

## WHO PUBLIC INSPECTION REPORT (WHOPIR)

### Finished Product Manufacturer

#### Part 1: General information

Name of Manufacturer	<b>MacLeods Pharmaceuticals Ltd - Baddi</b>
Unit number	Unit VI
Production Block	N2
Physical address	<b>Village Theda, P.O. Lodhi Majra, Tehsil Nalagarh, District Solan, Himachal Pradesh 174101, INDIA.</b>
Contact person and email address.	Mr. Sushil Jaiswal (Mobile: +91-98-6755 5463, e-mail: sushil@macleodspharma.com) Tel. HQ: +91-22-6676 2800, Site: +91-1795 661400 Fax: +91-1795 661452 E-mail: <a href="mailto:sushil@macleodspharma.com">sushil@macleodspharma.com</a>
Date of inspection	17, 18, 19 and 20 March 2009
Type of inspection	Routine Inspection
Dosage forms(s) included in the inspection	Hard gelatine capsules (plus tablets, oral solutions) with focus on Tuberculosis (TB) and HIV/AIDS products.
WHO product categories covered by the inspection	<b>Products used in the treatment of Tuberculosis (TB) and HIV/AIDS</b>
Summary of the activities performed by the manufacturer	Manufacturing, packaging, quality control and batch release of hard gelatine capsules (plus tablets, oral solutions).

## **Part 2: Summary**

### *General information about the company and site*

The facility inspected was Block **N2** of **MacLeods Pharmaceuticals Ltd, Unit VI**, located at Village Theda, P.O. Lodhi Majra, Tehsil **Nalagarh**, District Solan, **Himachal Pradesh 174101, INDIA, here after called MacLeods - Baddi**. According to the Site Master File, No.: MPL/N2/SMF/02, effective 02/09, MacLeods Pharmaceuticals Ltd had Corporate headquarters in Atlanta Arcade, Andheri (E), Mumbai India, Research & Development Centre in Mumbai and six manufacturing facilities across India.

MacLeods Baddi is located about 302km north of Delhi and the nearest airport is 60km away at Chandigarh on a 52732m<sup>2</sup> site of which 9013m<sup>2</sup> was built up. It had 3 independent manufacturing facilities, namely:

- 1) Block N1: Small Tablet and Soft Gelatine Block
- 2) Block N2: General Block
- 3) Block N3: Cephalosporin Block

**Block N2 of MacLeods Baddi, which was the only focus of this inspection**, was designed to manufacture Oral Solid Dosage forms (Hard Gelatin Capsules and Tablets) and Oral Liquid Dosage forms.

The site included storage areas for starting materials, manufacturing areas, testing areas (analytical and microbiological) finished goods stores, supportive engineering services and quality assurance.

According to the SMF, the plant employed a total of 165 people: 31 in Production, 56 in Quality Control, 34 in Quality Assurance, 9 in Stores for N2, 25 in Utilities, 4 in Personnel & Administration and 6 in Accounts/IT/Purchase.

### *History of WHO and/or regulatory agency inspections*

This was the first time the site of MacLeods Baddi (Unit VI) was being inspected by WHO Prequalification team. The manufacturing facility was licensed by the Food and Drug Administration of Himachal Pradesh (MB/07/593 and MNB/07/594).

### *Focus of the inspection*

The inspection focused on the production and control of the products listed in Part 1 above and activities in **Block N2**. The inspection covered all the sections of the WHO GMP text, including premises, equipment, documentation, materials, validation, sanitation and hygiene, production, quality control and utilities.

### *Inspected Areas*

#### **Day I**

WHO Public Inspection report (WHOPIR):

**MacLeods Pharmaceuticals Ltd - Baddi**, Theda, Nalagarh, Himachal Pradesh, **INDIA**

17, 18, 19 and 20 March 2009

Page 2 of 24

On arrival, the inspectors were directed into the conference room, introduced themselves and exchanged business cards. They explained the procedure for WHO Prequalification Programme, the procedures and standards used for inspection including the newly introduced Notice of Concern (NOC) and elaborated on the tentative inspection plan. After confirming the inspection plan, the company made a presentation about the company and the site to be inspected. The presentation highlighted the capacities, Quality Management System, product range and other specific features of the site. A copy of the presentation was obtained and will be filled in the company file.

This was followed by a review of documents related to quality management system:

- ⇒ Organization charts
- ⇒ Job descriptions of key personnel.
- ⇒ SOP on Preparation, Approval and Control of Standard Operating Procedures
- ⇒ SOP Indexes.
- ⇒ SOP on Document and Data Control
- ⇒ SOP on Issue and Control of Formats and Books/Registers
- ⇒ SOP on Handling of Deviations. The selected examples reviewed included:
  - Retesting of one product capsules to IP requirements.
  - Resanitising the water loop ahead of schedule to accommodate a weekend shut down.
  - Recording three separate product potency calculations when making one virgin batch from three separate batches of API.
- ⇒ SOP on Change Control. Records for the following changes were examined:
  - Transfer of a balance between coating area I to coating area 2
  - Access control between blocks N2 and N3 and QC
  - A coating pan replacement (Ganscoater)
  - Change of BPR for an Oral Suspension product. One lot to be repacked into different packing configuration.
  - Regulatory updates for Cephalosporin block SMF. Updated SMF of 14/2/09 confirmed the change.
  - Introduction of one product to the Baddi site.
  - BMR changes.
  - Regulatory change of impurity limits of one of the APIs.
- ⇒ SOP on Handling of Out-of-Specifications. An OOS report concerning a zero result on the 5<sup>th</sup> vessel of a tablet dissolution test was reviewed. Discussion showed that the sample taken from the vessel for analysis had been poorly prepared.
- ⇒ SOP on Simulated Hold Time Studies
- ⇒ SOP on Batch Release Procedure
- ⇒ SOP on Allotment of Batch Number
- ⇒ Several BMR/BPR Issue Registers.
- ⇒ SOP on Assigning of Manufacturing and Expiry Date
- ⇒ SOP on Self Inspection
- ⇒ SOP on Annual Review of Drug Product Quality. Selected reports were reviewed in detail.
- ⇒ SOP on Production Planning

WHO Public Inspection report (WHOPIR):

**MacLeods Pharmaceuticals Ltd - Baddi**, Theda, Nalagarh, Himachal Pradesh, **INDIA**

17, 18, 19 and 20 March 2009

Page 3 of 24

- ⇒ List of products.
- ⇒ SOP on Reprocessing, Recovery and Reworking. Whilst the company defined rework, reprocessing and recovery, none of these was permitted.

At the end of the day, the team reviewed progress of the activities of the day, gave feed back, received reactions from the management of the company and agreed on the tentative programme for the next day.

## **Day 2**

The inspectors started by reviewing the progress of the inspection and outlining the day's programme. Thereafter, the following documents related to the site layout and utilities were reviewed, followed by an orientation tour of the site:

- ⇒ Site plan, production block layout, indicating the area classification, HVAC system, AHU's and dust extraction system, material and personnel flow.
- ⇒ HVAC system schematic drawing and summary of specifications for HVAC
- ⇒ Qualification/Requalification/Monitoring the HVAC System. The qualification (URS, DQ, IQ, OQ and PQ) of AHU serving compression II and AHU serving the wet granulation, sifting and binder preparation rooms as described in the above reports were reviewed in detail.
- ⇒ SOP on Operation of Air Handling Systems
- ⇒ SOP on Filter Cleaning Procedures
- ⇒ PW system drawings and summary of specifications and capacities.
- ⇒ Qualification/Requalification/Monitoring the PW system (Sampling and trend analysis)
  - Phase 1 Qualification Protocol.
    - DQ: User Requirements and System Specifications.
    - IQ: Installation Qualification was by the maker. Examples taken for assessment included the two major circulation pumps, and the RO cartridge material.
    - OQ: Operational Qualification. Random selection of data for valves controlling flow rate were assessed together with the actual flow calculations.
    - PQ: The water was sampled daily from each take off point for three weeks. Sampling followed an SOP which described the scheduled sampling points and the sampling technique. A specified sample of raw water was filtered using the Millipore assembly.
  - Phase 2 Qualification: Water samples were taken over a period of 30 days.
  - Phase 3 Qualification: Water was regularly sampled throughout the year and covered all take off points. Water was tested using the membrane filtration method.
- ⇒ Compressed air system schematic drawing and summary of specifications for Compressed Air system
- ⇒ Qualification/Requalification/Monitoring the Compressed Air systems

The inspectors then proceeded to inspect installations of the HVAC Systems, Water Generation and Purification System and Compressed Air System.

WHO Public Inspection report (WHOPIR):

**MacLeods Pharmaceuticals Ltd - Baddi**, Theda, Nalagarh, Himachal Pradesh, **INDIA**

17, 18, 19 and 20 March 2009

Page 4 of 24

At the end of the day, the team reviewed progress of the activities of the day, gave feed back, received reactions from the management of the company and agreed on the tentative programme for the next day.

### **Day 3**

The day started with management showing the DVD of the airflow patterns during initial qualification and subsequent requalification.

The inspectors proceeded to inspect the change rooms, receiving areas, sampling areas, quarantine area, under test area plus warehouses for approved raw materials, primary packaging materials, secondary packaging materials and pre-printed packaging materials and the dispensing areas. SOPs and related records in these areas were reviewed, the following in detail:

- ⇒ SOP on Entry and exit of personnel in the factory premises.
- ⇒ SOP on Entry and exit of visitors into production area.
- ⇒ SOP on Entry and exit of Male and Female Staff in the Production Area.
- ⇒ SOP on Cleaning of primary change room of production area.
- ⇒ SOP on Receipt of Raw Materials and Packaging Materials.
- ⇒ SOP on Cleaning and operation of Vacuum Cleaner.
- ⇒ Approved Vendor List - Raw Materials.
- ⇒ SOP on Entry and exit into sampling booth area.
- ⇒ SOP on Sampling, testing, release and reject of Raw Materials.
- ⇒ SOP on Operation and Cleaning of Sampling booth (RM).
- ⇒ SOP on Cleaning and usage of sampler and sampling devices (Raw Materials).
- ⇒ SOP on Dispensing of Raw Materials.

The inspectors proceed to inspect the production area and activities following the flow of production of hard gelatine capsules, coated and uncoated tablets and oral solutions. The related SOPs use and cleaning logs, BMRs and BPRs were reviewed, the following in detail:

- ⇒ Sieving, granulation, FBD, milling, and blending of a specific lot of tablets in Granulation area.
- ⇒ SOP on Cleaning and utilization of FBD finger bag and RMG filter bag.
- ⇒ SOP on Cleaning and operation of Fluidized Bed Drier.
- ⇒ SOP on Cleaning and operation of vibrator sifter.
- ⇒ SOP on Issue, use and retrieval of punches and dies.
- ⇒ SOP on Inspection of punches and dies.
- ⇒ SOP on Polishing of punches and dies.
- ⇒ SOP on Cleaning and Operation of a Double Rotary Compression Machine.
- ⇒ Coating of one lot of tablets.
- ⇒ Compression of one lot of tablets.
- ⇒ SOP on Cleaning and operation of Sparkler filter press.
- ⇒ SOP on Cleaning and operation of process line in liquid orals.
- ⇒ SOP on Cleaning and operation of Lube transfer pump.
- ⇒ SOP on Sanitisation of drain points.

WHO Public Inspection report (WHOPIR):

**MacLeods Pharmaceuticals Ltd - Baddi**, Theda, Nalagarh, Himachal Pradesh, **INDIA**

17, 18, 19 and 20 March 2009

Page 5 of 24

- ⇒ SOP on In-process checks in liquid oral manufacturing, filling and packing line.
- ⇒ SOP on Cleaning and operation of leak test apparatus for filled and sealed bottle.

At the end of the day, the team reviewed progress of the activities of the day, gave feed back, received reactions from the management of the company and agreed on the tentative programme for the next day.

#### **Day 4**

The team started with a review of documents related to some of the outstanding issues from the previous day inspection.

The validation and qualification system was evaluated. Cleaning validation, approach, protocols and reports of selected equipment and products were reviewed together with report of the validation of the analytical methods used. The following related documents were evaluated in detail:

- ⇒ Validation policy.
- ⇒ Validation Master Plan.
- ⇒ Calibration policy.
- ⇒ Process validation protocol and report for one of the products.
- ⇒ Master Manufacturing formula and BMR for one of the products plus the corresponding executed BMRs for two batches.
- ⇒ Cleaning validation protocol and report.
- ⇒ Report of the Hold time study for dirty and clean equipment.
- ⇒ Equipment qualification (DQ, IQ, OQ and PQ for major equipment), Calibration and preventive maintenance. The qualification of the following equipment was reviewed in detail:
  - RLAF sampling booths (2).
  - RLAF dispensing booth
  - Capsule filling machine.
  - Metal detector.
  - Monoblock Filling and Sealing Machine, SOP and related training.
  - Vibro Sifter.

Vendor approval and qualification system was reviewed covering vendor development, qualification, dequalification and requalification procedures for Raw Materials. The audit report of the supplier of one of the anti-TB APIs by Macleods was assessed in details. Reports of evaluation of suppliers of randomly selected excipients and empty hard gelatin Capsules were reviewed.

Selected Batch Manufacturing Records of the products in focus were reviewed and the respective annual product review reports for the products for the year 2008.

The team then proceeded to inspect the following QC laboratory areas:

- ⇒ Sample receiving, storage and allocation procedure plus related records.
  - SOP on Sample receipt in QC.

WHO Public Inspection report (WHOPIR):

**MacLeods Pharmaceuticals Ltd - Baddi**, Theda, Nalagarh, Himachal Pradesh, **INDIA**

17, 18, 19 and 20 March 2009

Page 6 of 24

- SOP on Assigning of analytical reference number.
- SOP on Sampling, testing, release and rejection of raw materials.
- ⇒ Training and qualifications:
  - The training records for some analysts were selected at random and found to be satisfactory.
- ⇒ Wet chemistry laboratory (4)
- ⇒ Instrumental laboratory
  - Qualification, calibration, preventive maintenance
- ⇒ Laboratory materials management (Samples, Reagents, Stock Solutions, Reference and Working Standards)
- ⇒ Microbiological laboratory
  - Room and equipment
  - Media preparation and product testing
  - PW monitoring
  - Environmental monitoring
- ⇒ Starting materials and finished products Specifications
- ⇒ Validation of Analytical methods
- ⇒ Stability chambers and stability testing programme
- ⇒ Control samples
- ⇒ Packaging materials

The QA and QC SOPs, testing procedures, specifications and related records were reviewed, the following in detail:

- ⇒ SOP on Sample receipt in QC
- ⇒ Sample receipt record (in-process, validation, cleaning and finished product samples)
- ⇒ Format of RM sample receipt record
- ⇒ SOP on Assigning of Analytical Reference Number (ARN)
- ⇒ Work allotment record
- ⇒ Analyst validation report for one of the analysts for Assay of one of the APIs.
- ⇒ Specifications, Standard Testing Procedures and Analytical Data Sheets for selected APIs.
- ⇒ Standard Testing Procedures and Analytical Data Sheets for selected excipients.
- ⇒ SOP on Qualification and storage of laboratory working standards.
- ⇒ Records for preparation of selected Working Standards.
- ⇒ Certificates of selected RS and impurity standards.
- ⇒ Qualification report for the fridge used to store RS and WS for N2 block.
- ⇒ SOP on procedure for operation, calibration and monitoring of stability chambers.
- ⇒ Stability Chamber Charging Record for 25<sup>0</sup>C/60%RH conditions.
- ⇒ Stability Chamber Charging Record for 40<sup>0</sup>C/75%RH conditions.
- ⇒ Stability Chamber Charging Record for 30<sup>0</sup>C/65%RH conditions.
- ⇒ Sample Withdrawal and Reconciliation Record for 30<sup>0</sup>C/65%RH conditions.
- ⇒ SOP on Post production stability studies.

Records related to qualification, calibration and routine maintenance of laboratory equipment were reviewed, with detailed evaluation of records for randomly selected HPLC, UV visible spectrophotometer, Fourier Transfer IR, Dissolution Tester, analytical balances, pH meters, Melting Point apparatus, Conductivity Meter and Auto Titrators.

Records of sampling and testing selected APIs, excipients, finished products, components and packaging materials were reviewed.

The training policy, SOP, programme plus training records of specific sessions and selected individuals were reviewed.

The system for handling customer complaints, the customer complaints register and selected complaints plus the corresponding investigation reports were reviewed. This was followed by a review of the Product recall system and related mock recall report.

At the end of the day, the team reviewed progress of the activities of the day and the entire inspection, gave feed back and wrap up for the inspection and received reactions from the management of the company. There was consensus of the all the observations made.

## **2.1 QUALITY ASSURANCE**

The quality assurance procedures were summarized in the Quality Manual and enshrined in the Quality Policy.

There was an organization chart and job descriptions specifying the responsibilities and reporting relationships of the various staff. Although the job descriptions were very detailed, clarity of the designation and regrouping into major and lesser responsibilities was recommended.

Equipment and systems had been qualified and procedures and processes validated. The quality of the systems, procedures and products were regularly reviewed and monitored through an elaborate self inspection procedure and annual product review.

All the routine procedures were guided by clear, written and approved procedures and any changes were controlled and deviations were documented and their impact assessed.

### **Change control:**

Change was managed using an approved SOP and changes were classified as either documentation (CCD) or facility based items (CCF). The former comprised mainly of changes in support documents related to products being sequentially introduced into the plant. A conventional approach was adopted where the need for change was identified followed by an impact analysis which also considered regulatory aspects. Relevant departments were involved in the approval/rejection process.

### **Technology Transfer:**

Transfer of Technology was included in the change control programme. The transfer of one of the products from Kachigam-Daman to Baddi was well documented in a Change Control.

### **Handling Out-of-Specification results:**

Out-of-Specification (OOS) results were managed by following an approved SOP. The procedure included tracing assignable cause to laboratory error or production error. Details on

sampling and re-sampling were given. OOS did not necessarily result in a rejection. No outlier tests were permitted when data was assessed.

#### **Deviations:**

Deviations were managed by following an approved SOP. They were grouped into planned and unplanned categories. The records for 2008 and 2009 to date confirmed the company's assertion that no unplanned deviations had occurred. Planned deviations reflected the development of where changes are inevitable. All the deviations reviewed were well documented and authorized by the appropriate person/s.

#### **Annual Product Review:**

There was a system for annual product quality review managed by an approved SOP.

The reports of selected products of interest were reviewed in detail. As one of the products still had a short history at Baddi, only limited information was available. Three batches: were manufactured in January 2008 and had been placed on a stability trial. All had been reviewed before March 2009. Master Manufacturing formula and Packaging specifications were used. This was pertinent to primary packaging only as cartons; PIL's etc had yet to be developed. The Batch Manufacturing Record and Packing Record were complied with. Raw materials and components used were all tested and released. There were no non conformances noted nor were there any OOS incidents. Complaints, returns and recalls are not applicable in this case.

Although no matters of concern were noted, it was recommended that this aspect of the company's performance is closely monitored in the future.

## **2.2 GOOD MANUFACTURING PRACTICES (GMPs) FOR PHARMACEUTICAL PRODUCTS**

The available facilities at the site, the manufacturing and quality control procedures were comprehensive and well executed and maintained by adequately qualified personnel to ensure products of consistent quality.

There were minor observations, as described in the sections that follow and summarized in a separate table of observations, that required attention to further improve the degree of GMP compliance.

## **2.3 SANITATION AND HYGIENE**

There were procedures to enhance hygiene on the site. Personnel changing procedures, cleaning procedures for the equipment and the premises, waste collection procedures plus the design of the HVAC system ensured a high level of hygiene of premises.

## **2.4 QUALIFICATION AND VALIDATION**

WHO Public Inspection report (WHOPIR):

**MacLeods Pharmaceuticals Ltd - Baddi**, Theda, Nalagarh, Himachal Pradesh, **INDIA**

17, 18, 19 and 20 March 2009

Page 9 of 24

There was a Validation Master Plan which outlined the policy and approaches to be followed in qualification of equipment and validation of systems and processes. The approach qualification included definition of User Requirements Specifications (URS), Design Qualification (DQ), Installation, Commission, Installation Qualification (IQ), Operation Qualification (OQ) and Performance Qualification (PQ). The conditions requiring requalification were specified as major changes, repairs following major breakdowns, changes in computer hardware or software, change in specifications or acceptance criteria, relocation of equipment. otherwise requalification was required every 1 year  $\pm$  1 week for AHUs and 2 years  $\pm$  2 weeks for other equipment and systems. There were schedules for requalification, revalidation and preventive maintenance and records showed that they were being followed. Reports showed that equipment was qualified and systems and process were validated.

Cleaning validation had been done to validate cleaning procedures, hold times of uncleaned and cleaned equipment. Swab recovery studies, analysis of rinse residues and microbial limit studies were used and the acceptance criteria used included: visual clean, not more than 10ppm of residue, maximum allowable residue in the maximum dose of the next product and NMT 50cfu/m<sup>3</sup>. Validated HPLC and UV analytical methods were used concurrently during cleaning validation but UV methods were used for routine monitoring after cleaning for product change. Three consecutive validation commercial scale batches were used in validation.

### *Validation*

Process Validation was managed using a protocol and involved a multidisciplinary team. Responsible QA personnel signed off all stages when satisfactory. Process validation protocol and report of selected products were reviewed in detail and the process validation records gave no matters of concern.

### *Qualification*

There was a system and programme for qualification of key equipment. This followed definition of User requirement specifications (URS), Design Qualification (DQ), Installation Qualification (IQ), Operation Qualification (OQ) and Performance Qualification (PQ).

Review of qualification of selected equipment (RLAF sampling booths, RLAF dispensing booth, capsule filling machine, metal detector, mono block filling and sealing machine and vibro sifter) showed that the equipment were adequately qualified.

## **2.5 COMPLAINTS**

There was a system to record and investigate market complaints and feed back was promptly given and appropriate corrective and preventive action taken in most cases reviewed.

## **2.6 PRODUCT RECALLS**

There was a recall procedure which had described the deficiencies that would require a recall, the means of communication to be used, the timelines to conclude the recalls, composition of the recall committee and the parties to be informed while conducting a recall.

There was a procedure to conduct mock recalls at least once very two years in order to evaluate the effectiveness of the recall procedures. The last mock recall was initiated on 17<sup>th</sup> March 2007.

## **2.7 CONTRACT PRODUCTION AND ANALYSIS**

The company did not carry out any contract production. Only specialized analytical procedures were contracted out and in such circumstances there was a contract that complied with the principles of GMP. The contracts defined the responsibilities if the contract giver and contract receiver.

For example, there was a sub contractor laboratory for some aspects of raw material analysis. The laboratory had been audited and a technical agreement was in place. The laboratory was also audited by the Indian authorities.

## **2.8 SELF INSPECTION AND QUALITY AUDIT**

There were procedures to conduct self inspection on once in six months' basis for the purposes of monitoring the quality system and continuous improvement of the procedures. This procedure was comprehensive and covered all areas of production, quality control, quality assurance and engineering. There was a schedule with defined teams and the record showed that the schedule was complied with.

### **Vendor Audit Programme:**

Vendor audits were part of the vendor approval and qualification procedure. Audits followed an approved Standard Operating Procedure. The supplier reports seen followed the SOP in force at the time.

A detailed questionnaire preceded any actual audit. Manufactures supplying materials of animal origin were asked for TSE certification. The audit report of the supplier of one of the anti-TB API, by Macleod's was assessed. Several observations were reported in the audit report. A second audit report (follow – up audit) purporting to demonstrate some improvement was in draft form but was not presented for inspection. It was later presented showing that the supplier had improved and was now compliant.

## **2.9 PERSONNEL**

The personnel met were well qualified to perform the duties assigned and had a high consciousness of GMP. There was an organization chart and job description to guide personnel. The responsibilities of the key personnel like head of production, head of quality control and head of quality assurance were well defined and there were personnel designated

to deputise the key personnel in their absence. The responsibility for batch review and release was assigned to head of QA.

## **2.10 TRAINING**

The company had had a comprehensive training program for all the employees. This was coordinated by the QA department but the concerned department head identified the training needs of each employee based on qualification, previous experience and job assigned to the employee. Training programs were divided into two categories:

- ⇒ Basic training: general discipline, basics of GMP, Hygiene & Sanitisation, Safety, entry/exit procedures.
- ⇒ In-service training: Operating instruction of production machines, Job related Training (SOPs Training), maintenance of BMRs and GLP training.

Written and oral examinations were used to identify retraining needs and training records were monitor and evaluate the training activities.

## **2.11 PERSONAL HYGIENE**

Personnel were trained in personal hygiene procedure and facilities were provided in form of change rooms, protective garments and disinfectants.

The health of staff was monitored at least once year through medical examinations. Staffs with contagious diseases or open lesions were required to report to the immediate supervisor and were not allowed in areas that may potentially contaminate the product.

Eating, chewing of tobacco, smoking and consumption of alcoholic beverages was prohibited in the factory premises.

## **2.12 PREMISES**

### ***Raw material receiving areas and warehouses***

Areas were provided at the ground floor for goods receipt, initial clean down using a vacuum cleaner and quarantine/finished goods. The goods unloading dock was accessed via an airlock. Both sets of doors were open at times despite clearly displayed instructions to the contrary. There were separate sampling rooms each fitted with RALF cabinets for the raw materials and packaging materials.

The storage facilities allowed for effective segregation and security of materials and products at different stages of processing and those rejected. All areas were in a good state of cleanliness and maintenance.

Environmental conditions (Temperature and RH) in the warehouse were regularly monitored and mapping had been completed. Records showed that the conditions were appropriate for the goods held therein.

WHO Public Inspection report (WHOPIR):

**MacLeods Pharmaceuticals Ltd - Baddi**, Theda, Nalagarh, Himachal Pradesh, **INDIA**

17, 18, 19 and 20 March 2009

Page 12 of 24

Pest control was managed by an outside contractor. Glue traps for rodents were located at defined places near the entrances.

### ***Packaging Materials Warehouse***

Entrance to the warehouses was restricted. The packaging materials were housed on the ground floor. All areas were clean and tidy.

Temperature and RH in the warehouse were monitored using wet and dry bulb thermometers and mapping had either been completed in some areas or was on going in others. A discrepancy in the readings of two wet bulb thermometers in close proximity in the component store RG33 was noted. This was traced to one unit having a dry bulb instead of wet which resulted in an excessive temperature depression and was corrected instantly and recorded according to the deviation procedure.

### ***Dispensing Rooms***

There were two dispensing rooms, both for raw materials each fitted with a RALF cabinet. Entrance to the dispensing room was through change rooms where appropriate gowning took place.

### ***Production areas***

There were two floors in Block N2. Entry into the premises was restricted only through well designed change rooms using coded key cards. Toilet facilities were located on the side prior to hand wash and gowning. The entrance procedure was controlled using approved SOPs (for visitors change room, Entry and exit of personnel in the factory premises; Entry and exit of Male and Female Staff in the Production Area) and appropriate protective clothing were used. The Jewellery policy was neither rigorously nor consistently enforced. There was pictorial representation of gowning procedure. The area was cleaned following an approved SOP.

The location, design, construction and maintenance of the premises were suitable to support production and storage of quality products. The general condition of the room finishes was of a high order. Settlement cracks were repaired immediately upon discovery. The design supported unidirectional flow of the manufacturing processing and there was adequate space for placement and operation of the equipment. The construction of the premises plus the installation of equipment and utilities enabled effective cleaning and maintenance.

There was a well designed HVAC system and dedicated dust extraction system to provide a conducive environment for manufacturing and to avoid cross-contamination.

Exhaust air from several AHUs serving several rooms and corridors was collected and could potentially be mixed with fresh air in one Treated Fresh Air (TFA) Unit. Although the air to all critical areas was filtered through H13 HEPA filters, a risk assessment would be advisable to rule out any potential for cross contamination. It was not clear in the AHU qualification

protocol whether the limit of  $\pm 20\%$  variation of the air velocity across filters given as the acceptance criteria was with respect to the actual average velocity or design average velocity.

### ***Quality Control Laboratory***

The quality control laboratory consisted of the following main sections: sample receiving area, 3 chemistry laboratories, instrument room, Reference Standards room, Dissolution room, stability section, Polarimeter and TOC room. The facility was well decorated and in a good state of maintenance. The furniture and bench tops were well maintained. Standard services such as a fume extraction hood, water electricity, drainage were available. There were safety facilities in form of eye shower and safety shower in case of accidental contact with corrosive chemicals.

There was a separate microbiology laboratory with sample preparation; sample incubation and examination; maintenance of reference organisms; media and equipment preparation and sterilization; decontamination.

### ***Water purification system***

The installation was 2 years old. The detailed schematic was available in the Site Master File. The configuration was an orthodox RO system fed by bore well water, which had been softened in the conventional manner. Pre-softened water was stored in underground concrete storage tanks, which were regularly cleaned and sanitized with sodium hypochlorite solution by an outside contractor. A technical agreement was in place. The system was managed using an approved SOP. Treated raw water was then used to service Blocks N2 and N3, the boiler house, HVAC cooling tower and generator cooling tower.

An SOP described the operating instructions of the modules comprising the purification system.

The purification system was housed in a well-decorated and well-maintained room. No evidence of pipe leakage was seen. All gauges and flow meters were tagged with their service dates. The RO units were arranged in series. A flow rate of  $3.6 \text{ m}^3/\text{hour}$  was achieved and the in line conductivity meter gave a steady reading of  $9.2 \mu\text{s}$ .

The water was finally purified using an EDI unit followed by a final  $0.01\mu$  filtration and UV irradiation, the latter set to run for 7000 hrs before replacement. Continuous on line monitoring of pH, TOC and conductivity was in place. The conductivity regularly achieved was of the order of  $1.25\mu\text{s}$  and TOC was  $60\pm 10$  ppb. An outside contractor calibrated the in line TOC meter annually.

Water was stored in a stainless steel storage tank fitted with a  $0.45\mu$  hydrophobic vent filter. The take off points on the loop were incorporated into ceiling pendants in the work areas. Dead legs were minimal (less than 1.5 pipe diameters). Circulation was continuous and the flow rate of  $1.2\text{m}/\text{sec}$  satisfied the USP requirement, which prevents build up of bio-films.

WHO Public Inspection report (WHOPIR):

**MacLeods Pharmaceuticals Ltd - Baddi**, Theda, Nalagarh, Himachal Pradesh, **INDIA**

17, 18, 19 and 20 March 2009

Page 14 of 24

Not less than  $3 \times 10^3$  litres/hr was produced. And this comfortably satisfied the projected usage when in constant use.

The pipe work of the softening system was made of galvanized iron and thereafter it was in 316L stainless steel. The pipe work welding was electro polished and certified. Photographic evidence was provided.

The loop was regularly sanitized by circulating the hot water from the steam-heated jacketed holding tank. The pipe runs as far as the EDI unit were chemically sanitized while the EDI was hot water sanitized. Three solutions were used to remove in turn Silica, Iron and Bio-film Colloids from RO membranes.

The system went through DQ, IQ, OQ and three phases of PQ and the documents available showed that the system was well qualified, maintained, operated and sanitised.

PQ was satisfactory as evidenced by the water samples taken for microbial assessment. During Phase 1, the water was sampled daily from each take off point for three weeks following an approved SOP. The scheduled sample points and the sampling technique were all adequately described. A specified sample of raw water was filtered using the Millipore assembly. Initial results for raw water were 157cfu/ml (no pathogens) but fell to 85 by the third week. This was reportedly due to continuous flushing of the system. Initial results for the purified water were of the order of 40 cfu/ml (pathogens absent, McConkey and selenite growth media) but after three weeks continued sampling the last point in the return loop returned levels between 1 and 12 cfu/ml (USP specification NMT 100 cfu/ml).

During Phase 2 Qualification, water samples were taken over a period of 30 days. The results were satisfactory.

During Phase 3 Qualification, water was regularly sampled throughout the year and covered all take off points. Water was tested using the membrane filtration method. Raw data seen during the microbiology laboratory audit showed levels of the order of between 3 and 5cfu/ml with absence of pathogens. Computer generated trend charts showed a level performance with an alert limit set at 60cfu/ml. This is well below the USP maximum of 100cfu/ml. It was suggested that the alert limit could be lowered to a level more representative of the actual levels being found.

### ***Compressed Air***

Compressed air was supplied from an oil-free compressor with an installed air dryer. It was operated by following an approved SOP. The air was filtered at point of use and was subject to pre-programmed maintenance. The design and records showed that the system produced oil-free (non-lubricated) and moisture free compressed air.

### ***Nitrogen Generator***

Nitrogen was acquired by passing compressed air through a molecular sieve. The nitrogen was then scrubbed dry with activated alumina.

An oxygen analyser was used to monitor O<sub>2</sub> content and the level of 0.1% inferred that nitrogen was at least 99.9% pure.

### **2.13 EQUIPMENT**

There were adequate numbers of equipment for the production and testing products manufactured at the site. They were generally well designed, had been qualified and they were regularly calibrated and maintained. The contact parts for all equipment were made up of SS316 or SS316L. All pieces of equipment were identified and had the appropriate status labels (clean, previous product, current product) attached.

Some production equipment was designed with PLC control system and the related software had been validated. Some equipment had WIP/CIP systems for cleaning and these too had been validated.

There were use, cleaning and maintenance logs for each piece of equipment.

The preventive maintenance programme was managed using an SOP for each specific piece of equipment. SOPs and records of maintenance of selected equipment were reviewed and the preventive maintenance programme was assessed to be generally adequate and effective. The frequency of stoppages of the Monoblock Filling and Sealing Machine witnessed during the course of inspection indicated a need for requalification and/or maintenance. Requalification has been done.

### **2.14 MATERIALS**

#### *Goods in and materials management*

Receipt of goods followed the standard routine according to an approved SOP. A computer database (ERP system) was used to acquire and store data for inventory control. No claim was made to use it as a material/product release mechanism. It was currently under validation.

All materials used in manufacture and packaging were manually released by authorized QC/QA personnel. Goods were purchased from authorized suppliers by Mumbai central office. The system was configured to recognize a supplier by the supplier reference number. The computer would reject any attempt to purchase from non-authorized source. Baddi received an electronic copy of all purchase orders.

A goods-receipt-note (GRN) was generated upon arrival of the goods. A copy was sent to QC who made arrangements to sample the goods for subsequent testing and release/rejection.

Details of the delivery were entered into the system and status labels were generated for each container. The SOP made no provision for printing extra labels in the event of one or more being defaced during labelling. The analytical report (AR) number was entered manually.

Data entry cross checked with the handwritten goods receipt ledgers for actives and excipients held in the QC Laboratory.

WHO Public Inspection report (WHOPIR):

**MacLeods Pharmaceuticals Ltd - Baddi**, Theda, Nalagarh, Himachal Pradesh, **INDIA**

17, 18, 19 and 20 March 2009

Page 16 of 24

The component number, lot number and AR number would uniquely identify the material during its life cycle at Baddi.

After de-dusting samples were moved to the quarantine area. Upon release they were placed in the free stock area and location co-ordinates allocated and recorded.

The inventory listings were interrogated for materials movement (batch traceability) usage and current stock holding. All holdings were itemised by batch and issued using FEFO. The computer record of the stock holding of selected APIs agreed with on the spot check.

#### *Starting materials*

There was a system for development, qualification, dequalification and requalification of vendors of Raw Materials and Packaging Materials. This procedure was generally well implemented and a comprehensive list of approved vendors existed. This list was always followed in procurement and receiving of materials reviewed. The system of vendor approval included a comprehensive questionnaire filled by the manufacture, testing of a pre-shipment sample and, when found necessary, auditing of the facilities of the vendor and/or production of pilot batches. The vendors for all the APIs for products under WHO prequalification had been audited in 2008.

All containers of active and inactive materials were sampled and tested for identification. There was a procedure for making composites and the maximum number of samples that could be pooled was defined.

The storage conditions of all materials were defined and a list was available at the receiving area to guide the staff to place the material in the right area.

#### *Packaging materials*

Packaging materials were purchased from approved vendors. Each consignment was quarantined, sampled and tested before release for use.

The packaging materials were housed on the ground floor. All areas were clean and tidy. The goods were neatly stacked in quality steel racking. Location codes for each item were clearly displayed at the end of each lane. All items were stored in containers with their status clearly displayed.

#### *Intermediate and bulk products*

Granules, uncoated tablets, coated tablets and capsules were stored in sealed SS in process containers (IPCs) and their holding time had been validated.

#### *Finished products*

Each batch of finished products was held in quarantine until it was tested and its production, packaging and testing records reviewed and found in compliance with GMP and regulatory requirements.

#### *Rejected materials and products*

There were separate storage facilities in which rejected material were securely stored until either they were disposed off by return to the supplier or destruction, or they were reviewed and approved by QA for further testing and repackaging.

#### *Reagents and culture media*

Standard stock reference culture and subcultures were used and subcultures were discarded after 5 generations. Both positive and negative growth test were performed on all media.

#### *Reference Standards*

There were dedicated facilities (*LAF, humidity chambers, refrigerator and controlled boxes with desiccators*) for the preparation and storage of reference and working standards. The procedures for preparation of working standards were comprehensive. Reference and working standards were well labelled and the records for standardization of working standards were well maintained.

### **2.15 DOCUMENTATION**

There was a procedure for preparation, review, approval and authorization of standard operation procedures. For products reviewed, there was a master formula, specification of starting and packaging materials, production and packaging instructions, batch processing and packaging records, finished product specifications, standard testing procedures and corresponding results. The documents carried a unique number and their documentation, change and retrieval were well controlled by the quality assurance department.

There were some minor observations on the clarity and cross-referencing of some SOPs and documents as specified in the tabulated observations.

### **2.16 GOOD PRACTICES IN PRODUCTION**

There were written procedures and records to manage the receipt, quarantine, sampling, labelling, storage and dispensing of materials; cleaning of equipment and premises; processing, packaging and distribution of products. All production operations followed the written and approved SOPs and all operating conditions were properly recorded in the BMR.

Any deviations from the approved procedures were investigated and their impact assessed before taking appropriate action. Limits for yield had been set at different stages of production and packaging and any results beyond the limits were investigated and documented. Whilst the company defined rework and reprocessing and recovery, none of these is permitted.

The equipment used in processing and packaging had been qualified and the processing and cleaning procedures had been validated

#### *Compression and Capsulation*

The procedures employed in production included wet granulation using a Rapid Mixer Granulator, dry granulation using a Roll compactor. Drying was done in a Fluid Bed Dryer while blending was done using Bin blender.

Compression was using single or double rotary compression machines, while ether film was done in Auto coaters. There were on line metal detectors and dedusters. Metal detectors performed satisfactorily when challenged with ferrous, non ferrous and SS test pieces.

Punches and dies were cleaned and inspected for damage on return to the stores. Cleaned tools were stored in custom built drawers and were coated with food grade oil. Punch and die dimensions were periodically checked using calibrated measuring equipment. The maintenance kit included all the necessary tooling for measurement of critical dimensions.

Capsulation was done by tamping and dosing using Automatic Capsule Filling Machines.

There was a separate laboratory for IPQC containing all the necessary equipment like the Tablet Hardness Tester, Tablet friability Tester, Tablet Disintegration Apparatus, Tablet weight check balance, Infra-red moisture balance and vernier Callipers' all of which were regularly calibrated.

Packaging was done either in strips (Alu/Alu), blisters (Alu/Alu, Alu/PVC, Alu/PVdC), bottle containers, or pouches. The calibration and/or operation of the leak tester was not appropriate as it was set to apply a vacuum pressure of up to 300mmHg but went up to 305mmHg. This was resolved.

#### *Liquid manufacturing and filling*

Materials were sifted before transferring into the manufacturing tanks. Sugar was charged separately by vacuum. Decartoning was done in a separate room from the bottle washing area. The bottle washing cycle included validated alternate cycles of purified water and filtered compressed air. Water was supplied through a water circulation loop. The syrup tank had a capacity of 2000L while the preparation tank had a capacity of 1000L and the manufacturing tank had a capacity of 3000L. Use and cleaning logs were maintained and those of the basket filter, filter press and Lobe Transfer Pump were reviewed in detail.

Filling and capping took place in an enclosed room operating at a positive air pressure relative to the packing hall. Liquid filling on the Bottle Filling and Sealing line was in progress at the time the area was inspected. SOPs were available for set up, operation and cleaning of the machine and records were made in the respective BMR/BPRs and Use/Cleaning logs. PET bottles were used. Inspectors witnessed frequent stoppages of the filling and sealing process as a result of several malfunctioning aspects. Although these reduced when the operators was changed, they were not totally eliminated by this change.

WHO Public Inspection report (WHOPIR):

**MacLeods Pharmaceuticals Ltd - Baddi**, Theda, Nalagarh, Himachal Pradesh, **INDIA**

17, 18, 19 and 20 March 2009

Page 19 of 24

There was a dedicated laboratory for IPQC for the liquid line. It contained equipment for Leak test, Measuring cylinder and pH Meter. Calibration certificates were available and so were records for preparation of the buffer solutions.

Secondary packaging included addition of a measuring cap, bottle labelling, Package Insert, insertion into individual bottle carton and then placing the bottles into a shipper carton. The labelling and packaging process was adequately monitored to avoid mix up and errors.

## **2.17 GOOD PRACTICES IN QUALITY CONTROL**

There were quality control and quality assurance departments whose functions were independent of other units including production. Corporate Quality assurance department was involved in approving new vendors for starting and packaging materials and equipment.

The quality control laboratory had adequate facilities in form of space, equipment, reagents and chemicals to test all starting material, packaging materials, intermediates and finished products before release for use or distribution.

Adequate sampling procedures and plans were used and the testing procedures were documented and appropriately validated. Quality assurance staff reviewed all the production and testing records for each batch before it was released for distribution.

Retention samples were kept from each batch of starting materials and finished products to facilitate any future investigation, if necessary.

There was an adequate stability testing programme supported by several stability chambers (25<sup>0</sup>C/60%RH, 30<sup>0</sup>C/65%RH, 30<sup>0</sup>C/75%RH and 40<sup>0</sup>C/75%RH) and a separate dedicated laboratory. Records of stability testing were maintained and could support the storage conditions and shelf life claimed for the products.

### ***Sample Management***

Receipt of samples in the QC laboratory followed an approved SOP. The receipt of each type of material was entered into the appropriate ledger and the sample was allocated a unique AR (Analytical Report) number in accordance to an approved SOP. Samples each block were adequately segregated from those from other blocks during storage.

Sampling followed an approved SOP. Samples were distributed to appropriately trained technicians for a particular analytical test. The training records for selected staff were selected at random for review and found to be satisfactory.

All individual containers of a batch of starting materials in a consignment were sampled and tested for identity before pooling into a composite (maximum 5 containers) for other tests and general composite for the retention sample.

WHO Public Inspection report (WHOPIR):

**MacLeods Pharmaceuticals Ltd - Baddi**, Theda, Nalagarh, Himachal Pradesh, **INDIA**

17, 18, 19 and 20 March 2009

Page 20 of 24

Randomly selected examples were reviewed in detail. Records showed that, in all the cases reviewed, the procedures for sampling, preparation of composite and testing were followed and results in compliance with the specifications.

### ***Reference Materials***

Primary, Working and Impurity Standards were stored in the fridge 2 - 8<sup>0</sup>C. Records for preparation, storage, issuance and use of reference standards were maintained.

Primary Reference materials were used to qualify Working Standards according to an approved SOP. Triplicate determinations were made and the acceptance criteria were Assay with RSD of NMT 0.5% and LOD of NMT 0.1% plus RSD of NMT 0.03%. Each time 13 vials were prepared one for each months and one being a spare for one month. Records for preparation of selected WS were reviewed and they had been standardized against pharmacopoeial RS USP. Certificates for the pharmacopoeial RS were reviewed and found satisfactory.

The SOP did not specifically require the reference materials kept in the fridge to be equilibrated to room temperature before use and did not specify that the RS be kept in the desiccator once out of the fridge.

### ***General Wet Chemistry***

All testing followed compendial requirements or authorized in house methods. Volumetric solution preparation records were properly reported and standardization followed standard practice.

All volumetric glassware was calibrated. Certificates for a pipette, a burette and a volumetric flask, all chosen at random, were available.

Reagent solutions are prepared according to compendial requirements (e.g. BP, EP, USP, IP) all are numbered and date expired. Preparation of arsenic trioxide was taken as an example. The authorized method of preparation was followed but there was no written record of the actual weight of the AS<sub>2</sub>O<sub>3</sub> required.

### ***Laboratory Equipment***

The laboratory had all the basic equipment like Analytical Balances, pH meters, Auto Titrators, Melting point apparatus, Conductivity meter which were maintained and calibrated according to authorized SOPs.

The fume chambers in the Chemistry laboratory had not been qualified.

### ***Instrumentation***

(a) *FTIR and UV/visible spectrometers*

WHO Public Inspection report (WHOPIR):

**MacLeods Pharmaceuticals Ltd - Baddi**, Theda, Nalagarh, Himachal Pradesh, **INDIA**

17, 18, 19 and 20 March 2009

Page 21 of 24

FTIR and UV/visible spectrometers were regularly calibrated and were within specification for resolution, wavelength accuracy, absorption accuracy and stray light. Apart from the UV/visible silica cuvettes looking in need of a cleaning, no matters of concern were noted.

*(b) HPLC*

The IQ/OQ/PQ protocol and reports for HPLC was assessed and they were satisfactory. The software controlling the pumps and UV detector were part of the OQ and PQ protocol. Flow checks, injection repeatability, detector wavelength accuracy and linearity of response were well documented.

The reporting integrator collects raw data but did not have the capacity to calculate assay results. The peak areas generated were used to manually calculate results.

Peak threshold settings were set manually after visual assessment of the peak printouts. Similarly for the peak cut off point. System suitability checks were automatically calculated. Once set, the integration parameters were adhered to for both sample and standard injections.

Column usage logs are kept and HETP trends were used to ascertain the useful life of a column.

*(c) Dissolution Apparatus*

One of three modules was selected for assessment. The Dissolution Apparatus was operated and calibrated according to an approved SOP. The routine checks for bath temperature, shaft revolutions, shaft eccentricity and basket position were all satisfactory. The SOP specified the location in the vessel from which the analyte sample must be taken.

***Microbiology***

The laboratory was well equipped to carry out the necessary testing for bio-burdens, purified water monitoring and environmental studies.

*(a) Media Preparation*

A full range of solid media was available for the culturing of yeasts, moulds and bacteria. Media were prepared either for plate pouring or slants. The SOP gave details of preparation and any special requirements or checks such as pH adjustments.

The sterilization cycle reference number formed part of the BMR. A log of usage was maintained. Details of growth promotion checks and negative controls were also recorded.

Standard reference cultures were maintained in the refrigerator. They were renewed from stock cultures after 5 generations

*(b) Equipment*

Twelve (12) incubators were in use: Two on  $55^{\circ}\text{C}\pm 2.5^{\circ}\text{C}$ , two  $42.5^{\circ}\text{C}\pm 2.5^{\circ}\text{C}$ , four at  $22.5^{\circ}\text{C}\pm 2.5^{\circ}\text{C}$ , and four at  $32.5^{\circ}\text{C}\pm 2.5^{\circ}\text{C}$ . They had all been validated for even temperature distribution and were constantly monitored.

The autoclave was validated using a protocol based on HTM2010 and included temperature distribution studies (empty chamber and load configurations) vacuum and pressure hold tests and heat penetration checks.

Records chosen at random showed media had been held at 121<sup>0</sup>C for a minimum of 20 minutes at 1-1.3 Kg / cm<sup>2</sup> pressure. F<sub>0</sub> of the order of 18 was achieved. (F<sub>0</sub> of 18 was regarded as a minimum value using the standard reference of B stereothermophilus with D value of 1.5 minutes).

*(c) Environmental Monitoring*

The programmes of microbial air monitoring and general testing procedures were managed by following approved SOPs.

A sample of air was collected under active air sampling and while Petri dishes were exposed for 4 hours under passive air sampling. Growth promotion tests had validated the 4 hour exposure time. The SOP gave details of both frequency and location of sampling. The work areas were claimed to be class 100,000 (Class D) at rest. The alert and action limits for passive air samples and for active air had been set.

Results for locations pertinent to tableting areas were chosen for scrutiny. These included: Dispensing area air lock, Dispensing area LAF, Granulation room, the paste preparation room, Compression room and Coating room. The counts reported were considered typical for the whole of the manufacturing units in Block 2 and well within limits. No matters of concern were noted.

*(d) Purified Water.*

The findings are included in the report of the phase three validation of the purified water system.

*(e) Validation of Sanitising Agents*

Several disinfectants were used. All had been challenge tested using the standard stock cultures (10<sup>3</sup>-10<sup>4</sup>/0.1ml) in order to ascertain the minimum dilutions to effect a kill.

Various test pieces including 316 SS, epoxy coated gypsum and Kota stone tiling were loaded with 10<sup>3</sup> organisms and allowed to stand in contact with the sanitising agents for five minutes. Swab recoveries showed results that supported the application of the disinfectants. No swab recovery test had been performed which casts doubt on the validity of any results generated.

### **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, **MacLeods Pharmaceuticals Ltd, Unit VI, Block N2**, located at Village Theda, P.O. Lodhi Majra, Tehsil **Nalagarh**, District Solan, **Himachal Pradesh** 174101, **INDIA**, was considered to be operating at an acceptable level of compliance with WHO GMP guidelines.

WHO Public Inspection report (WHOPIR):

**MacLeods Pharmaceuticals Ltd - Baddi**, Theda, Nalagarh, Himachal Pradesh, **INDIA**

17, 18, 19 and 20 March 2009

Page 23 of 24

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

The WHOPIR is valid for a maximum of 3 years, unless the site is found to be non-compliant in another inspection before the 3 years had lapsed.