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தேசிய மருந்துகள் ஒழுங்குபடுத்தல் அதிகார சபை
National Medicines Regulatory Authority

මගේ අංකය எனது இல. My No.	GMP/FGM/Med/p8/04/2023	ඔබේ අංකය உங்கள் இல. Your No.	N/A	දිනය திகதி Date	20.03.2023

Mr. Mahesh Premaratne,
Deputy Chairman,
Slim Pharmaceuticals (Pvt) Ltd
98/10, Namal Mawatha Kahantota Road, Malabe.

Dear Sir/Madam,

Final decision relevant to GMP inspection on an overseas manufacturing site
GMP Inspection Report & CAPA request

Theon Pharmaceuticals, Plot No.400 Industrial area, Phase -I Panchkula-134113, (Haryana)-India
Site: Village-Saini Majra, Tehsil- Nalagarh, Distt: Solan-174101, (Himachal Pradesh)-India

According to the findings of the inspection including documents reviewed and follow up conducted through video presentation, live video demonstration conduct via zoom. based on CAPA received and evaluated, the manufacturing site can be considered to be operating at an acceptable level with reference to GMP compliance for

- non-sterile pharmaceutical products relevant to general formulations (Tablet/Capsules/Dry powder syrup/ Ointment/ Cream/Sachet),
- non-sterile pharmaceutical products relevant to penicillin formulations (Tablet/Capsules/Dry powder syrup),
- non-sterile pharmaceutical products relevant to cephalosporin formulations (Tablet/Capsules/Dry powder syrup),
- sterile pharmaceutical products relevant to cephalosporin formulation (injectable),

Dr. Vijith Gunasekera
MBBS, MSc, MEcon, MD
Chief Executive Officer
National Medicines Regulatory Authority
No. 120, Norris Canal Road,
Colombo 10.

Thank you

Director General/Chief Executive Officer
National Medicines Regulatory Authority

Cc: Manufacturing Regulatory Division

GMP Inspection Report

Part 1	General information
Manufacturers Details	
Company information	Name of Manufacturer : Theon Pharmaceuticals, India Corporate Office : Plot No. 400, Industrial Area, Phase-I, Panchkula-134113, (Haryana) – INDIA Telephone : +91-0172-5011077, 5033850 Fax : +91-0172-5033851 Email : admin@theonpharma.com Website : www.theonpharma.com Contact person during outside working hours :Mr.Adheesh Malhotra E-mail : adheeshmalhotra@theonpharma.com
Inspected site	Site address : Village -Saini Majra, Tehsil-Nalagarh, Distt.: Solan- 174101, (Himachal Pradesh) - INDIA Telephone : +91-01795-669200 (100 lines), 265303-04 Email : info@theonpharma.com GPS Coordinates : Latitude: 31.0303388/N 31^0 1' 49.2204" Longitude : 76.64723500000002 /E 76^0 38' 50.0454"
	Site master file number : SMF/001-16
	General description of the site: **Theon Pharmaceuticals Ltd** is established in year 2005 and located on the Nalagarh-Ropar highway at Nalagarh, Distt.:Solan, Himachal Pradesh, INDIA. Manufacturing site is in an industrial area at distance of about 50KM from Chandigarh on the Nalagarh – Roper highway, accessible by road (nearest railway station at Chandigarh) and nearest airport is Mohali. Shipment facility is available at Mumbai Port, which is approx. 1400 Km away from manufacturing site for export and import requirements. **Theon Pharmaceuticals Ltd.**, have separate & dedicated blocks for manufacturing of Penicillin Products in Penicillin Block (OSD), Cephalosporin Products in Cephalosporin Block (OSD), Cephalosporin Dry Powder Injection in Cephalosporin Injection Block and General Products & External Preparation in General Block (OSD).
Brief summary of planned activities to be performed at the site	Manufacturing, packaging and batch release of oral solid dosage forms including tablets, capsules and dry powder syrup and small volume dry powder injectable sterile pharmaceutical finished dosage forms relevant to Cephalosporin formulations in the Cephalosporin blocks.

	Manufacturing, packaging and batch release of oral solid dosage forms including tablets, capsules and dry powder syrup relevant to Penicillin formulations in the Penicillin block. Manufacturing, packaging and batch release of oral solid dosage forms including tablets, capsules, dry powder syrup and External Preparations relevant to general formulations in the general block.
Inspection details	
Dates of inspection	23rd of January 2023
Type of inspection	Desk review of submitted CAPA documentation, video presentation, live video demonstration conduct via zoom.
Inspector(s)	1. Mr. Chaminda Dissanayake (Lead Inspector) 2. Ms. Ishani Sandamali Weerasinghe (Inspector/NMQAL)
Introduction	
Brief summary of the manufacturing activities	Manufacturing, packaging and product release of tablets, capsules, dry powder syrup and external preparations of general formulations, Tablets, capsules, dry powder syrup and small volume sterile dry powder injectable dosage forms of cephalosporin formulations, tablets, capsules, dry powder syrup dosage forms of penicillin formulations consisted of glass vials, blisters, strips, HDPE bottles tubes and sachets.
History	Pre-approval inspection on 26th September to 30th September 2022 conduct by NMRA team. GMP compliance report was issued to Penicillin Products in Penicillin Block (OSD), Cephalosporin Dry Powder Injection in Cephalosporin Injection Block, General Products & External Preparation in General Block (OSD) and other cephalosporin product range in Cephalosporin Block (OSD), and CAPA were requested for manufacturing of dry powder syrup cephalosporin block. Manufacture has submitted the documentation and video presentation in connection with above requested CAPA for the dry powder syrup relevant to cephalosporin block and for the other observation made by the team during the previous inspection report.

Brief report of inspection activities undertaken		
Focus of the inspection	Desk review of documentation on CAPA implementation by the manufacture for the observation made by the NMRA team in their GMP report in connection to GMP visit of the Manufacturing plant pay in special focus on CAPA implementation for the dry powder syrup relevant to general formulations in the cephalosporin block and follow up of CAPA implementation relevant to pre-approval inspection.	
Areas inspected	Production areas, particularly the manufacturing lines for, • tablets, capsules, ointments, creams, sachets and dry powder syrups of general formulations, (G BLOCK) • tablets, capsules, dry powder syrups – (C Block) • dry powder sterile dosage forms of cephalosporin formulations, (Dry powder injection block- I BLOCK) • tablets, capsules, dry powder syrups of penicillin formulations, (B-BLOCK) • Documentation reviewed, during the pre-approval inspection process. • In reviewing CAPA implementation plan desk review of the submitted CAPA implementation document with video presentation and live video demonstration via zoom meeting were done.	
Key persons met	**Name**	**Designation**
	1. **Mr. P.C. Joshi**	**Plant Head**
	2. **Mr. Kamal Deep Sharma**	**Sr. Manager QA/Microbiology**
	3. **Ms. Lakhvir Kaur**	**Manager- QA**
	4. **Mr. P.C.S. Negi**	**Head – Engineering**
	5. Krishna soni	**Officer - Quality Assurance**
	6. Kuldeep Kumar	**Officer - Quality Assurance**
Out of scope and limitations	QC laboratories and utility areas	
	API	Active Pharmaceutical Ingredient
	AHU	Air Handling Unit
	APQR	Annual Product Quality Review
	BMR	Batch Manufacturing Record
	BPR	Batch Packing Record
	CAPA	Corrective and Preventive Actions
	GMP	Good Manufacturing Practices

	IPQC	In Process Quality Control
	OSD	Oral Solid Dosage Form
	QA	Quality Assurance
	QC	Quality Control
	QMS	Quality Management System
	QRM	Quality Risk Management
	NMQAL	National Medicines Quality Assurance Laboratory
	NMRA	National Medicines Regulatory Authority
	OOS	Out-of-specification
	R & D	Research and Development
	RM	Raw Material
	SMF	Site Master File
	SOP	Standard Operating Procedure

Part 2
Brief summary of the findings and comments

Pharmaceutical quality system	Pharmaceutical quality system incorporating GMP and QRM has been established. Resources such as premises, equipment and facilities were adequate for the planned processors. There were sufficient staff with appropriate qualifications and experience. Responsibilities were adequately specified in job descriptions. Head of QA and Assistant Manager QA were responsible for batch release. <u>CAPA implementation</u> Document management system has been improved by revising the SOPs through change control (TPL/CCP/13/011, CCP/C/QA/14/004, CCP/C/QA/16/002, CC/17/014, CC/18/202, CC/Q/19/009, CC/I/21/017, CC/Q/22/042) and corrected SOPs (SOP No. QA/001-010, SOP No.QA/001/F07) had been submitted <u>Management Review Meetings:</u> Management review meetings were conducted periodically and when required. <u>Batch Release</u> SOP No. QA/046-05 on procedure for batch release existed. As per the job description, QA senior manager was responsible for the approval and release of the batch. Packaging record has been revised to incorporate the actual number of primary label to be dispatched for the production of cephalosporin at the cephalosporin (OSD) block.
Good Manufacturing Practices for Pharmaceutical Products	Required resources including suitable premises with adequate space, appropriately qualified and trained staff, and suitable equipment and services had been provided. All relevant equipment had been qualified and validated, and records were being maintained.

	Process were generally well defined in relevant SOPs. BMR and BPR had been well designed to capture the history of respective batches. Implementation of CAPA • BMR of cefuroxime (BMR/CFML/001-08) revise as (BMR/CFML/001-09) through the change control (CC/I/22/017) including the provision to mention the carry over quantity in case of campaign batches production. • BPR revised to mention the number of labels to be dispatched for the scrap rather than the weight in Kg for better tracing of the actual quantity transferred. Attendance sheet of the trainees had been provided as an attachment 11.
Sanitation and hygiene	A system had been established to maintain an acceptable level of sanitation and hygiene with adequate cleaning SOPs for specific areas and individual equipment. Premises and equipment were generally clean. (SOP No: HR/002-02)
Qualification and validation	Validation Master Plan VMP (VMP/001-07) presented an overview the validation policy of the company and described the validation approach, the organization for validation, the life cycle management program and the basis of the acceptance criteria. Process validation SOP No. QA/032-05 on process validation was in place. Process validation protocols relevant to manufacturing were available. Revalidation done for the equipment (TPL/AHU/G/SF/08 according to SOP No. QA/081-00 (Submitted first document had been expired at the time of inspection and later company has submitted correct document.) Validation done for the equipment (TPL/AJC/C/09/01 – Air jet bottle cleaning machine) and submitted OQ and IQ report. The training has been conducted for the operation of bottle cleaning machine of the dry powder syrup of the cephalosporin formulation for rise CAPA relevant to the dust observed the outer container with relevant to the CAPA number 12 of the previous inspection.
Complaints and Product recalls	A complaint handling system had been established and the procedure was described in QA/017-07 for handling of market complaints. SOP No. QA/023-03 described the recall procedure. CAPA implementation Explanatory provided by the manufacture training has been imparted as a preventive measure, but only attendance sheet of the trainees had been provided as an attachment 5.

Contract production, analysis and other activities	The documents relevant to contract analysis were reviewed during the previous inspection.
Self-inspection, quality audits and Suppliers' audits and approval	**Self-inspection** SOP for internal audits (SOP No- QA/008-09) was in place. QA, Plant head and section heads were responsible for preparation of self-inspection schedule and maintain the self-inspection record. Implementation of CAPA ● SOP No QA/008-09 was revised through change control No.- CC/Q/22/042 as QA/008-10 adding to incorporate the provisions for the checking of training programme and training of the persons in the IT department during self-inspections, ● Self-inspections carried out as per the pre designed format (QA-008/F01-04, QA-008/F02-02, QA-008/F03-02, QA-008/F04-01, QA-008/F05-02, QA-008/F06-01, QA-008/F07-03, QA-008/F08-00)
Personnel	The key personnel were sufficiently qualified and experienced. The number of persons were adequate for the planned activities. The employees interacted were well versed with duties which they were tasked.
Training	Employee training calendar would be prepared in every year, in the month of December. Personal training file maintained for each individual employee and contained induction training report, job description (QA/C2233-00), job specific training schedule and training evaluation records of the relevant employee.
Personal hygiene	An acceptable level of personal hygiene was being maintained. The personnel were provided with appropriate clean garments.
Premises	Entry to the premises was controlled with adequate security measures. Total area of plant was 283881.768 Sq.ft. Total Constructed Area was 142327.48 Sq.ft and open area was 73565.608 Sq.ft. Manufacturing Area was divided into different Blocks I.e. General Block (OSD), Penicillin Block (OSD), Cephalosporin Block (OSD), Cephalosporin Block (Dry Powder Injection) and Quality Block. Implementation of CAPA Submitted CAPA has provided the documentation and video presentation for the installation of air curtain at Airlock entrance of RM receiving area. Video presentation show the floor of raw materials, packing materials store and corridor were epoxy in the penicillin block (OSD).

Equipment	The equipment was sufficient for the planned activities. Each equipment had a unique identification number. For most of the equipment, qualifications had been done and documents were available. Implementation of CAPA Ionizer was installed for the Air jet cleaning machine in the dry powder syrup manufacturing in Cephalosporin Block. Live demonstration provided operation of the ionizer.
Materials	Sufficient space had been provided for storage of incoming material. Material were kept in coded racks. Separate cold rooms were available to store quarantined and approved thermos-liable material in general block. Implementation of CAPA • Video presentation shows that, racks was adequately labeled as "Quarantine", 'under test" and "approved" and raw materials were stored there in the general block with demarcation.
Documentation	The documents had been designed and prepared appropriately and had been approved by the relevant responsible persons. CAPA implementation SOPs and document included but not limited to following: • SOP NO: QA/008-10 Internal Audits • SOP NO: QA/001-11 Sop On Sop • SOP NO: WG/004-11Receipt and storage of raw materials • SOP NO: QA/116-06 Cleaning, Operation and Calibration of Weighing Balance • SOP NO: WI/008-06 Dispensing of Raw Material • SOP NO: QA/104-05 Batch Numbering System • BMR No- BMR/CFML/001-09 • Protocol No: EQ/PQP/004-03 Performance Qualification protocol for Automatic high speed linear vial washing machine. • Protocol No: ADD/OQ/AJC/O/PC/01-00 Addendum - Operational Qualification protocol cum report for automatic air jet bottle cleaning machine. • Validation protocols and records of Equipment No: TPL/AHU/G/SF/08
Good practices in production	Entry to production areas were access controlled. Designated rooms had been assigned for specific processes. The facilities consisted of manual as well as automated equipment and qualification of them had been completed. The production line layout and flow of personnel and material was complying with GMP. Products were subjected to visual inspection prior to packing.

	The manufacturing operations in the cream, ointment and sachets in the general block lines could not be inspected. Production operations in comparison with relevant SOPs was reviewed.	
Good practices in quality control	The QC function was independent from other departments and two IPQC lab were G Block and C Block. Implementation of CAPA The SOP No QA/116-05 of procedure for cleaning, Operation and Calibration of weighing balance revision through the change control (CC/Q/22/036). SOP No. QA/116-06 has been initiated for revision of SOP for incorporating the format QA/116/04-00 for usage record of weighing balance and the photograph of the placement on drift free and anti-vibration desk of the balances in the QC lab.	
Utilities	Utility areas were not visited during the inspection.	
Part 3 **Inspection outcome**		
Deficiencies		
1. Critical	1.1 None	
2. Major	2.1 None	
3. Other		
3.1	**Premises (Production and Warehouses)** • During the site visit the team observed pressure difference was not maintained properly in de dusting room and the air lock in the I block and that alarm system was not properly functioning in the I block. Submitted CAPA document deficiencies that action taken for the non-proper function of alarm system in the I block were not provided • Although the air curtain had been installed for the area, which opens raw material receiving bay to air lock entrance of RM receiving area of I block, details of corrective action taken to maintain differential pressure not provided in the submitted CAPA document. pressure difference was not maintained properly from the receiving bay to the air lock area. hence suggested to be placed air shower between the de dusting area and air lock area which leads to the main corridor.	WHO TRS 986 Annex 2; 16.7, 12.15

3.2	**Good Practices in Quality Control was deficient in that:** Explanatory provided by the manufacture, training has been imparted as a preventive measure for the observation made for the deficiencies in CAPA management, but only the attendance sheet of the above training had been provided as an attachment 5.	WHO TRS 986 Annex & 15.2

Definition of deficiencies classification

Critical deficiency
A *critical* deficiency may be defined as an observation that has produced, or may result in a significant risk of producing, a product that is harmful to the user.

Major deficiency
A *major* deficiency may be defined as a non-critical observation that:

- has produced or may produce a product that does not comply with its marketing authorization and/or prequalification application (including variations);
- indicates a major deviation from the GMP guide;
- indicates a failure to carry out satisfactory procedures for release of batches;
- indicates a failure of the person responsible for quality assurance/quality control to fulfil his or her duties;
- consists of several other deficiencies, none of which on its own may be major, but which together may represent a major deficiency and should be explained and reported as such.

Other deficiency
A deficiency may be classified as other if it cannot be classified as either critical or major, but indicates a departure from GMP. A deficiency may be other either because it is judged as minor or because there is insufficient information to classify it as major or critical.

Classification of a deficiency is based on the assessed risk level and may vary depending on the nature of the products manufactured, e.g. in some circumstances an example of another deficiency may be categorized as major.

Part 4
Conclusion & Signature

Conclusion	Based on the desk review of documents, video presentations and live video demonstration As CAPA submission for the finding of the previous GMP inspection including the Observation listed in the inspection, Theon Pharmaceuticals, located at Plot No.400, Industrial Area, Phase-I, Panchkula-134113, (Haryana) – INDIA can be considered as operating at an acceptable level of compliance with GMP guideline for;

	• non-sterile pharmaceutical products relevant to general formulations (Tablet/Capsules/ Ointment/ Cream/Sachet), • non-sterile pharmaceutical products relevant to penicillin formulations (Tablet/Capsules /Dry powder syrup), • non-sterile pharmaceutical products relevant to cephalosporin formulations (Tablet/Capsules/Dry powder syrup), • sterile pharmaceutical products relevant to cephalosporin formulation (injectable),
Name(s) &Signature(s)	..... 1. Mr. Chaminda Dissanayake, Pharmacist (Lead Inspector) ..... 2. Mrs. Ishani Sandamali Weerasinghe, Pharmacist (Inspector/ NMQAL)
Date	20 March 2023