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**Prequalification Unit Inspection Services**
**WHO PUBLIC INSPECTION REPORT**
**(WHOPIR)**
**Finished Pharmaceutical Product Manufacturer**

| **Part 1** | **General information** |
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| **Manufacturers details** | |
| Name of manufacturer | **Macleods Pharmaceuticals Ltd** |
| Corporate address of the manufacturer | Macleods Pharmaceutical Limited<br>Research & Development Centre<br>G-2, Saket Bldg., Near Onida House<br>Mahakali Caves Road, Andheri (E)<br>Mumbai, India. 400093 |
| | |
| Name & address of inspected manufacturing site if different from that given above | Block No. N2, Village Theda,<br>P.O. Lodhi Majra, District Solan<br>Tehsil Baddi, Himachal Pradesh 174 101<br>India |
| Unit/block/workshop number | Block-N2 (General Block) including GB-1, GB-2, GB-3 |
| | |
| Dates of inspection | 12-16 May 2025 |
| Type of inspection | Routine GMP inspection |
| **Introduction** | |
| Brief description of the manufacturing activities | The Baddi (Unit VI) has two independent manufacturing facilities, the Foil Printing Unit and the Carton Printing Unit, within a common premise.<br>1. Block N1 (Small Tablet and Soft Gelatin Block).<br>2. Block N2 (General Block)<br>3. Foil Printing Unit<br>4. Carton Printing Unit<br>Macleods Baddi (Unit VI) is identified as Block N2 (General Block), having three separate blocks:<br>1. General Block -1 (Solid orals and liquid orals) (GB1)<br>2. General Block -2 (Solid orals) (GB2)<br>3. General Block-3 (Solid orals) (GB3) |
| General information about the company and site | Macleods Pharmaceuticals Limited was established in 1986. Macleods manufactures and markets a wide range of pharmaceutical formulations from Tablets to sterile dosage forms and from inhalation to novel drug delivery systems. It is engaged in the manufacturing of both primary and secondary anti-Tuberculosis formulations. Macleods is a vertically integrated global pharmaceutical company. The company has the following manufacturing facilities across India:<br>1. Pharmaceutical Formulation (Unit I), Palghar, Thane, Maharashtra<br>2. Pharmaceutical Formulation (Unit II), Daman, UT |

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| | 3. Pharmaceutical Formulation (Unit III), Kabra, Daman, UT<br>4. Pharmaceutical Formulation, Foil Printing (Unit VI), Baddi, HP<br>5. Pharmaceutical Formulation (Unit VII), Daman, UT<br>6. Pharmaceutical Formulation (Unit IX), Sikkim<br>7. Pharmaceutical Formulation (Unit XI), Pithampur, MP<br>8. API & Pharmaceutical Formulation (Unit V), Sarigram, Gujarat<br>9. Research and Development (R&D) centre, Andheri, Mumbai<br>10. Foil printing Unit, Daman, UT<br>11. Carton Printing Unit, Baddi, Himachal Pradesh<br>12. KSM / Intermediate, API Unit X, GIDC Dahej, Bharuch, Gujarat |
| History | The WHO Prequalification Inspection Services has regularly inspected Macleod's Baddi site (Unit-VI). The last WHO PQ inspection was conducted in November 2022. |
| **Brief report of inspection activities undertaken – Scope and limitations** | |
| Areas inspected | The following areas were inspected:<br>- Pharmaceutical quality system, including documentation<br>- Personnel, training, hygiene<br>- Facilities, equipment, and utilities (including qualification, calibration, and maintenance<br>- Process and computerized system validation<br>- Production and packaging<br>- Quality control<br>- Material management ( warehouse) |
| Restrictions | None |
| Out of scope | The inspection was limited to Block N2, covering the General Block (GB-1, GB-2, and GB-3), where WHO Prequalified Products were produced. Products and facilities not related to prequalification were outside the scope of this inspection and were therefore not inspected. |
| WHO products covered by the inspection | |

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| HA424 | Lamivudine Tablets | 150mg |
| HA459 | Lamivudine and Zidovudine Tablets | 150 mg + 300 mg |
| HA514 | Lamivudine and Tenofovir Disoproxil Fumarate, Tablets Film Coated | 300 mg + 300 mg |
| HA516 | Tenofovir Disoproxil Fumarate Tablets | 300 mg |
| HA523 | Lamivudine Oral Solution | 10 mg/ml |
| HA526 | Zidovudine Oral Solution | 50 mg/5ml |
| HA561 | Emtricitabine and Tenofovir Disoproxil Fumarate Tablet Film-coated | 200 mg + 300 mg |
| HA562 | Efavirenz, Emtricitabine, and Tenofovir Disoproxil Fumarate Film-coated Tablets | 600 mg+ 200 mg + 300 mg |
| HA573 | Lopinavir and Ritonavir Film Coated Tablets | 100 mg + 25 mg |

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| | HA574 | Lopinavir and Ritonavir Film Coated Tablets | 200 mg + 50 mg | |
| | HA713 | Dolutegravir (Sodium), Lamivudine, and Tenofovir disoproxil fumarate Tablet, Film-coated | 50mg + 300mg + 300mg | |
| | HA714 | Efavirenz, Lamivudine, and Tenofovir Disoproxil Fumarate Tablet, Film-coated | 400mg + 300 mg + 300 mg | |
| | HA735 | Sulphamethoxazole and Trimethoprim Tablets | 400mg + 80mg | |
| | HA736 | Sulphamethoxazole and Trimethoprim Tablets | 800mg + 160mg | |
| | HA740 | Abacavir and Lamivudine Tablets | 600mg + 300mg | |
| | HA765 | Dolutegravir Dispersible Tablets | 10mg | |
| | MA176 | Primaquine Phosphate Tablets | 15 mg | |
| | TB154 | Cycloserine Capsules USP | 250 mg | |
| | TB179 | Isoniazid Tablets | 300 mg | |
| | TB230 | Moxifloxacin (as Hydrochloride) Tablets | 400mg | |
| | TB277 | Levofloxacin Tablet, Film Coated | 250mg | |
| | TB278 | Levofloxacin Tablet, Film Coated | 500mg | |
| | TB279 | Levofloxacin Tablet, Film Coated | 750mg | |
| | TB297 | Linezolid tablets | 600mg | |
| | TB307 | Pyrazinamide Dispersible Tablets | 150 mg | |
| | TB326 | Levofloxacin Dispersible Tablets | 100mg | |
| | TB342 | Moxifloxacin (hydrochloride) Dispersible Tablets | 100 mg | |
| | TB390 | Bedaquiline (as Fumarate) Tablets | 100 mg | |
| | DI005 | Zinc (as Sulfate monohydrate) Dispersible Tablets | 20mg | |
| | CV029 | Nirmatrelvir Tablet, Film-coated + Ritonavir Tablet, Film-coated | 150mg + 100mg | |
| | IN014 | Oseltamivir Phosphate Capsules | 30 mg | |
| | IN015 | Oseltamivir Phosphate Capsules | 45 mg | |
| | IN016 | Oseltamivir Phosphate Capsules | 75 mg | |
| | NT004 | Praziquantel Tablet, Film-coated | 600 mg | |

| **Abbreviations** | **Meaning** |
|---|---|
| AHU | Air handling unit |
| ALCOA | Attributable, legible, contemporaneous, original, and accurate |
| API | Active pharmaceutical ingredient |
| APR | Annual product review |
| APS | Aseptic process simulation |
| BMR | Batch manufacturing record |

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| BPR | Batch production record |
| CC | Change control |
| CFU | Colony-forming unit |
| CIP | Cleaning in place |
| CoA | Certificate of analysis |
| CpK | Process capability |
| DQ | Design qualification |
| EDI | Electronic deionization |
| EM | Environmental monitoring |
| FMEA | Failure modes and effects analysis |
| FPP | Finished pharmaceutical product |
| FTA | Fault tree analysis |
| GMP | Good manufacturing practices |
| GPT | Growth promotion test |
| HEPA | High-efficiency particulate air |
| HPLC | High-performance liquid chromatography |
| HVAC | Heating, ventilation and air conditioning |
| IQ | Installation qualification |
| LAF | Laminar air flow |
| LIMS | Laboratory information management system |
| MB | Microbiology |
| MBL | Microbiology laboratory |
| MF | Master formulae |
| MFT | Media fill Test |
| MR | Management review |
| NC | Non conformity |
| NRA | National regulatory agency |
| OQ | Operational qualification |
| PHA | Process hazard analysis |
| PLC | Programmable logic controller |
| PM | Preventive maintenance |
| 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 |
| RO | Reverse osmosis |
| SIP | Sterilization in place |
| SMF | Site master file |

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| SOP | Standard operating procedure |
| URS | User requirements specifications |
| UV | Ultraviolet-visible spectrophotometer |
| WFI | Water for injection |

| **Part 2** | **Summary of the findings and comments** |
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## 1. Pharmaceutical quality system

General

The site had a quality system that met the requirements of the current WHO GMP Guidelines, Indian Schedule M, EUDRA GMP, and US FDA CFRs. The QA/QC and production departments were independent, and both QC and QA reported to Corporate QA. The Corporate QA controls and governs the implementation and operation of the quality system. Some elements of the quality management system were assisted by computerized systems:

- TrackWise - change control, out of specification and out of trends, CAPA, deviation, and market complaints.
- Caliber DMS - Document Management System

Management review

The performance of the quality management system was reviewed monthly by management, including all department heads.

Product quality review (PQR)

The SOP outlined the objective, scope, responsibilities, and procedures for preparing PQRs, which were carried out on a rolling basis. The data were collected product-wise. The PQR documents included detailed product descriptions, batch details, investigations, RA status, validations, quality complaints, and process capability evaluations.

Change management system

The SOP on the change management system was discussed. The procedure was applied to all changes related to the manufacturing, validation, testing, holding, sampling, storage, handling, packaging, release, and distribution of drug products and drug substances. The changes were categorized as minor, major, and critical, but no specific timelines for their closure were provided.

Deviation Management

The events were defined as divergences or disobedience from written procedures or instructions. They were categorized as Critical, Major, and Minor events and addressed as incidents or investigations. The incidents were recorded in the appropriate document (e.g., BMR), then reported and managed in the TrackWise system in accordance with SOP Event Management. The required CAPAs were based on formal root cause analysis. The investigation considered the impacts on product quality, process performance/yield, GMP, qualification, calibration, validation, training, and other documents, as well as on equipment/instruments and systems. The quality tools used were FMEA (risk categorization) and HACCP (risk categorization).

Corrective and Preventive Actions (CAPA)
The corrective and preventive actions were triggered by investigations into deviations, events, incidents, and quality complaints, and were managed in the TrackWise system. The QA head approved the closure of the CAPA.

Quality risk management (QRM)
The SOP for QRM was recently revised to comply with current requirements. The procedure described the use of FMEA and HACCP tools for assessing risks. The cross-functional team evaluated risks and maintained physical logbooks.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

**2. Good manufacturing practices for pharmaceutical products**
Macleods Pharmaceutical Limited, Baddi, manufactures oral solid and liquid dosage forms in General Blocks (GB) 1, 2, and 3. The WHO prequalified products were manufactured in all three GBs. This is a shared, multi-product facility that manufactures products from different therapeutic areas. The products were manufactured on a campaign basis. The risk of contamination and cross-contamination has been minimized by providing adequate gowning, airlocks, and pressure differential.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

**3. Sanitation and hygiene**
The SOP for Fumigation in Block N2 outlined the requirements for fumigating the manufacturing areas. Fumigation was performed once per month. The fumigation was performed with a 20% Virosil solution (10% $H_2O_2$ and 0.01% Silver Nitrate) using a fogger for a minimum hold time of 1 hour. Garment washing was performed in-house using two washing machines and four dryers. After washing, garments were checked for damage before being sent for ironing.

**4. Qualification and validation**
The VMP was updated annually, identifying areas, equipment, and utilities to be validated in accordance with the respective procedures and protocols. The VMP covered the following:

- qualification of equipment/instruments,
- process validation,
- analytical method validation
- computerized system validation,
- HVAC,
- transport validation,
- vendor qualification

The validation plan was available for validating processes, cleaning, and analytical methods. Similarly, computerised systems and requalification of facilities were periodically revalidated and requalified.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

## 5. Complaints

The complaints were received by corporate QA, recorded in the TrackWise system within one working day, and the concerned manufacturing site was informed immediately. Within 2 working days of the recording, the manufacturing site acknowledges receipt of the report and initiates the investigation. The investigation deadline depends on the case classification: critical, 5 days; major, 20 days; and minor, 35 days. The investigation report was expected to be sent to the complainant within 45 days.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

## 6. Product recalls

The Procedure for Product Recall described the recall procedure, including voluntary and statutory recalls. The recall records of the Levofloxacin 500 tablet were discussed. The recall was initiated on 29/12/22 with a recall submission on 30/12/22. It was categorized as Class II at the retail level. The interim status report is sent monthly to the relevant NCA (USFDA), with the closing report on 03/12/24. The recalled units were discarded by a US local company. The discard reports were available. According to the corresponding SOP, the mock recall is due annually unless a real recall has occurred during the period. No WHO products were affected by the product recall since the previous WHO inspection.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

## 7. Contract production, analysis, and other activities

The WHO products are manufactured at Baddi (Unit-VI) without contracting out to any third parties. Some of the laboratory tests are contracted to the laboratories. This section was not inspected in detail due to time constraints.

## 8. Self-inspection, quality audits and suppliers' audits, and approval

Self-Inspection Program

The QA head or deputy certified the auditors in the qualification program's framework. Audits were performed as Level 1 (intra-department) or Level 2 (inter-department). The internal audit covered all departments and functions involved in GMP activities, including production, QC/microbiology, engineering, IT, warehouse, HR, and environmental health and safety. Level 1 audits were due quarterly by the internal team. In contrast, Level 2 audits were due twice a year by a cross-functional team. The observations were classified as Critical, Major, and Minor. The report was to be issued within 7 days, and CAPA close-out was targeted at 30 days/ or as per the action plan, with the option of extension for effective CAPA close-out.

Vendor qualification

The audits were conducted on the vendors based on red, yellow, and green flags (2, 3, and 5 years, respectively). The vendors were evaluated annually against the testing criteria. The vendor qualification reports for various suppliers were reviewed. The vendor audit schedule for APIs for the Baddi site was reviewed. The schedule included the API names, vendor names, the audit due date, and the actual date the audit was performed. Some vendors had accepted the proposed audit dates, whereas in other cases, Macleods performed a risk assessment.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

**9. Personnel**

Organograms were provided as Annexure V of the site master file. The roles and separation between production and QA were adequately depicted. The manpower details were as follows:

Production: 1136, QC: 439, QA: 305, Warehousing: 122, Engineering: 163
Human resources: 45, Accounts: 7, Information Technology: 12, Operations: 1
Production planning and inventory control: 4, Purchase: 2, Operational excellence: 1
Technical service: 17, CQA: 6, Regulatory affairs: 2

The site activity was performed in three shifts.

**10. Training**

The training was governed by the PLMS (Pharma Learning Management System). The training was mandatory for the permanent and temporary staff involved in GMP activities, covering an induction program, induction training, on-the-job training, advanced training, and required (scheduler) training. The training was delivered through self-study and classroom sessions, and the NLT criterion of 80% was set for staff members. The trainers were identified from each department based on their experience and training. The PLMS has been in use since 2019. The 2025 annual training calendar or schedule was available. The employee's tasks, responsibilities, and reporting lines were captured in up-to-date job descriptions. The job descriptions and training records of 4 production personnel were discussed (a junior officer and 3 technical associates). The training records were available and in line with the written job descriptions.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

**11. Personal hygiene**

Health and hygiene rules were outlined in the SOPs. Medical examinations were mandatory for all employees upon joining the company and then annually thereafter. The proof of the regular health checks for the four randomly selected production employees was available. The gowning of personnel entering controlled facilities was described in the SOP under the entry and exit procedure. In the production areas, a boiler suit over primary gowns, shoe covers, head covers, and masks was required. The garments were changed once daily. The general hygiene rules defined the personnel cleanliness and weekly hygiene records. The last record of the production staff was discussed.

**12. Premises**

The number of production areas by function in the inspected production blocks was as follows.

Block N2, GB-I

| | |
|---|---|
| Granulation areas | 9 |
| Compression areas | 7 |
| Coating areas | 5 |
| Capsule filling | 1 |
| Liquid line | 1 |
| Packaging lines | 1 (Bulk), 5 (blister), 1 (Pouch filling) |

| Block N2, GB-II | |
|---|---|
| Granulation areas | 11 |
| Compression areas | 7 |
| Coating areas | 5 |
| Capsule filling | 1 |
| Packaging lines | 4 (Bulk), 2 (blister) |

| Block N2, GB-III | |
|---|---|
| Granulation areas | 3 |
| Compression areas | 4 |
| Coating areas | 3 |
| Packaging lines | 2 (Bulk) and 1 (blister) |

Clean areas for manufacturing non-sterile OSD products were classified (ISO 8) and were multiproduct facilities.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

**13. Equipment**

Manufacturing equipment

The list of manufacturing equipment was included in the Validation Master Plan. The equipment had a unique ID and was part of the regular qualification, calibration, and maintenance program, including IQ/OQ/PQ and regular requalification, as outlined in the annual qualification planner compiled based on the equipment's criticality (Annual Qualification Planner, VMP Annex 12). The requalification was due every 3 years for critical equipment. The cleaning and operating procedure and the recent qualification records for the Rapid Mixer Granulator were discussed.

Measuring devices

Measuring devices were classified as “critical” and “not critical” and regularly calibrated. Critical devices: 2 times a year; non-critical devices: annually, according to the calibration policy, using the calibration planner form. The calibration protocol for pressure-type measuring devices and the recent calibration certificates for the pressure sensors installed in RMG were discussed.

Preventive maintenance program

The equipment was part of the preventive maintenance program. The program was summarized in the annual schedule, with maintenance due quarterly for critical and half-yearly for non-critical equipment. The maintenance protocol and the recent maintenance records were discussed.

Water System

The production areas were supplied with purified water by the following systems, which have not changed substantially since the last WHO inspection:

- GB1 System I/II/V( system V is for QC)
- GB2 System III
- GB3 System IV

The qualification and monitoring of System III were discussed. The loop included 13 user points, in addition to the sampling points in the supply and return loops. The PW generation and distribution layouts were available and up to date.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

**14. Materials**

The materials in GB1 were received through the receiving bay, where warehouse personnel received a phone call from the security gate notifying them of the material's arrival. After verification of the material through the SAP system, the vehicle was allowed to unload the materials. A checklist was used to record details of the material, including container conditions. The warehouse personnel prepared the GRN; labels were printed in SAP and pasted on the incoming containers. The QC was informed about the receipt of the material and the request for sampling. Until then, the material was placed in a quarantine area. At the time of the inspection, Opadry and Lactose monohydrate sampling were conducted in two separate sampling rooms. The sampling was performed by QC personnel, with a helper providing support. Similarly, primary packaging material (Aluminium printed foil) was sampled in another sampling booth. The APIs and excipients were sampled 100% for identification using Raman spectroscopy. The library was maintained in the Nano Raman handheld device. The sampling plan for the printed aluminium foil was verified and adequate. The approved raw material store was maintained at 15- 25 °C.

The procedure for dispensing raw materials was reviewed. It was noted that the materials were dispensed in accordance with the BMR and the received material list. The warehouse personnel performed the dispensing, which was verified by another warehouse personnel member and, finally, by the production personnel. A separate procedure was available for dispensing primary, secondary, and tertiary packaging materials.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

**15. Documentation**

The documentation system was hybrid. The SOPs were already managed by the Caliber DMS (Document Management System), but some documents, such as BMRs and BPRs, were still maintained as controlled hard copies. The preparation, identification, review, modification, approval (by the QA head or two deputies), and the format of the documents were well-defined. The documents were signed electronically. The printouts were time-stamped. The SOPs were prepared locally or at the corporate level. The corporate SOPs were deemed applicable after the concerned staff were trained.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

**16. Good practices in production**

The GB 1 covered the ground and first floor, whereas liquid products were manufactured on the GF and solid products on the FF. In the liquid oral manufacturing areas, the temperature was maintained at 15-25ºC, with no requirement for relative humidity. The differential pressure was maintained between 1.5 and 2.5 mm of water column and recorded twice per shift using a magnehelic gauge. Generally, the primary and secondary change rooms were adequately equipped with gowning requirements, including instructions and pictorial presentations. Separate lockers were provided for the staff to store their street clothes and shoes before entering the controlled environment. A hand-wash facility was provided, and 70% IPA was used for sanitization.

The GB 2 was spread over the ground floor, first floor, second floor, and third floor. At the third and second floors, granulation was performed; at the first floor, compression/coating was performed; and at the ground floor, packaging was performed. A similar gowning procedure was followed in GB 2 and GB 3 manufacturing areas.

The GB 3 facilities were spread across the ground, first, and second floors. The second floor performs granulation, the first floor performs compression/coating, and the ground floor performs packaging activities. Before entering the production areas, staff members go through a hand-washing facility and sanitization with 70% IPA. The materials were stored in the dispensed material hold area on the second floor. The warehouse personnel carried out the dispensing, which was verified by the production personnel. The dispensed materials were stored between 15-25ºC and less than 55% relative humidity. These materials were placed on the pellets rather than in locked cages.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

**17. Good practices in quality control**

The quality control laboratory was located on the 1st and 3rd floors of the administration building. Approximately 439 staff members were responsible for testing materials, in-process products, and finished goods.

- 1st floor: physico-chemical testing of finished products and Microbiology laboratory
- 3rd floor: RM and stability testing

The entrance to the laboratory was controlled through change rooms for chemistry and microbiology laboratories. The laboratory activities were supported by a Laboratory Information Management System (LIMS), which managed sample management, electronic test records, and the storage of chemicals, reagents, reference materials, instruments, and chromatography columns. Without interfacing with SAP, chromatography software, balances, and other electronic or computerized systems, all the data was manually entered into the LIMS. As such, the analytical test results (release) were manually uploaded to SAP. The materials were labelled, including the “Use before” date, set at 2 years after opening for general materials and 6 months for hygroscopic materials. Chromeleon and LabSolutions were used to operate and acquire data for chromatography systems. The analytical instruments were regularly qualified in accordance with the general policy, written procedures, and the annual planner. The IQ, OQ, and PQ records of the HPLC were discussed. The analytical balances were verified daily and calibrated monthly. The balance's verification and calibration records were available in the LIMS. The specification, test methods, and test records of a raw material (Tenofovir

Disoproxil Fumarate - TDF) and a finished product (Primaquine Phosphate Tablet 15 mg) were discussed.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

| Part 3 | Conclusion – Inspection outcome |
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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, ***Macleods Pharmaceuticals Limited***, located at ***Block No. N2, Village Theda, P.O. Lodhi Majra, District Solan, Tehsil Baddi, Himachal Pradesh 174 101,*** India, was considered to be operating at an acceptable level of compliance with WHO GMP 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 WHO Guidelines referenced in the inspection report |
|---|---|

1. 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. ***Short name: WHO TRS No. 986, Annex 2***
   https://digicollections.net/medicinedocs/documents/s21467en/s21467en.pdf

2. 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***
   untitled (digicollections.net)

3. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 3.
   ***Short name: WHO TRS No. 1033, Annex 3***
   9789240020900-eng.pdf (who.int)

4. 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***
   https://digicollections.net/medicinedocs/documents/s21440en/s21440en.pdf

5. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8. **Short name: WHO TRS No. 1010, Annex 8**
https://digicollections.net/medicinedocs/documents/s23455en/s23455en.pdf

6. 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***
https://digicollections.net/medicinedocs/documents/s20108en/s20108en.pdf

7. WHO good practices for pharmaceutical quality 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. 961, 957), Annex 1***
https://digicollections.net/medicinedocs/documents/s18681en/s18681en.pdf

8. 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 3.
***Short name: WHO TRS No. 957, Annex 3***
https://digicollections.net/medicinedocs/documents/s22358en/s22358en.pdf

9. 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***
https://digicollections.net/medicinedocs/documents/s19959en/s19959en.pdf

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***
https://digicollections.net/medicinedocs/documents/s18677en/s18677en.pdf

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**
https://digicollections.net/medicinedocs/documents/s18683en/s18683en.pdf

12. General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-first Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3. ***Short name: WHO TRS No. 943, Annex 3***
https://digicollections.net/medicinedocs/#d/s21438en

13. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2.
***Short name: WHO TRS No. 961, Annex 2***
https://digicollections.net/medicinedocs/documents/s18682en/s18682en.pdf

14. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2.
***Short name: WHO TRS No. 981, Annex 2***
https://digicollections.net/medicinedocs/#d/s20177en/

15. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3.
***Short name: WHO TRS No. 981, Annex 3***
https://digicollections.net/medicinedocs/#d/s20175en/

16. WHO guidelines for drafting a site master file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 14.
***Short name: WHO TRS No. 961, Annex 14***
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

17. Good Manufacturing Practices: Guidelines on validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-third Report Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 3. ***Short name: WHO TRS No. 1019, Annex 3***
https://digicollections.net/medicinedocs/documents/s23697en/s23697en.pdf

18. WHO General guidance on hold-time studies WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4. ***Short name: WHO TRS No. 992, Annex 4***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

19. WHO Technical supplements to Model Guidance for storage and transport of time – and temperature – sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 5. ***Short name: WHO TRS No. 992, Annex 5***
Essential Medicines and Health Products Information Portal (digicollections.net)

20. WHO Recommendations for quality requirements when plant – derived artemisin is used as a starting material in the production of antimalarial active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 6
***Short name: WHO TRS No. 992, Annex 6***
https://www.who.int/publications/m/item/who-recommendations-for-quality-requirements-when-plant-derived-artemisinin-is-used-as-a-starting-material-in-the-production-of-antimalarial-active-pharmaceutical-ingredients---trs-992---annex-6

21. Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4. ***Short name: WHO TRS No. 1033, Annex 4***
9789240020900-eng.pdf (who.int)

22. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
***Short name: WHO TRS No. 996, Annex 10***
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

23. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 10.
***Short name: WHO TRS No. 1010, Annex 10***
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

24. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditionning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-third Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1019), Annex 2. **Short name: WHO TRS No. 1019, Annex 2**
https://digicollections.net/medicinedocs/documents/s23699en/s23699en.pdf

25. Points to consider when including Health-Based Exposure Limits in cleaning validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 2. **Short name: WHO TRS No. 1033, Annex 2**
9789240020900-eng.pdf (who.int)

26. Points to consider for manufacturers and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 6. **Short name: WHO TRS No. 1025, Annex 6**
9789240001824-eng.pdf (who.int)

27. Production of water for injection by means other than distillation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 3. ***Short name: WHO TRS No. 1025, Annex 3***
https://www.who.int/publications-detail/978-92-4-000182-4

28. Good chromatography practice. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 4. ***Short name: WHO TRS No. 1025, Annex 4***
https://www.who.int/publications-detail/978-92-4-000182-4