DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
1401 Rockville Pike, Ste 200N (HFM-650) Rockville, MD 20852-1448 (301)827-6220 Fax:(301)827-1944	1/16/2017-1/24/2017* FEI NUMBER 3004540906

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Dr. Bhimavarapu Rami (B.R.) Reddy , Director - Formulations

FIRM NAME	STREET ADDRESS
NATCO Pharma Limited	Kothur Village, Mahaboob Nagar District
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Mahaboob Nagar, Telangana, 509 228India	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

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

Specifically,

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

A. Complaint investigations are inadequate. For example,

1) Complaint N/IV/MC/15/016, received 20Jul15 due to lack of effectiveness of (b) (4) (b) (4) mg capsules, concluded the product met specifications; however, the QC laboratory failed to perform an assay on the returned sample and did not evaluate the retention sample.

2) Complaint N/IV/MC/15/009, received 09Apr15 due to lack of effectiveness of (b) (4) mg (b) (4) tablets concluded the complaint was unsubstantiated because the lot number was unavailable. SOP IVQA/001-06, "Handling of Complaints", requires at least two (2) attempts to obtain the product sample; however the investigation report does not document the dates, times, or persons contacted to request the product lot number or sample.

B. Incident investigations are not conducted in a timely manner. For example, the following incident investigations regarding stability samples not tested within their required timeframe were not closed within the (b) (4) working days required by SOP GQA/01-02, "Reporting, Investigation, and Disposition of Incidents":

Investigation #	Date Open	Date Closed	# days open

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Linda F Murphy, Consumer Safety Officer Anastasia M Shields, Generic Drug User Fee Amendments (GDUFA) 1/24/2017 X Linda F Murphy Linda F Murphy Consumer Safety Officer Signed by: Linda F. Murphy -S	1/24/2017

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IR/IV/15/079	31-Mar-15	09-Feb-16	315
IR/IV/15/086	9-Apr-15	12-Feb-16	309
IR/IV/15/137	1-Jun-15	12-Feb-16	256
IR/IV/15/164	16-Jun-15	12-Feb-16	241
IR/IV15/210	17-Jul-15	28-Dec-15	164

C. The Quality Unit did not initiate or implement CAPAs as required by SOP GQA/043-02, "Corrective and Preventive Action (CAPA). For example, CAPAs were not initiated regarding:

1) Repeated incidents regarding 227 stability samples tested outside their required timeframe.

2) Market Complaint N/IV/MC/16/027, dated 26Jul16, regarding incorrect barcode labels on shipping cartons of (b) (4) ablets USP.

3) Laboratory investigations N/V/OOS/15/006, dated 17Apr15, and N/V/OOS/15/035, dated 27Aug15, in which the assigned cause for both investigations was the use of dirty septa or vials during related substance testing of (b) (4) mg stability samples.

D. Complaint investigations are not completed within the timeframe required by SOP IVQA/001-06, "Handling of Complaints". For example, the SOP requires a final complaint investigation report to be sent to the customer within (b) (4) business days; however, complaint investigation report N/IV/MC/15/030 regarding a literature review of (b) (4) tablets (b) (4) mg was not finalized until 64 days after receipt.

LABORATORY CONTROL SYSTEM

OBSERVATION 2

The written stability testing program is not followed.

Specifically,

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A. Five (5) incident reports dated between 31Mar15 and 17Jul15 show 227 stability samples were not tested at the required time point. Furthermore, samples were removed from the stability chamber and maintained in a cabinet located within the QC laboratory prior to analysis.

The following table shows the dates samples were removed from the long term condition (25°C, 60%RH) stability chamber and the dates they were tested:

Product	Lot Number	Stability Interval (Month)	Date pulled from chamber	Date test complete	# Days past required test date
(b) (4) Tablets (b) (4) mg	(b) (4)	36 M	3-Jun-15	31-Jul-15	(b) (4)
(b) (4) Capsules (b) (4) mg		12 M	7-Feb-15	16-Mar-15	
(b) (4) tablets (b) (4) mg		12 M	7-Feb-15	18-Mar-15	
(b) (4) Capsules (b) (4) mg		6 M	13-Feb-15	28-Mar-15	
Capsules mg		6 M	13-Feb-15	19-Mar-15	

B. Records of stability sample quantities are not accurately maintained. For example, I discovered a discrepancy in the quantity of (b) (4) USP (b) (4) mg capsules remaining in the 40°C/75% RH stability sample chamber as compared with the quantity recorded on the Stability Study Samples Log. According to the log, (b) (4) blister packs of (b) (4) lot (b) (4) in the chamber; however, actual count of the samples revealed (b) (4) blister packs were present. This is a repeat observation.

OBSERVATION 3

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

Specifically,

A. Master label specifications are not maintained in the QC Laboratory for (b) (4) capsules (b) (4) mg; the approved primary labels were found in the AR&D office in a separate building. In addition, the Quality Unit

has not approved master labels for shipping cases, which include information such as product name, storage conditions, NDC number and barcoded NDC number.

B. According to SOP GQC/083-04, "Procedure for Management of Empower Chromatography Data Station in Quality Control", a single standard may be injected prior to the assessment of system suitability; however, failed "pre-system suitability injections" are not entered into the quality management system for tracking, trending, or root cause analysis.

C. Placebo powder formulations used during related substance testing of finished products have not been tested for stability; however, the formulations have assigned expiration dates based on the expiration date of excipients used in the preparation, or (b) (4) years, whichever is earlier.

D. System suitability testing of (b) (4) drug substance (DMF Grade) is insufficient in that the Related Substances test procedure, STP K/STP/RMS/594-00, does not require replicate standard injections for evaluation of HPLC system precision during system suitability testing.

PACKAGING AND LABELING SYSTEM

OBSERVATION 4

An (b) (4) Field Alert Report was not submitted within three working days of receipt of information concerning an incident that caused a drug product or its labeling to be applied to another article.

Specifically,

The Quality Unit failed to submit an (b) (4) field alert form when they learned that shipping cartons of ten (10) batches of (b) (4) tablets USP, (b) (4) mg, (b) (4) count bottles, were barcode labeled with the incorrect NDC number. The cartons were labeled with the barcode for (b) (4) count bottles of (b) (4) (b) (4) tablets USP, (b) (4) mg , NDC # (b) (4) instead of the barcode for (b) (4) count bottles, NDC # (b) (4)

According to market complaint N/IV/MC/16/027, on 26Jul16, the Quality Unit was notified the barcode did not match the human-readable NDC number for lot (b) (4) The investigation revealed case labels were incorrect for the following lots of (b) (4) tablets USP (b) (4) mg, pack style: (b) (4) count bottles:

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(b) (4) [redacted]

Although the investigation was closed on 09Aug16, an (b) (4) [redacted] field alert form was never submitted.

Section 7.1 of SOP GRA/002-03, titled "Field Alerts", includes the following example of an issue requiring initiation of a Field Alert Form (FAR): "any incident that causes the drug product or its labeling to be mistaken for or applied to another article."

PRODUCTION SYSTEM

OBSERVATION 5

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established, written and followed.

Specifically,
SOP#VPD/106-02, titled, "Entry and Exit Procedure for Aseptic Processing Area" which is applicable to all areas utilized in the manufacturing of pharmaceuticals destined for the U.S. market, including the drugs (b) (4) [redacted] (b) (4) [redacted] requires use of sterile garments and goggles prior to entry into the clean room area. However, the QA department has not validated the number of cleaning and sterilization cycles through which the garments or goggles can be processed without compromising the integrity of the sterile equipment.

Additionally the firm is reusing numbers to identify the goggles and garments instead of a unique numbering system. Garments are numbered 1-28 and goggles are numbered 1-50; once a garment or set of goggles is taken out of service the number on that piece of equipment is reassigned to the replacement piece of equipment. Numbering of garments and tracking of these numbers is not covered in any SOP.

FACILITIES AND EQUIPMENT SYSTEM

OBSERVATION 6

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Separate or defined areas to prevent contamination or mix-ups are deficient regarding operations related to the storage of drug products after release.

Specifically, the disposition status of approved and quarantined drug product is not well controlled or identified to prevent a mix-up. For example, finished goods in quarantine status are stored in the designated areas of the warehouse allocated for "Finished Goods" and the disposition status labels are not always identified.

***DATES OF INSPECTION**

1/16/2017(Mon),1/17/2017(Tue),1/18/2017(Wed),1/19/2017(Thu),1/20/2017(Fri),1/23/2017(Mon),1/24/2017(Tue)

1/24/2017

X Anastasia M Shields
Anastasia M Shields
Generic Drug User Fee Amendments (GDUFA)
Signed by: Anastasia M. Shields -S

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1/24/2017
X Linda F Murphy
Linda F Murphy
Consumer Safety Officer
Signed by: Linda F. Murphy -S