

**Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
of the Active Pharmaceutical Ingredient (API) Manufacturer**

Part 1	General information
Manufacturers Details	
Company information	
Name of manufacturer and address	Neuland Laboratories Ltd. Unit-I Sy. 347, 473, 474, 490/2 , Veerabhadraswamy temple road, Bonthapalli (V), Gummadidala (M), Sanagreddy (dist)-502313, Telangana, India North latitude: 17° 39.339' East Longitude: 78° 21.972' D-U-N-S Number: 675596335
Corporate address of manufacturer	Neuland Laboratories Limited Sanali info Park, 'A' Block, Ground Floor, 8-2-120/113, Rd No. 2, Banjara Hills, Hyderabad –500 034 Telangana, India Phone: +91-40-30211600,66518682, Fax : +91-40-30211602
Inspected site	
Address of inspected manufacturing site if different from that given above	As above
Manufacturing blocks	Block-I, Pharm area B
Inspection details	
Dates of inspection	06 – 09 February 2018
Introduction	
Brief summary of the manufacturing activities	The manufacturer is involved in manufacturing, packaging, labelling, testing and storage of intermediates and active pharmaceutical ingredients (APIs).
General information about the company and site	Company was established in 1984, commercial operations started in 1986. Intermediates and APIs are manufactured Unit I. Another manufacturing site (Unit-II) is located in Pashmylaram, Sangareddy district which is 30 kms away from Unit-I. At Unit II the company manufactures intermediates and active pharmaceutical ingredients (APIs) and finished dosage forms.

WHOPIR Neuland Laboratories Ltd. Unit-I, February 2018

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Contact: prequalinspection@who.int

	Neuland Pharma Research Centre is located at Sy no: 488G, 489A Veerabhadraswamy temple road, Bonthapalli (V), Gummadidala (M), Sanagreddy (dist)-502313, Telangana, India																					
History	<p>This was first WHO inspection. The site has been inspected by the following authorities in the recent years:</p> <table border="1"> <thead> <tr> <th>Authority</th> <th>Date/s of inspection</th> </tr> </thead> <tbody> <tr> <td>China Food and Drug Administration (CFDA)</td> <td>04-08 Dec 2017</td> </tr> <tr> <td>Food and Drug Administration (USFDA)</td> <td>03-07 April 2017</td> </tr> <tr> <td>Korea Food & Drug Administration (KFDA)</td> <td>21-23 July 2014</td> </tr> <tr> <td>The National Health Surveillance Agency, Brazil (ANVISA)</td> <td>05-09 May 2014</td> </tr> <tr> <td>Food and Drug Administration (USFDA)</td> <td>21-25 April 2014</td> </tr> <tr> <td>Federal Commission for the Protection against Sanitary Risk, Mexico (COFEPRIS)</td> <td>24-28 Feb 2014</td> </tr> <tr> <td>European Medicines Agency (EMA)</td> <td>08-11 Jan 2013</td> </tr> </tbody> </table>		Authority	Date/s of inspection	China Food and Drug Administration (CFDA)	04-08 Dec 2017	Food and Drug Administration (USFDA)	03-07 April 2017	Korea Food & Drug Administration (KFDA)	21-23 July 2014	The National Health Surveillance Agency, Brazil (ANVISA)	05-09 May 2014	Food and Drug Administration (USFDA)	21-25 April 2014	Federal Commission for the Protection against Sanitary Risk, Mexico (COFEPRIS)	24-28 Feb 2014	European Medicines Agency (EMA)	08-11 Jan 2013				
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Brief report of inspection activities undertaken																						
Scope and limitations																						
Areas inspected	<ul style="list-style-type: none"> • Pharmaceutical Quality System • Documentation system • Production System • Facilities and Equipment System • Laboratory Control System • Packaging and labeling system 																					
Restrictions	Inspection focused only at manufacture and quality control of the API under WHO assessment																					
WHO product covered by the inspection	API used for treatment of Antibacterial diseases.																					
Abbreviations	<table border="1"> <tbody> <tr> <td>AHU</td> <td>air handling unit</td> </tr> <tr> <td>ALCOA</td> <td>attributable, legible, contemporaneous, original and accurate</td> </tr> <tr> <td>AQL</td> <td>Acceptance quality limit</td> </tr> <tr> <td>API</td> <td>active pharmaceutical ingredient</td> </tr> <tr> <td>APQR</td> <td>annual product quality review</td> </tr> <tr> <td>BDL</td> <td>below detection limit</td> </tr> <tr> <td>BMR</td> <td>batch manufacturing record</td> </tr> <tr> <td>BPR</td> <td>batch packaging record</td> </tr> <tr> <td>CAPA</td> <td>corrective actions and preventive actions</td> </tr> <tr> <td>CC</td> <td>change control</td> </tr> </tbody> </table>		AHU	air handling unit	ALCOA	attributable, legible, contemporaneous, original and accurate	AQL	Acceptance quality limit	API	active pharmaceutical ingredient	APQR	annual product quality review	BDL	below detection limit	BMR	batch manufacturing record	BPR	batch packaging record	CAPA	corrective actions and preventive actions	CC	change control
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CFU	colony-forming unit
CoA	certificate of analysis
CpK	process capability index
DQ	design qualification
EM	environmental monitoring
FAT	factory acceptance test
FBD	fluid bed dryer
FG	finished goods
FMEA	failure modes and effects analysis
FPP	finished pharmaceutical product
FTA	fault tree analysis
FTIR	Fourier transform infrared spectrometer
GC	gas chromatograph
GMP	good manufacturing practice
HACCP	hazard analysis and critical control points
HPLC	high-performance liquid chromatograph
HVAC	heating, ventilation and air conditioning
ID	identity
IR	infrared spectrophotometer
IPC	In process control
IQ	installation qualification
KF	Karl Fisher
LAF	laminar air flow
LIMS	laboratory information management system
LoD	limit of detection
LOD	loss on drying
MACO	maximum allowable carry over
MB	Microbiology
MBL	microbiology laboratory
MF	master formulae
MR	management review
NIR	near-infrared spectroscopy
NMR	nuclear magnetic resonance spectroscopy
NRA	national regulatory agency
OQ	operational qualification
PHA	preliminary hazard analysis
PM	preventive maintenance
PpK	process performance index
PQ	performance qualification
PQR	product quality review
PQS	pharmaceutical quality system
PW	purified water
QA	quality assurance

QC	quality control
QCL	quality control laboratory
QMS	Quality management system
QRM	quality risk management
RA	risk assessment
RCA	root cause analysis
RH	relative humidity
RM	raw materials
RS	reference standard
SAP	system applications products for data processing
SFG	semi-finished goods
SOP	standard operating procedure
STP	standard test procedure
T	Temperature
TAMC	total aerobic microbial count
TFC	total fungal count
TLC	thin layer chromatography
TMC	total microbial count
TOC	Total organic carbon
URS	user requirements specifications
UV	ultraviolet-visible spectrophotometer
VMP	Validation Master Plan
WFI	water for injection
WS	working standard

Part 2	Brief summary of the findings and comments (where applicable)
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Brief summary of the findings and comments

1. Pharmaceutical quality system

The quality management system was generally well established, documented and implemented; the system encompassed organizational structure, procedures and processes. QA and QC departments were independent of production. In general, deviations from established procedures were documented and explained. A procedure was in place for notifying responsible management of regulatory inspections, serious GMP deficiencies, product defects and related actions.

Data integrity

An SOP “Data integrity” was briefly reviewed. SOP dealt with electronic data and paper data and was focused on ALCOA.

Product Quality Review (PQR)

An SOP “Annual Product Quality Review” was briefly reviewed. The PQR covered:

- Brief description of manufacturing process
- Number of batches manufactured
- Review of critical control parameters, in-process control parameters, quality parameters and yields of intermediates and APIs
- Reworked and reprocessed batches
- Laboratory incidents
- OOS/laboratory incidents
- Failed batches
- Deviations, non-conformances and related investigations
- Changes
- Process validation status
- Complaints, returns and recalls
- Stability monitoring
- CAPAs
- Approved vendors
- Control samples
- Actions identified/recommended from previous

Environmental monitoring trends and water trends were presented as separate file.

CkP and 3 sigma were used to calculate trends for related substances by HPLC, assay and yield.

According to the SOP PQR should be prepared from 1st Jan to 31st December and shall be completed before March of the following year. Data was trended.

Management review (MR)

An SOP “Management Quality Review Meeting” was briefly reviewed. According to the SOP MR Meetings should be organized every 6 months. SOP listed personnel who should attend the meetings.

The following items should be covered during the MR:

- Status of actions from previous MR
- Changes
- Information on the performance and effectiveness of the quality management system, customer satisfaction and feedback
- Non-conformities and corrective actions
- Monitoring and measurement actions
- Audit results
- Performance of external providers
- Adequacy of resources
- Effectiveness of actions taken to address risks and opportunities
- Opportunities of improvement

Agenda and MR minutes related to the last MR were presented to the inspectors.

Quality risk management (QRM)

An SOP “Risk Management for Manufacture of Drug Substance” was briefly reviewed. Quality risk management of API XX was available and briefly reviewed. RA was performed starting with purchase of raw materials till packaging and included impurities and stability studies. Risk assessment of clean room was briefly reviewed.

Deviations (Incidents)

An SOP “Handling of deviations” was briefly reviewed. There was a comprehensive system for handling deviations which was followed.

A number of deviation reports were briefly reviewed.

Change control (CC)

A formal change control system was in place to evaluate the changes that may affect the production and control of the manufactured products. An SOP “Change Management” was briefly reviewed. “Change initiation form” and “Change evaluation form” should be completed for all CC. In case GMP related documents were modified, copies of the modified documents were attached to the CC. A number of CC forms were briefly reviewed.

Complaints

An SOP “Handling of Customer Complaints” was briefly reviewed. Designated person from QA was responsible for investigation and implementation and follow up of CAPAs. Complaints were received via marketing department. XX complaints were registered in 2017. Complaints were trended yearly.

A number of complaint investigation forms were briefly reviewed.

Recalls

An SOP “Product Recall” was briefly reviewed. There were no product recalls in the site history. Recall effectiveness was evaluated by mock recall every three years. Site Quality Assurance head was responsible for notifying the recall and maintaining recall records.

Self-inspection

An SOP “Self-Inspection” was briefly reviewed. SOP specified three types of audits:

- Internal Quality Audit (cross functional), should be conducted every 4 months
- Intra Unit Quality Audit, should be conducted every 6 months
- Quality assurance & compliance (self-department) Quality Audit, should be conducted once in a week
- Blind audit – process of verifying the capabilities of reviewer.

Self-inspection was conducted using department dedicated check lists.

Quality Control and Quality Assurance Department self-inspection check lists and last reports were reviewed. After self-inspection non-conformity report was prepared, root cause analysis and CAPAs were proposed by audited department. CAPAs implementation was checked by Head/designee of QA or management representative. List of qualified internal auditors was presented to the inspectors. Conflict of interest was avoided.

Supplier qualification

An SOP “Vendor Qualification for Raw Materials” was briefly reviewed. Vendor qualification different steps were explained. A number of vendor audit reports were briefly reviewed.

Quality Agreement with XX and a number of KSM suppliers Authorization letters were briefly reviewed.

Personnel

Current organization chart of the company was available. The company had sufficient number of personnel with responsibilities according to their respective unit and department. Personnel were wearing suitable clothing for the manufacturing activities.

According to the Company presentation, the site employed approximately 431 full time employees:

Contract workers were involved in physical operations e.g. transfer of materials, cleaning, documentation shifting.

An SOP “SOP on Training of Employees” was briefly reviewed. The following trainings were specified in the SOP:

- Induction
- On-the-Job training
 - Phase I training – SOPs training
 - Phase II training – operations to be carried out
 - Phase III training – evaluation: practical and theoretical
- GMP & Safety training
- On-going training
- Remedial training
- External training
- On-site training

An SOP “Qualification of an Analyst” was briefly reviewed. After Induction training analyst was allocated to the respective section. Fresheners as well as experienced analyst were provided with the SOPs related to the job allocation. When analysts were familiar with SOPs then on-job training was initiated. Analysts were given previously approved sample to analyze, results were compared. The % variations between analyst and initial analysis results were specified for different tests. Training effectiveness was evaluated by true/false, single answers questions and multiple choice questions.

A number of employees training records were briefly reviewed.

An SOP “Contract Workmen” was briefly reviewed. General instructions what “to do” and what “not to do” were available in local language.

An SOP “Personal Hygiene” was briefly reviewed. Smoking, eating, drinking, chewing and the storage of food was restricted.

An SOP “SOP on Medical Examination of Employees” was briefly reviewed. All employees need to undergo medical examination before joining the company and annually/bi-annually depending on work allocation.

Medical examination of the permanent employees and contract workers working in Pharma area was performed every six months. Medical examination records were presented to the inspectors.

2. Documentation system

Documentation system was generally well established. Documents related to the manufacture of intermediates and APIs were prepared, reviewed, approved and distributed according to written procedures. The issuance, revision, superseding and withdrawal of documents were controlled with maintenance of revision histories. Specifications were established for raw materials, intermediates and APIs. The Company had a policy to archive logbooks and other documents.

An SOP “Batch Coding and Numbering System” was briefly reviewed.

An SOP “Preparation, Control, Issue / Distribution, Retrieval and Filing up of the Batch Manufacturing Sheets (BMS) & Batch Packaging Records (BPR)” was briefly reviewed. BMSs and BPRs were under QA control.

The electronic copies of the Master Batch Records were stored on two servers located in different areas. The access to the files was restricted to selected QA persons who have the right to modify the electronic version based on a change control form approved by QA.

An SOP “Preservation and Destruction of Records” was briefly reviewed. According to the SOP, production, control and distribution records were retained for one year after the expiry date of the batch. For APIs with retest dates, records were retained for three years after assigned retest date. Destruction of the documents were recorded and done using the shredder. Documents were archived in QA archive. Access to QA hard copies of master documents, records and archives was limited to authorised personnel.

An SOP “Batch Release” was briefly reviewed. Final batch release was performed by qualified persons from QA. Batch release was done using check list.

An SOP “Testing of Samples and Reporting Results” was briefly reviewed. Review of analytical raw data and calculations was carried out by reviewers using check list. Test results were approved by the Head QC / Designee.

An SOP “Preparation of Protocols, Reports, Method of Analysis, Specifications, Master Labels and Certificate of Analysis” was briefly reviewed. Master labels (API labels) were prepared by authorizer person from QA.

Printing of API labels was explained in the SOP “Packing, Labelling, Commercial Transfer and Storage of Commercial Products”.

3. Production system

In general, production operations followed defined procedures. Process flows (with IPCs) and routes of synthesis were available. Deviations from procedures were recorded; major deviations were investigated. Access to production premises was restricted to authorized personnel. Weighing and measuring devices were of suitable accuracy for the intended use.

Blending

An SOP “Operation of Blender” was briefly reviewed. As stated by the Company blending of API batches under WHO assessment was not performed.

Reprocessing and Reworking

An SOP “Reprocessing/Reworking of APIs and Intermediates” was briefly reviewed. According to the SOP reprocessing of the non-conforming intermediates and APIs shall not be carried for more than two times.

Log for Reprocess/Rework was presented to the inspectors.

An SOP “Handling of Returned Good” was briefly reviewed. Returned good register for 2017 was presented to the inspectors.

Material management

All materials used in production were supplied by qualified suppliers. The list of qualified suppliers was available in the warehouse and updated when necessary. Upon receipt, materials were kept in a quarantine status under ambient or controlled temperature depending of the requirement until tested. A yellow quarantine label was affixed and a yellow rope was tied around a group of containers. Solid raw material was sampled in an air controlled sampling booth (ISO 5).

After QC approval a green label was affixed to cover the yellow label and yellow rope was changed to green rope. Locations for rejected/returned materials were available.

Bulk deliveries of solvents were received in tanks and stored in tank farm. Product dedicated hoses were used to connect the trucks to the tanks. Two QC tests were performed, one from the truck and one from the tank after discharge. When the tanker was product dedicated a certificate was issued confirming the previous product load. For non-dedicated tankers a certificate of cleaning was received.

Process Validation

The process of API under WHO assessment was well documented and one of the 3 validation batch records was reviewed. Process validation document XX and the Process validation protocol ZZ were reviewed.

Cleaning Validation

An SOP “Cleaning validation” was briefly reviewed. Three different types of cleaning were described and used:

- Type 0 (zero) cleaning was used for early stages where the cleanliness of the equipment was checked only visually. No validation was required
- Type I cleaning was used for batch to batch cleaning. Validation was required to clean after several batches for example during a campaign
- Type II cleaning was used for product change over and had to be validated using the MACO calculation for the cleaning of equipment located in the pharma area.

A number of equipment cleaning SOPs and records were briefly reviewed.

Computer system Validation

Provision for Computer system validation was given in the validation master plan.

However, neither the warehouse or production blocks use GMP related computer systems to support their processes. Only the quality control lab was using computerized systems.

4. Facilities and equipment system

Buildings and facilities of block I, including Pharma area B used in the manufacture of intermediates and APIs were located, designed, and constructed to facilitate cleaning, maintenance and operations as appropriate to the type and stage of manufacture. Facilities were designed to minimize potential contamination. Adequate space was provided for orderly placement of equipment and materials to prevent mix-ups and contamination. Permanently installed pipework was appropriately identified. Solvent pipelines had different colour codes.

Dedicated sampling tools were used for in process sampling, cleaned and wrapped near the place of use. A label was affixed informing about the product, the status the date of cleaning. Non permanently installed hoses, also product specific, were identified, and stored horizontally on racks, cleaned and wrapped on both ends.

Equipment status boards indicated calibration status with due dates and preventive maintenance due dates. Equipment was identified as to its contents and cleanliness status.

An SOP “Handling of Preventive Maintenance (PM)”, PM schedule and PM check list for reactor and centrifuge were briefly reviewed. Spot checks showed that PM schedule was followed.

An SOP “Calibration of Measuring, Monitoring Instruments and Calibration Master Instruments”, calibration schedule and compliance report were briefly reviewed. Spot checks showed that calibration schedule was followed.

An SOP “Calibration of Instruments and Equipment’s” and calibration schedule were briefly reviewed. This SOP was applicable to QC instruments.

An SOP “Temperature Distribution Study of Process Equipment’s, Temperature Control Rooms” and Validation protocol and report “Temperature and humidity mapping of approved finished goods storage room II” were briefly reviewed.

An SOP “Laboratory Network Systems” was briefly reviewed. Access levels/privileges to lab computers were defined. According to the SOP audit trails shall be reviewed by QA monthly using “Batch analysis audit trail review” check list. For every batch a brief audit trails report was done by reviewer according to the “Audit trail summary report” check list.

An SOP “Backup and restoration of Analytical data” was briefly reviewed. Hot back-up of electronic data was done daily on server. Cold backup was done weekly on server and tape drives as well. Data restoration exercises were performed for every three months.

Utilities

PW was used for production and for cleaning of equipment and tools. The system had 3 distribution tanks and 3 loops. From the main storage tank PW was distributed to the smaller storage tank supplying water to Block-I. Designed flow rate was NTL 1.2 m/sec and gradient 1:100. Storage tanks and loops were made from stainless steel 316 L. PW was in continuous circulation at ambient temperature. Conductivity, flow rate and temperature on the return loops were monitored on-line. PW system was installed on 11/01/2017. PW system 1st Phase and 2nd Phase validations were carried out for one month each. 2nd Phase validation was finished 16/08/2017. During inspection PW system validation was in 3rd Phase. 3rd Phase validation was planned for one year and started on 20/11/2017. The following documents related to the PW system were briefly checked:

- Welder performance qualification record
- Industrial X-Ray & Allied Radiographers radiographic inspection report
- Boroscopy report (10% of joints)
- SS316 test report
- 1st Phase chemical and microbiological test results (trends). Analyses were carried out every day
- 2nd Phase chemical and microbiological test results (trends). Analyses were carried out every day. Action and alert limits were set up after 2nd Phase. Action limit for total aerobic microbial counts was 80 cfu/ml, alert limit was 60 cfu/ml. Sanitisation frequency was established 15 ± 2 days. Sanitisation was performed by hot water 80 – 85 °C for 1 hour.
- 3rd Phase sampling plan
- Change control CC/16/385 regarding installation of the new PW loop was also briefly reviewed.

The Calibration certificate of the conductivity Meter installed at the PW distribution storage tank outlet was reviewed.

Pharma B clean area was supplied with 100 % fresh air. Filter cascade was following: G2 (20 microns) → G4 (10 microns) → M5 (5 microns) → M5 (2 microns). Terminal HEPA filters H13 were installed in rooms. Pressure differentials between filters were monitored daily. HEPA filters integrity tests were performed once per year.

Qualification of the AHU No XX was briefly reviewed. HVAC system was installed in 2008 and was re-qualified every six months for the following parameters:

- Air flow rate
- Pressure difference
- Particle counts (viable and non-viable)
- T & RH

Air flow patten and recovery study was performed initially and in case of major modifications.

Technical areas of AHUs, PW system as well as compressed air and nitrogen production areas were well maintained and in good state of art.

An SOP “Checking/cleaning/ replacing of compressed air Nitrogen gas filters” was briefly reviewed with the corresponding records and logbooks.

Laboratory premises

Laboratory areas and operations were separated from production areas. Microbiological laboratory premised were recently modified and separated from the QC laboratory.

5. Laboratory control system

Quality control laboratory (QCL) appeared to be adequately organized and equipped. In process control (IPC) tests were performed in QCL. QCL was working in 3 shifts.

Analytical balances were located in the Instrumental laboratory room. Balances qualification was performed daily and monthly.

All laboratory instruments usage was recorded in instruments log books. Instruments calibration certificates indicating calibration due date were affixed to the instruments. Routine calibration was carried out by QCL staff; PM was carried out by service providers. HPLC columns were stored in locked cabinets in good order.

As an example of data integrity API XX batch No ZZ analytical work sheets, electronic metadata, standards and columns usage, printouts and other relevant data were cross checked. No discrepancies were noted.

Out of specification (OOS)

An SOP “Out of specification results” was briefly reviewed. A comprehensive system was described and followed to handle OOs results. Reports on OOS results comprise a Phase I investigation followed by a Phase II A and if required there was a phase II B investigation. A number of OOS investigation reports were reviewed.

Analysts Specimen Signature - full signature and initials was presented to the inspectors.

An SOP “Analytical Method Validation” was briefly reviewed. According to the SOP pharmacopoeia methods should be verified.

An SOP “Good chromatographic practice” was briefly reviewed. Document was detailed and contained pictorial examples of different peaks.

An SOP “Sampling” was briefly reviewed. SOP was applicable to raw materials, KSM, intermediates, APIs and packaging materials sampling procedure. $\sqrt{n+1}$ sampling plan was applied to KSM sampling.

An SOP “Control samples” was briefly reviewed. Control samples were stored in in the same packaging system in which the API was stored. Sufficient quantities were retained to conduct at least two full analyses.

An SOP “Handling and maintenance of Laboratory standards” was briefly reviewed. Working standards were standardized against Pharmacopoeia standards and dispensed in 13 amber color vials, one vial for use within one month. Standards were stored according specified storage condition in special chambers and in desiccators.

Access to the standards storage chambers and stability chambers was controlled and restricted to dedicated employees. T and RH in chambers were recorded by MACK software every hour. Printouts were taken and checked daily. Chambers were equipment with visual and audio alarm, system.

Stability studies

A comprehensive testing program of API under WHO assessment was in place. Long term and accelerated stability studies were conducted. The three validations batches had been placed under long term stability and tested according to the planned schedule. As requested by the WHO assessors 3 batches were maintained under intermediate conditions: 30° and 65% of humidity and tested.

6. Packaging and labelling system

Packaging of the final API was performed in the Pharma area under ISO 8 conditions. APIs were labelled in finished good warehouse by production personnel in the presence of QA personnel. Some of the pre-printed labels were kept in a closed room with restricted access in individual cupboards each closed by a lock. Another part of the labels was kept in a common area within individual locked cupboards. QA personnel were in charge of the keys and were issuing the labels.

Miscellaneous	
<i>Samples taken</i>	N/A
<i>Assessment of the site master file</i>	SMF was submitted before inspection and was considered to be in compliance with requirements
<i>Annexes attached</i>	N/A

PART 3

CONCLUSION

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report Neuland Laboratories Ltd. Unit-I, located at Sy. 347, 473, 474, 490/2, Veerabhadraswamy temple road, Bonthapalli (V), Gummadidala (M), Sanagreddy (dist)-502313, Telangana, India was considered to be operating at an acceptable level of compliance with WHO good manufacturing practices for active pharmaceutical ingredients guidelines.

All the non-compliances observed during the inspection that were listed in the full report as well as those reflected in the WHOPIR, were addressed by the manufacturer, to a satisfactory level, prior to the publication of the WHOPIR.

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

PART 4

List of GMP guidelines used for assessing compliance

1. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2.
Short name: WHO TRS No. 957, Annex 2
<http://www.who.int/medicines/publications/44threport/en/>
2. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2.
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/
Short name: WHO TRS No. 986, Annex 2
3. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 6
Short name: WHO TRS No. 961, Annex 6
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

4. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth-sixth Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2
Short name: WHO TRS No. 970, Annex 2
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/
5. WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4
Short name: WHO TRS No. 929, Annex 4
http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1
6. WHO guidelines on good manufacturing practices for heating, ventilation and air-conditioning systems for non-sterile pharmaceutical dosage forms. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 5
Short name: WHO TRS No. 961, Annex 5
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1
7. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4
Short name: WHO TRS No. 937, Annex 4
http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf?ua=1
8. WHO Good Practices for Pharmaceutical Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 1
Short name: WHO TRS No. 957, Annex 1
<http://www.who.int/medicines/publications/44threport/en/>
9. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2
Short name: WHO TRS No. 957, Annex 3
<http://www.who.int/medicines/publications/44threport/en/>
10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7
Short name: WHO TRS No. 961, Annex 7
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

11. Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 9
Short name: WHO TRS No. 961, Annex 9
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