelated to their respective department.

2) During the inspection, I observed the Quality Unit of your firm allowed destruction of original GMP documents such as balance weight printouts, controlled forms/formats. For example,

On 04-Dec-2023, I observed a balance printout pertaining to Balance ID: GPN/IN/545, Dated/Timed: 01-Dec-2023 (b) (4), Weight: 8.007 g that was disposed inside your firm's main scrapyard. The Production Technician that disposed this printout stated the practice of disposing the balance printout is normal by all employees in his department in the event of printing and weighing errors.

The firm only began recording the justification and type of document that was placed into the disposal bins less than one month ago on 06-Nov-2023. However, reconciliation of the documents disposed of on 11-Nov-2023 as noted in the logbook revealed the number of pages disposed inside the bin were less than the total number of pages of the controlled forms. For example, the entry made in the logbook dated 11-Nov-2023 for the disposal of Cleaning Checklist - Form 037989TP-59 and Form 037989TP-60 were

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Pratik S Upadhyay, Investigator	X Pratik S Upadhyay Investigator Signed By: Pratik S. Upadhyay -S Date Signed: 12-15-2023 08:20:09	12/15/2023

two separate entries pertaining to nine (9) pages forms. However, the number of pages received for disposal were eight (8) for Form 037989TP-59 and two (2) for Form 037989TP-60. Your Quality Unit provided no justification for the missing one (1) page for Form 037989TP-59 and six (6) pages for Form 037989TP-60. The total of eight (8) pages remained missing for which your firm conducted no investigation to ensure the missing pages does not get misused in the lack of Quality Unit's oversight on the issuance, retrieval, and reconciliation of GMP documents.

B) Your QC Microbiology laboratory has no equipment usage logbook or any other document that records incubator usage details for a total (b) (4) incubators across various temperature ranges that are used to incubate microbial and environment monitoring plates. The lack of an issued logbook violates your SOP No.: SOP008866, Titled: "Issuance, Handling and Retrieval of Logbook/Bounded Book", Version No.: 8.0, Section: 5.0 and SOP No.: SOP009405, Titled: "Instrument usage log", Version No.: 3.0, Section: 5.0.

As a result of no equipment usage logbook or documentation for the incubators, there is no assurance over its usage, breakdown (if any) and whether calibrations were performed on time. Per the above referenced procedures, the Quality Unit of the firm is required to verify logbook entries (b) (4) for usage and accuracy of data entered. However, given the lack of logbooks this verification is not happening and there was no justification provided by your Microbiology management about not conducting these activities.

OBSERVATION 4

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

Specifically, your Quality Unit has failed to investigate Product Quality Complaints (PQCs) thoroughly. For example,

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	12/4/2023-12/15/2023*
	FEI NUMBER 3004561553

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Reem Malki, Chief Quality Officer

FIRM NAME	STREET ADDRESS
Sun Pharmaceutical Industries Limited	Survey No. 1012
CITY, STATE, ZIP CODE, COUNTRY Dadra, Dadra & Nagar Haveli and Daman, 396191 India	TYPE ESTABLISHMENT INSPECTED Finished Drug Products Manufacturer - OSD

A. Your firm restricted PQC's trend evaluation for a period of (b) (4) only while you marketed drug products into the US with a shelf life of over (b) (4) for which you received many market complaints post (b) (4) period. For example,

Count variability market complaints:

Product Name	Batch No.	Date PQC received	PQCs in (b) (4)	PQCs in (b) (4)
(b) (4) Tablets, (b) mg	(b) (4)	01/02/2023	(b	(b
(b) (4) Tablets, (b) mg	(b) (4)	14/12/2022	(b) (4)	(b) (4)
(b) (4) Tablets, (b) (4) mg	(b) (4)	21/07/2022	(b) (4)	(b) (4)

According to your procedure SOP008928, Titled: "Product Quality Complaint handling process", Version: 7.0, Section 5.12.10 your firm restricted evaluation of the historical trend of Product Quality Complaints (PQCs) only for a period of (b) (4) to identify the repetitive trend of complaint while the drug products are marketed in the US with the expiry date of over (b) (4) i.e. (b) (4) (b) (4). As a result of limited historical trend evaluation of PQCs, your firm's complaint investigations are incomplete and not thoroughly investigated to determine the root cause and to take appropriate market actions such as filing a Field Alert and potentially recalling batch(es).

B. Your firm has not thoroughly investigated count variability market complaints for (b) (4) (b) (4) Tablets (b) (4) mg, and (b) (4) drug products. On 11-Dec-2023, I observed your firm received mainly between 7 to 22 complaints each month since year 2019 to 01-Dec-2023 for count variability complaints. The evaluation of randomly selected twelve (12) PQCs for the period of year 2021 to 01-Dec-2023revealed that the complaints were closed based on the similar investigation

summary, root cause and CAPAs repetitively simply by rewriting these sections or copy and pasting upon changing the batch information. Your firm took no meaningful efforts to determine the root cause and establish CAPAs to overcome the count variability PQCs.

C. The firm does not provide procedures or guidance to the contracted third-party PQC call center that receives incoming product quality complaints so product specific questions can be asked to the complainants during follow-up attempts to get a meaningful information that would be significant to determine the root cause.

OBSERVATION 5

An (b) (4) -Field Alert Report was not submitted within three working days of receipt of information concerning significant chemical, physical, or other change or deterioration in a distributed drug product.

Specifically,

Your firm failed to submit a Field Alert for Product Quality Complaints (PQCs). For example,

A. In the period of January 2019 to 01-Dec-2023, your firm received 468 complaints out of 1355 complaints relating to count variability (short and excess count) issues globally of which around 457 complaints out of 1209 complaints were reported from the US market. The details are as follows:

Year	Total Complaint Received	No. of Short/Excess count Complaint Received	% of Complaint received (Short/Excess)
2019	269	42	15.61
2020	282	119	42.20
2021	230	77	33.48
2022	225	106	47.11
Till 01st Dec 2023	203	113	55.67

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	12/4/2023-12/15/2023* FEI NUMBER 3004561553

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Reem Malki, Chief Quality Officer

FIRM NAME	STREET ADDRESS
Sun Pharmaceutical Industries Limited	Survey No. 1012
CITY, STATE, ZIP CODE, COUNTRY Dadra, Dadra & Nagar Haveli and Daman, 396191 India	TYPE ESTABLISHMENT INSPECTED Finished Drug Products Manufacturer - OSD

Total	1209	457	37.80

Total 407 complaints out of 457 complaints i.e. about 89% complaints were received for (b) (4) (b) (4) Tablets (b) (4) mg, and (b) (4) drug products as follows:

S.no.	Product	2019	2020	2021	2022	Dec-23	Total	% Complaint in 05 years
1	(b) (4) Tablets, (b) (4) Mg	33	79	53	67	33	265	57.99
2	(b) (4) mg (b) (4) Tablets	1	11	4	15	15	46	10.07
3	(b) (4) and (b) (4) Tablets (b) (4) mg	4	4	11	8	18	43	9.41
4	(b) (4) and (b) (4) Tablets (b) (4) mg"	0	11	2	4	11	28	6.13
5	(b) (4) Mg (b) (4) Tablets	1	4	2	2	16	25	5.47

Out of 407 complaints about 219 complaints are repeated count variability complaints that were reported for about 73 batches. Your firm categorized these complaints as "Minor" without conducting any Health Hazard Evaluation (HHE). About 95% of these complaints were substantiated (confirmed/valid) upon investigation and some through verification of controlled samples by your Quality Unit. However, there was no Field Alert filed by your firm to the agency. This is in deviation of your SOP No.: SOP008879, Titled: "Field Alert Report (FAR) Management and Process", Version: 3.0, Effective date: 29-Dec-2020. Per Sections 5.1.7 of this procedure "Any failure of (b) (4) or more distributed batches of the drug

product to meet the specification established in the application. Examples, include but are not limited to" 5.1.7.5 "Investigation of a product quality complaint indicates that the defect is substantiated in the retention sample" requires filing a Field Alert.

Further, your firm received several complaints related to short count of tablets of which as many as 22 complaints are for 2 tablets short, 5 complaints for 3 tablets short, 3 complaints for 4 tablets short, 4 complaints for 6 tablets short, 2 complaints for 7 tablets short, 2 complaints for 10 tablets short, 2 complaints for 13 tablets short and 1 complaints each for 27, 35, 42, 46, 49, 53, 56, 66, 69, tablets short along with 3 complaints for <100 and 2 complaints for >100 tablets for (b) (4) Tablets (b) (4) mg. Your firm substantiated one (1) and two (2) count variability (short and high count) complaints only.

Based on the observation of repeated substantiated count variability complaints and your Quality Unit's deviation from SOP No.: SOP008879, on 11-Dec-2023 your firm filed six (6) individual Field Alerts to the agency pertaining to (b) (4) Tablets (b) (4) mg, and (b) (4) drug products for (b) (4) # (b) (4), and (b) (4)

B. As a result of receiving repeated count variability Product Quality Complaints (PQCs) for (b) (4) (b) (4) Tablets (b) (4) mg, and (b) (4) drug products, your firm initiated five (5) Corrective Action and Preventative Actions (CAPAs) and two (2) Change Controls (CCs) since July 2018. In the three (3) out of five (5) CAPAs, the objective was related to powder/dust generation followed by broken tablets, half tablets and crumpled tablets related issues. There was not mention of CAPAs being taken for count variability issues. However, your firm kept on referring to these three (3) CAPAs being taken to resolve the count variability issues.

CAPA PR ID: 89147, CAPA initiation date: 25-Jul-2018, CAPA closure date: 18-May-2019
CAPA PR ID: 723955, CAPA initiation date: 24-Oct-2020, CAPA closure date: 29-Dec-2020

CAPA PR ID: 513656, CAPA initiation date: 08-Feb-2020, CAPA closure date: 27-Aug-2021

Moreover, the CAPA effectiveness check was pertaining to the issues of broken tablets, half tablets and crumpled tablets issues and there was no reference of these CAPA's applicability to count variability (short/high tablets) complaints. Further, the CAPAs effectiveness check was limited to very few batches of the drug products for which there was not even a meaningful historical trend of count variability complaints. Your firm provided no justification for restricting these complaints to a limited number of batches and conducting the CAPA effectiveness check on irrelevant drug products.

C. Your firm Product Quality Complaints (PQCs) pertaining to lack of efficacy and ADE are not thoroughly investigated to determine the root cause and no adequate CAPA was taken. For example,

1. Your firm received 166 complaints pertaining to lack of efficacy in the period of January 2019 to 01-Dec-2023 for the US market. Your Quality Unit did not have an adequate oversight on the functioning of your third-party service group that received complaints to determine if the adequate number of attempts were made to complainant requesting a batch information, physical sample of complaint product and pictures. As a result of this for about 111 (67%) out of 166 lack of efficacy complaints, the batch number remained unknown. Your firm non-substantiated all 111 (67%) of complaints based on the sole justification of unknown batch number. Your PQC investigation was not thorough to include the following, but not limited to:

- **a.** Controlled samples evaluation
- **b.** Impact on the quality of product due to subsequent process validations
- **c.** Historical trend of the product behavior over the period of shelf life from the date of receiving the market complaint considering the unknown batch number
- **d.** Historical trend of similar nature of complaints
- **e.** Evaluation of quality events in the laboratory and in product both substantiated and non-

substantiated

Your firm restricted complaint investigation to a period of (b) (4) only from the date of receiving complaint and not the entire shelf life a product.

2. Your firm did not thoroughly investigate the PQCs related to lack of efficacy complaint when the product details including batch number was provided by the complainant. For example,
Your firm received multiple PQC related to lack of efficacy for (b) (4) Tablets USA ((b) (4) # (b) (4)) process validation batches from the US market:

(b) (4) Tablets (b) (4) mg USA, Batch Number: (b) (4) Total complaints: 10
Tablets (b) (4) mg USA, Batch Number: (b) (4) Total complaints: 12
Tablets (b) (4) mg USA, Batch Number: (b) (4) Total complaints: 11
Tablets (b) (4) mg USA, Batch Number: (b) (4) Total complaints: 5

In each of these PQCs, your firm simply relied upon stability study timepoint data while the repetitive complaints were being filed and conducted no controlled samples physical evaluation and testing for any of the above stated batches. Your firm did not conduct Health Hazard Evaluation (HHE) and there were no Field Alerts filed to the agency.

Your firm concluded the above PQCs pertaining to four (4) different batches of (b) (4) Tablets simply by rewriting the similar information in the sections of investigation summary, root cause, CAPA, etc. These practices of simply rewriting the investigation has resulted in no meaningful investigation as the repetitive PQCs were being reported to the firm for the lack of efficacy.

3. PQC PR ID: 1533634, Product: (b) (4) and (b) (4) (b) (4) Tablets (b) mg/(b) mg, Date of initiation: 12-Jul-2023, Date closed: (b) (4),

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	12/4/2023-12/15/2023* FEI NUMBER 3004561553

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Reem Malki, Chief Quality Officer	
FIRM NAME Sun Pharmaceutical Industries Limited	STREET ADDRESS Survey No. 1012
CITY, STATE, ZIP CODE, COUNTRY Dadra, Dadra & Nagar Haveli and Daman, 396191 India	TYPE ESTABLISHMENT INSPECTED Finished Drug Products Manufacturer - OSD

Nature of complaint: Lack of efficacy, Batch Number: Unknown, Description of complaint: "These tablets do NOT contain even a fraction of the (b) mg stated!", Complaint classification: Non-substantiated.

The investigation simply referred to the evaluation of finished product analytical trend, stability trend and Annual Product Review (APR) (Period: 05th Aug 2020 to 04th Aug 2021 and 05th Aug 2021 to 04th Aug 2022). However, there was no mention of the total number of batches manufactured verses quality events for both valid and invalid trend. Your firm restricted evaluation of historical trend of PQC to (b) (4) only while this product is marketed in the US with (b) (4) shelf life.

During the inspection, I observed your firm did not evaluate (b) (4) complaint log between July 2022 to (b) (4). During this period, your firm received three (3) complaints PR#1260415, PR# 1435243 & PR# 1441694 relating to lack of efficacy. However, there was no mention of these complaint logs and its correlation to the repetitive lack of efficacy complaints received by your firm.

Your firm has limited the control samples evaluation to a limited number of batches on an (b) (4) basis for all drug products manufactured by your site. There was no evaluation of controlled samples data performed by your firm in the event of complaint investigations.

4. PQC PR ID: 1519034, Product: (b) (4) and (b) (4) (b) (4) Tablets (b) mg/(b) mg, Date of initiation: 27-Jun-2023, Date closed: (b) (4), Nature of complaint: Lack of efficacy, Batch Number: Unknown, Description of complaint: The complainant has to take 2 pills of the Sun brand and only one of the other manufacturer, Complaint classification: Non-substantiated.

Additionally, the investigation simply referred to the evaluation of finished product analytical trend, stability trend and Annual Product Review (APR) (Period: 05th Aug 2020 to 04th Aug 2021 and 05th Aug 2021 to 04th Aug 2022). However, there was no mention of the total number of batches

manufactured verses quality events for both valid and invalid trend. Your firm restricted evaluation of historical trend of PQC to (b) (4) only while this product is marketed in the US with a (b) (4) shelf life.

Your firm has limited the control samples evaluation to a limited number of batches on an (b) (4) basis for all drug products manufactured by your site. There was no evaluation of controlled samples data performed by your firm in the event of lack of efficacy related PQC investigations.

OBSERVATION 6

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,

A) Each lot of Controlled/Reserve (Retain) samples of drug products is not examined at least once a year for the evidence of deterioration and physical defects. Your firm's rationale based on (b) (4) for the selection of limited number of batches is not justifiable while there are significant gaps identified in your firm's Quality and Production Systems along with several repeated product quality complaints pertaining to count variability, broken, half tablets, and lack of efficacy.

As per your procedure SOP018076, Titled: "Sampling, Storage, Observation and Destruction of Finished Products Control Samples", Version: 13.0, Section: 5.4.1 "For each product, (b) (4) batch out of total commercial batches packed during calendar year shall be selected for visual inspection (All pack style & counts)". (b) (4) batches selection per section 5.4.4 for visual inspection is defined in table-1. For example, but not limited to:

No. of batches of a product packed	No. of batches of a product

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	12/4/2023-12/15/2023* FEI NUMBER 3004561553

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Reem Malki, Chief Quality Officer

FIRM NAME	STREET ADDRESS
Sun Pharmaceutical Industries Limited	Survey No. 1012
CITY, STATE, ZIP CODE, COUNTRY Dadra, Dadra & Nagar Haveli and Daman, 396191 India	TYPE ESTABLISHMENT INSPECTED Finished Drug Products Manufacturer - OSD

during a calendar year	to be inspected
Up to (b)(4) Batches	(b)(4)
(b)(4) to (b)(4)	(b)(4)
(b)(4) to (b)(4)	(b)(4)
(b)(4) to (b)(4)	(b)(4)
(b)(4) to (b)(4)	(b)(4)
(b)(4) to (b)(4)	(b)(4)

In the firm's current practices, the limited number of batches selected for the annual verification are the only ones that are verified throughout the products shelf life.

This reduced examination based on selection of few batches would be ineffective in identifying the issues pertaining to physical defects along with empty bottles and count variabilities until defected drug products reach to the customers and gets reported through product quality complaints as it has been observed during many product quality complaints.

B) Your firm's Controlled/Reserve (Retain) samples examination is deficient.

Specifically, there is no provision provided in your Controlled samples logbook to record discrepancy or observations pertaining to physical and count variability issues during annual verification. Your QA Officer (3 years in the current position) and QA Manager (10 years in current position) reported annual verification as "Ok" during each of the annual verification of controlled samples since their joining. These employees stated that they have not observed any discrepancy for any of the product's description and count (short/high) in their entire employment with the firm. Whereas your PQC Investigation Manager has observed count variabilities in controlled samples while investigating complaint investigations.

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	12/4/2023-12/15/2023*
	FEI NUMBER 3004561553

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Reem Malki, Chief Quality Officer

FIRM NAME	STREET ADDRESS
Sun Pharmaceutical Industries Limited	Survey No. 1012
CITY, STATE, ZIP CODE, COUNTRY Dadra, Dadra & Nagar Haveli and Daman, 396191 India	TYPE ESTABLISHMENT INSPECTED Finished Drug Products Manufacturer - OSD

***DATES OF INSPECTION**

12/04/2023(Mon), 12/05/2023(Tue), 12/06/2023(Wed), 12/07/2023(Thu), 12/08/2023(Fri), 12/11/2023(Mon), 12/12/2023(Tue), 12/13/2023(Wed), 12/14/2023(Thu), 12/15/2023(Fri)

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE

Pratik S Upadhyay, Investigator

X Pratik S Upadhyay
Investigator
Signed By: Pratik S. Upadhyay -S
Date Signed: 12-15-2023
08:20:09

DATE ISSUED
12/15/2023