

**WHO PUBLIC INSPECTION REPORT
(WHOPIR)
API Manufacturer**

Part 1: General information

Name of Manufacturer	IPCA Laboratories Ltd
Unit number	89A-B/90/91, Pologround, Indore, Madhya Pradesh, India
Production Block	Plant 5
Physical address	Same as above
Postal Address	Same as above
Contact person and email address.	Mr. S. K. Darh Corporate Quality Assurance sanjay.darh@ipca.com
Dates of inspection	14-15 and 18 September 2012
Type of inspection	Follow-up inspection
Active Pharmaceutical Ingredient(s) included in the inspection	APIMF 030: Amodiaquine HCl
Summary of the activities performed by the manufacturer	Production, quality control

Part 2: Summary

General information about the company and site

IPCA Laboratories Ltd., India has 15 manufacturing sites in India manufacturing key API intermediates, API's, finished dosage forms, and R&D. The headquarter was located in Mumbai (administration, IT and R&D).

The Indore site is specialized in the manufacturing of active pharmaceutical ingredients and key intermediates.

History of WHO and/or regulatory agency inspections

This inspection was a follow-up inspection to verify effective implementation of corrective actions. The site had been inspected by the WHO Prequalification of Medicines team on 26-29 March, 2012.

Focus of the inspection

The inspection focused on the implementation and effectiveness of CAPAs of the deficiencies discovered in the last inspection.

Inspected Area

The following facilities were in the scope of the re-inspection because of their involvement in the CAPAs:

- Synthesis workshop in Plant No 5
- Powder Processing Area in Plant No 5 (controlled area)
- Micronizing Area in Plant No 1 (controlled area)
- Water plant
- Warehouse

The other facilities and products manufactured at the site did not change since the last inspection.

2.1. QUALITY MANAGEMENT

General

The QA/QC department was independent from production.

There was no change in the organisation, key personnel and the operation of the QA system since the last inspection.

Quality management system was established, implemented and operated in a proper manner in general. There was no product complaint recorded since the last inspection.

2.2 PERSONNEL

Job descriptions

Some of the managers in key positions was promoted since the last inspection, but their functions and described job responsibilities did not change.

The job descriptions of the following personnel were discussed:

- General Manager Operations,
- General Manager QA,
- General Manager QC,
- General Manager Technical,
- QA Manager,
- Manager QC,
- Assistant Manager Production,
- Assistant Manager PPA.

The personnel met during the inspection were experienced, skilful and conscientious.

The deficiencies discovered during the last inspection regarding the job descriptions were resolved. The updated job descriptions were available.

The procedure for assessing training efficiency was implemented.
See observations (section 5)

Training

The training SOP was revised since the last inspection.

The training records, trainer qualification and the assessment records of the training regarding procedures were discussed.

Personnel hygiene

The procedures for entering the clean areas were described in SOPs.

The hand washing requirement before entering the clean areas was implemented into the procedures.

2.3 BUILDINGS AND FACILITIES

Toiletry and hand washing facilities

There were new toiletry and washing facilities constructed belonging to the controlled areas.

Production workshop

In the workshop the flooring was repaired, some rooms (Technical zone, Wash area, Air passage, and Quarantine room), the HVAC system reconstructed, and a new dust collector device installed.

The HVAC system was re-qualified following to the plant reconstruction and the installation of the dust collector device.

The air filters were identified according to the SOP.

The maintenance and cleaning records of the air filters were available.

The filter IDs were also indicated in the facilities (controlled areas).

The dust collector was installed in the “Milling-Sifting-Packing Room”.

SOP on cleaning procedure and operating procedure were reviewed.

DM water generation system

DM (demineralized) Water was used as a solvent in different manufacturing steps including the last stages of the processes and as cleaning agent in controlled areas (facility, manufacturing equipment and air filter cleaning).

As a corrective action the purified water system improvement has been initiated since the last inspection.

Following to the deviation discovered during the last inspection, a UPS (uninterruptible power supply) was installed to stabilize the power supply of the measuring devices connected to the DM water system.

The washing area of air filters (on “Terrace”) was supplied by DM water from a 1m³ water tank connected to the DM water loop. The 1m³ water tank and the pipeline towards the filter washing area ended with the user point.

The access of pigeons to the DM water generation area was prevented by mounting a protection net around the “Terrace”.

Raw material warehouses

Rain protection roofs were mounted at the entrances of the raw material warehouse, and the open roof-blowholes were provided with framed mesh. The emergency door was repaired to prevent entry of insects and any solid particles into the raw material warehouse.

Sewage and refuse

The handling of plant waste was regulated in SOP.

For non-chemical solid waste a new storage area was designated outside of the manufacturing site, closed to the raw material warehouse.

2.4 PROCESS EQUIPMENT

The equipment and facilities used to manufacture Amodiaquine were not dedicated. The last stages of the processes were carried out in multi-functional equipment and controlled clean areas.

The critical manufacturing equipment did not change since the last inspection, but their identification and calibration was dealt with.

The identification codes and the serial numbers were indicated in a table. The randomly checked device was properly identified, and the last calibration records were available.

2.5 DOCUMENTATION AND RECORDS

The documentation system did not change since the last inspection.

The modified SOPs master formula, validation documents and the corresponding records were discussed during the inspection (see the relevant sections).

2.6 PRODUCTION AND IN-PROCESS CONTROLS

The Company intended to implement a modified manufacturing process of Amodiaquine HCl, the change in the solvent list in the new process.

The master formula and the corresponding BMRs were available and discussed during the inspection.

2.7 MATERIALS MANAGEMENT

There was no change since the last inspection in procedures of the receipt, labelling, quarantine, storage, and handling of materials, as well as the procedures for sampling, testing and approval or rejection of materials.

The generation of GIM and AR numbers was regulated in SOP.

2.8 STORAGE AND DISTRIBUTION

There was no change in the storage and distribution procedures, but the raw material warehousing facilities were improved since the last inspection.

2.9 LABORATORY CONTROLS

The instrumentation and the procedures regarding laboratory controls did not change since the last inspection.

The Corporate SOP on analytical method validation/verification was reviewed in August 2012. The methods were claimed to be validated by the Corporate R&D Department then transferred to the Site according to the SOP on method transfer. The validation status of analytical test methods for raw materials (Mannich base, Denatured ethanol, 4,7-DQC), was discussed.

The change control investigation regarding a modification of an analytical test method omitting an extra peak belonging to a degradation product was discussed.

The procedure for OOS investigation was revised since the last inspection.

2.10 VALIDATION

Manufacturing process validation

The SOP on manufacturing process validation was reviewed. The validation of the modified manufacturing process was based on three consecutive batches.

Before the validation batches 3 trial batches were manufactured. The trial batches are intended to be marketed in domestic market when the validation report is completed and approved.

The manufacturing process validation protocol was available, the manufacturing of the validation batches accomplished and the validation report under review and approval by the company at the time of the inspection.

The validation documents were discussed during the inspection.

2.11 CHANGE CONTROL

The change control procedure was reviewed and considered to be acceptable.

The changes concerning the CAPAs of the inspection observations were listed in the “Change Control Proposal Register” and documented.

2.12 REJECTION AND RE-USE OF MATERIALS

The SOP on reprocess/rework was reviewed and considered to be acceptable.

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, as well as the corrective actions taken and planned, APIs manufactured at IPCA Laboratories Ltd. Indore, India, 89A-B/90/91, Pologround, Indore, Madhya Pradesh, India was considered to be manufactured in compliance with WHO GMP for Active Pharmaceutical Ingredients.

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.