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	1/28/2019-2/5/2019*
	FEI NUMBER 3012448465

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Umesh Kale, President & Chief Quality Officer

FIRM NAME	STREET ADDRESS
Strides Pharma Science Limited	Formulation Unit, Pims Road; 33 & 34 R S No 32
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Puducherry, Puducherry, 605014 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:

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,

(A) Your Out of Specification Investigation (OOS) PYF/OOS/2018/0074 (initiated on July 5, 2018) for (b) (4) USP API batch number (b) (4) is deficient. This investigation was initiated when OOS results were obtained for an individual unknown impurity value of (b) (4) % and total impurity value of (b) (4) % generated against a specification limit of NMT (b) (4) % and NMT (b) (4) %, respectively. The identified root cause as due to usage of old reagents was not conclusively substantiated during the investigation. Your hypothesis testing No. 1 with (a) original aliquot sample solution, (b) (b) (4) (b) (4) did not yield any OOS values for the individual unknown impurity and all results were within the specification limits of NLT (b) (4) %. Additionally, your hypothesis No. 2 yielded failing results ((b) (4) %) with a different individual unknown impurity peak at an RRT of (b) (4) (vs. the original analysis where the RRT was (b) (4) . From the 2nd hypothesis testing, your investigation concluded that "…the RRT of the unknown impurity which is falling out of specification was not same in the initial and hypothesis analysis, this may be due to usage of new bottle of (b) (4) '. The next statement in the investigation reports reads that "…it is confirmed that the usage of old reagents during initial analysis is the most

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Yvins Dezan, Investigator Jogy George, Generic Drug User Fee Amendments (GDUFA) X Yvins Dezan Investigator Signed By: 2001697410 Date Signed: 02-06-2019 13:06:42	2/5/2019

probable cause of the elution of unknown peak". The investigation fails to acknowledge that hypothesis no. 1 using the same reagents produced results within specification (i.e. results ranged from (b) (4) to (b) (4) % for individual unknown impurity against a specification limit of NMT (b) (4) %). Additionally, the investigation fails to probe why there was a difference in RRTs noted during initial analysis (RRT = (b) (4) and during hypothesis testing No. 2 (RRT = (b) (4) for the individual unknown impurity. The initial failing results were subsequently invalidated through reanalysis by analyst 1 and analyst 2.

(b) (4) USP API batch number (b) (4) was used in finished product batches released to the U.S. market as follows:

- (b) (4) Tablets USP (b) (4) mg, batch # (b) (4) Expiry date: July 2020
- Tablets USP mg, batch # Expiry date: July 2020
- Tablets USP mg, batch # Expiry date: July 2020

In addition, OOS No. PFY/OOS/2017/0090 is a similar investigation (initiated on October 23, 2017) for (b) (4) USP API batch number (b) (4) where the root cause for individual unknown impurity OOS value of (b) (4) % (RRT (b) (4) against a specification limit of NMT (b) (4) % was attributed to HPLC column aging.

(B) Written records are not always made of investigations into unexplained discrepancies and the failure of a batch or any of its components to meet specifications. For example, your record of the analyst interview process during Out-of-Specification (OOS) investigations is deficient. The current inspection discovered a pattern of template-based question and answers being recorded as analyst-provided information during the investigation process. Examples included, but are not limited to, the question and answer sessions recorded in the following OOS investigations in 2017 and 2018:

OOS Number	Batch Number	Product Name / Material Name	OOS Type	Product Type

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PYF/OOS/2018/0060	(b) (4)	(b) (4) (b) (4) Tabs USP (b) (4) mg (b) (4)	In process	Commercial
PYF/OOS/2018/0067		(b) (4) (b) (4) Tablets USP (b) (4) mg	Stability	Commercial
PYF/OOS/2018/0068		(b) (4) (b) (4) Tablets USP (b) (4) mg	Stability	Commercial
PYF/OOS/2018/0082		(b) (4) Capsules USP (b) (4) mg	In process	Commercial
PYF/OOS/2018/0074		(b) (4) USP	Raw Material	Commercial
PFY/OOS/2017/0090		(b) (4) USP	Raw Material	Commercial

Approximately 33 out of 121 OOS investigations since Jan 2017 to Jan 2019 have been recorded as due to Analyst error (for U.S. marketed products). Your Sr. Team Leader for QC (b) (6) acknowledged during the inspection on February 2, 2019 that answers provided by the analysts are "paraphrased" for recording on the investigation documents. Due to the template-based question and answers included in the investigation reports, there is no assurance that the information depicted in the OOS investigation accurately represents the circumstances and conditions that may have contributed to (or caused) the generation of OOS results.

OBSERVATION 2

Employees engaged in the manufacture and packing of a drug product lack the training and experience required to perform their assigned functions.

Specifically,

We reviewed all the firm's officially established SOPs, test methods, master manufacturing and packaging batch records and noted that they are written in the English language. The firm did not have translated copies of SOPs and test methods in the local languages for employees who cannot read

English.

A. During the walkthrough of the QC Laboratories (Analytical & Microbiology) on 01/29/2019, 02/01/2019, and 02/04/2019, we noticed that several QC personnel interviewed in QC Laboratories (Analytical & Microbiology) could not explain their assigned functions, testing of U.S. marketed products (b) (4) ((b) (4) Capsules, USP (b) (4) mg and (b) (4) mg), (b) (4) Capsules USP, (b) (4) Tablets USP, and processes after repeated opportunities (by us and their management). These QC employees are trained based on the review of their training records. It took approximately an hour for three QC Laboratory personnel GM QC (SMN), Team Leader Raw Material Testing ((b) (6) , Executive QC (AM) to explain the process of collecting water samples from sampling ports (b) (4) from the Mobile Phase Prep Area (b) (4)

B. On 01/29/2019, we asked the GM QC (SMN) and Team Leader Raw Material Testing ((b) (6) if he could explain the errors messages displayed on the (b) (4) (ID #SSFP-(b) (4) -0050) located in the Mobile Phase Preparation Area-(b) (4) in QC Laboratories which is used to prepare mobile phases: "Warning 20: Con Measurement out of range/ interval active" and "Warning 14: TOC above setpoint/ interval active". It took approximately 40 minutes for them to explain these error messages. The GM QC reviews and approves analytical and microbial testing results for all U.S. marketed products.

C. On that same day, a similar occurrence was observed when we inquired why the collected water samples were being stored in the Wash Area in the microbiology laboratory. We asked Group Leader Microbiology QC ((b) (6) if it is the area used for water sampling storage, he could not answer the question and called on another employee to answer the question.

D. We asked the GM QC (SMN) and Group Leader Microbiology QC ((b) (6) to call the employee who collects microbiology sampling water to demonstrate how he collects water sampling from point of use in the QC Laboratory. The employee collected samples for chemistry testing. When asked why

he collected water samples for chemical analyses, he stated this is what he was instructed by the GM QC and Group Leader Microbiology QC.

E. On 02/04/2019 we asked your Executive Production (ES) if he could explain to us why the blue binder was discarded inside the plastic drum found in the scrap yard. He could not answer in English although we repeated and rephrased the questions several times. He kept speaking in local language. When we asked him to write down the response in English for the following questions (Q2, Q5, Q1, Q6, Q7) which he purportedly completed on 02/03/2019 in English as part of the interview by your firm to probe why the blue binder was discarded. The answer provided in writing did not corroborate to the one he submitted earlier on 02/03/2019. It took him approximately 45 minutes to provide us with an explanation.

F. On 02/04/2019, we asked the Assistant Manager, HR (b) (6) if he could explain to us how he managed contract labor (Contracted personnel) training. He could not explain the training program and process for contract labor despite repeating and rephrasing the question and with management assistance. It took approximately 20 minutes (b) (4) for him to answer questions and could not fully explain the program. We asked him if there are requirements for training matrices, records, and job descriptions for the contract employees by providing him with SOP #F2/HR/018/R0 (*Management of Contract Labour*, 05/02/2017 effective date) that he brought with him into the conference room to show us how he managed training. He could not answer the questions. He provided us with a one-page document (Contract Labour Induction Form #F2/HR/018/F-01/R0) which does not cover the actual training provided to contracted employee (Initial (b) (7) with no last name on Document #004) who works in secondary packaging. The document for the contracted employee identified the person as a contract employee.

G. Your training program for permanent employees who perform GxP activities (i.e. Secondary Packaging) is different for contracted employees. For example, you have not established training matrices, job descriptions, and learning assessment for contracted employees who perform similar

activities as permanent employees. In addition, you do not provide them with training on all established SOP for packaging operations.

Facilities & Equipment System

OBSERVATION 3

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

Specifically, the following pieces of equipment used to manufacture U.S. marketed products and scale-up process validation batches to support (b) (4) (b) (4) Capsules, USP (b) (4) mg and (b) (4) mg) were observed visibly dirty, including multiple product contact surfaces, during facility walkthroughs. All equipment noted below were in a cleaned state during our visual observation.

A. (b) (4) (b) (4) equipment (b) (4) (ID #M (b) (4) C4004) in (b) (4) were found as follows on 01/28/2019:

1. We observed presence of whitish (b) (4) material inside the lower chamber and inside the wall of the (b) (4) although the equipment was issued a "Cleaned" status on 01/28/2019. The equipment was used on 01/17/2019 for (b) (4) Capsules (b) (4) MG Batch # (b) (4)

B. (b) (4) Tank (ID #M (b) (4) T4013) located in (b) (4) was found as follows on 01/28/2019:

1. Presence of white and (b) (4) product buildup in disassembled parts stored inside the tank (i.e. metal screw and other product contact surfaces) although the equipment was issued a "Cleaned"

status on 01/28/2019. The equipment was last used on 01/13/2019 for (b) (4) Batch # (b) (4)

C. (b) (4) Equipment/Tank (ID #M (b) (4) 4002) located in (b) (4) (b) (4) was found as follows on 01/28/2019 and was last used for (b) (4) Batch # (b) (4)

1. The (b) (4) tank has presence of water condensation inside the view glass.
2. The product ((b) (4) connection pipes were found disconnected and the opening exposed to the environment.

D. "Cleaned" inspection (b) (4) were observed uncovered and without cleaning status tags in the Cleaned Equipment Room.

Production System

OBSERVATION 4

The building lacks adequate space for the orderly placement of equipment and materials to prevent mix-ups between different components, drug product containers, closures, labeling, in-process materials and drug products and to prevent contamination.

Specifically,

On 01/30/2019 during the walkthrough of the raw materials warehouse, we observed Controlled Temperature Storage Area (b) (4) packaging components (containers, closures, and unprinted labels) were excessively crowded all the way to the front of the door including aisles. Per your Deputy General Manager Warehouse (b) (6), your firm is having a space issue in the warehouse. There is no assurance

that all hot spots (for temperature/humidity) identified during temperature mapping of the warehouse would continue to remain as hot spots due to the excessive raw material storage. The temperature mapping of the warehouse was not performed with any material stored in front of the racks.

OBSERVATION 5

All records of production, control, distribution, components, drug product containers, closures and labeling associated with a batch of drug product were not maintained at least one (1) year after the expiration date.

A. Specifically, a "blue binder" that contained GMP manufacturing data was observed discarded in a 50-gallon blue drum located in the scrap yard where materials are staged for destruction, shredding, and disposal. The "blue binder" contained several documents (which is not inclusive) including the following:

a) Record for Preparation of (b) (4) Agent (b) (4) % (b) (4) Solution) prepared and checked by on 01/18/2019 (Logbook #F2/PR/161/F-01/R1, Page 004).
b) Record for Preparation of (b) (4) Agent (b) (4) % (b) (4) Solution) prepared and checked by on 01/17/2019 (Logbook #F2/PR/161/F-01/R1, Page 003).
c) Record for Preparation of (b) (4) Agent (b) (4) % (b) (4) Solution) prepared and checked by on 01/14/2019 (Logbook #F2/PR/161/F-01/R1, Page 002).
d) Batch Report: (b) (4) for Product Name/Test (b) (4) Batch # (b) (4) Lot # (b) (4) and printed on 01/19/2019.
e) Batch Report: (b) (4) for Product Name/Test (b) (4), Batch # (b) (4) Lot # (b) (4) and printed on 01/12/2019.
f) (b) (4) Bag Integrity, Usage and Cleaning Logbook #F2/PR/196/F-01/R1 with the following completed pages: (b) (4) which were used for the manufacturing operation of the following U.S. marketed products:

- (b) (4) Tablets USP (b) (4) mg, Batch # (b) (4)
- (b) (4) Tablets USP (b) (4) mg, Batch # (b) (4) 7704582
- (b) (4) Tablets USP (b) (4) mg, Batch # (b) (4)
- (b) (4) Capsules USP (b) (4) g, Batch # (b) (4)

g) (b) (4) Usage Logbook #F2/PR/196/F-06/R1 with completed page 166: which was used for the manufacturing operation of the following U.S. marketed products:

- (b) (4) Tablets USP (b) (4) mg, Batch # (b) (4)
- (b) (4) Tablets USP (b) (4) mg, Batch # (b) (4)

h) (b) (4) Bags ((b) (4)) August 2018
i) (b) (4) Bags ((b) (4)) manually recorded on a loose white sheet
j) Calculation data
k) (b) (4) Stock List (May 2018) with data information.
l) Original Certificate of Conformity for (b) (4) Bag-067
m) Declaration of Conformity for the (b) (4) bag.
n) Several sheets of manual data including weighing information on loose sheet.

Management explained that their SOP allows them to discard GMP documents when discovered.

B. Specifically, multiple trash bags containing shredded documents that appear to be from QC (Yellow color), Manufacturing (White color), and packaging (Blue/Green color) that are too numerous to count such as GMP documents with QA approval (Green ink), Production Stability studies data, analytical testing sheets, analysis calculations, and release forms were found in the "Shredding Area" located in the scrap yard area during the walkthrough on 02/01/2019. No explanation was

provided for why these documents were discarded in this manner and no explanation was provided for how the contents of these documents relate to released products. For example,

a. We observed shredded document associated with the (b) (4)
b. Shredded documents with QA "Green" ink approvals.

OBSERVATION 6

The batch production and control records are deficient in that they do not include documentation of the accomplishment of each significant step in manufacturing, processing, packing and holding.

Specifically,

A. Batch records are not contemporaneously recorded at the time of the activity. We observed on 01/28/2019 the "Weighed by" and "Chd. By (b) (6)" were signed off in the Batch Manufacturing Record for (b) (4) Tablets USP (b) (4) ng Batch # (b) (4) (Page 162/236) although the "weight in Kg" section (Tare/Net/Gross) for Compressed Tablets Weighing Record were blank.

B. We observed that several manufacturing batch records were not readily available to manufacturing personnel. They are being kept in the "Men Entry" area where operators /Executive Production are to come out their process areas to record entries in the batch records. Your Executive Compression Department (b) (6) stated on 01/28/2019 that only Executive personnel in Production are allowed to record entries in the manufacturing batch records not even operators.

OBSERVATION 7

Appropriate controls are not exercised over computers or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel.

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Specifically, on 02/04/2019 during the walkthrough of the Control Room where Formulation Plant process are being monitored using Building Automation System, we observed that the system is being used. The system is being used to monitor the Formulation Process. However, the system has not been qualified and has no audit trail capabilities. In addition, when asked your Sr. Assistant Instrumentation what he does when there is an alarm in the system, he stated that he reset and clear the alarms.

Laboratory System

OBSERVATION 8

Laboratory records do not include the initials or signature of a second person showing that the original records have been reviewed for accuracy, completeness and compliance with established standards.

Specifically, we observed on 01/29/2019 during the walkthrough of the Microbiology Laboratory that your Microbiologists are recording petri dish readings for environmental monitoring in a notebook and the results for products/materials testing are recorded into the iLab software (the data acquisition used to record laboratory results and equipment calibration/verification). Once these results are recorded by your microbiologist both in the logbook and iLab, your microbiologists then remove the labels from the petri dishes, autoclave the petri dishes, and then discard them. However, the actual petri dishes are not being verified by a second person to ensure the results are accurate. Your QC personnel perform an independent review of the reported results and approved the reported results.

***DATES OF INSPECTION**

1/28/2019(Mon), 1/29/2019(Tue), 1/30/2019(Wed), 1/31/2019(Thu), 2/01/2019(Fri), 2/04/2019(Mon), 2/05/2019(Tue)

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