

WHO PUBLIC INSPECTION REPORT Finished Product Manufacturer
**WHO PUBLIC INSPECTION REPORT
(WHOPIR)**
Finished Product Manufacturer
Part 1: General information

Name of Manufacturer	Ipca Laboratories Limited,
Unit number	NA
Production Block	NA
Physical address	Plot No.255/1, Village Athal, Silvassa, 396230 Union territory of Dadra & Nagar Haveli, India
Contact address	Mr. Sanjay Kapur, Vice President – Operations sanjay.kapur@ipca.com Mr. Rajendra Dadhich Vice President – Corporate Quality rajendra.dadhich@ipca.com
Date of inspection	20 to 23 November 2012
Type of inspection	Follow up inspection
Dosage forms(s) included in the inspection	Tablets
WHO product categories covered by the inspection	<u>Prequalified products:</u> MA038 Artesunate 50 mg tablets MA001 Amodiaquine HCl tablets 150mg + Artesunate Tablets 50 mg MA062 Artemether/Lumefantrine 20 mg / 120 mg tablets MA080 Amodiaquine/Artesunate 67.5/25mg tablets MA081 Amodiaquine/Artesunate 135/50mg tablets MA082 Amodiaquine/Artesunate 270/100mg tablets
Summary of the activities performed by the manufacturer	Production and control of oral dosage forms

Part 2: Summary

General information about the company and site

Ipca Laboratories Limited is one of the leading manufacturers of Active Pharmaceuticals Ingredients (APIs), Finished Pharmaceutical Products (FPP) and intermediates in India. It has facilities located at Athal, Kandla, Piparia (Silvassa), Ratlam, Dehradun, Indore and Sikkim.

The facility inspected was Ipca Laboratories Limited located at Plot No.255/1, Village Athal, Silvassa, 396230, Union territory of Dadra & Nagar Haveli, India, hereafter called Ipca, Athal. It was established in 1995 and manufactures oral solid dosage forms. The site underwent major expansion in 2004. Currently, more than 800 employees are employed at the Athal site.

History of WHO and/or regulatory agency inspections

This was a follow up inspection to the last routine GMP inspection conducted in April 2012. This inspection was performed with UK MHRA as a joint inspection.

From the opening meeting presentation, it had been noted that Athal site had been inspected by UK MHRA, MCC South Africa, ANVISA Brazil, TGA Australia, Health Canada, Medsafe New Zealand, UNICEF etc.

Focus of the inspection

The inspection focused on the production and control of Artesunate/Amodiaquine (67.5/25mg, 135/50 and 270/100mg) tablets products. 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

- Quality assurance
- Good manufacturing practices for pharmaceutical products
- Sanitation and hygiene
- Qualification and validation
- Complaints
- Product recalls
- Contract production and analysis
- Self inspection and quality audits
- Personnel hygiene
- Premises
- Equipment
- Materials
- Documentation
- Good practices in production
- Good practices in quality control.

2.1 QUALITY ASSURANCE

There was an organizational chart and job descriptions specifying the responsibilities and reporting relationships of the various staff. There were documented and approved procedures to guide routine operations and activities. Starting materials, intermediate products, finished goods were controlled and approved by QC/QA before release for use or distribution.

Policies and procedures were in place for qualification and validation of equipment and systems, change control and deviation management, self-inspection and product quality review.

The observations raised from this section have been addressed adequately.

2.2 GOOD MANUFACTURING PRACTICES (GMPs) FOR PHARMACEUTICAL PRODUCTS

Good manufacturing practices were implemented. The necessary resources were generally provided. Manufacturing steps were recorded in batch manufacturing and packaging records. Instructions and procedures were generally written in clear and unambiguous language. Qualifications and validations were performed, adequate premises and equipment were available for production, in-process controls and storage, and operators were trained.

The observations raised from this section have been addressed adequately.

2.3 SANITATION AND HYGIENE

The site had facilities and procedures for sanitation and hygiene. Materials for production, containers and products for cleaning were handled in a manner to minimize their chances of becoming a source of contamination to the product.

The observations raised from this section have been addressed adequately.

2.4 QUALIFICATION AND VALIDATION

There was a general validation master plan which outlined the policy and approaches to be followed in qualification of equipment and validation of systems and processes. Qualification included Design Qualification (DQ), Installation Qualification (IQ), Operation Qualification (OQ) and Performance qualification (PQ).

Validation and qualification were guided by approved protocols. The schedules and frequencies for executed and planned requalification, validation and revalidation were outlined in annexes to the VMP.

The principles for cleaning validation were established plus the policies on number of cleaning cycles, discussion of worst case, setting of limits, justification of the limits and analytical methods used and general documentation.

2.5 COMPLAINTS

There was a procedure for handling customer complaints. The cases reviews revealed that the investigation of complaints and documentation on follow up of implementation of CAPAs were generally well handled.

The observations raised from this section have been addressed adequately.

2.6 PRODUCT RECALLS

The company had an established product recall procedure which classified the deficiencies (Class I, II and III) 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 and Health Authorities to be informed while conducting a recall.

The observations raised from this section have been addressed adequately.

2.7 CONTRACT PRODUCTION AND ANALYSIS

Production activities were not contracted out. Some analysis was carried out on contract basis. Other outsourced activities and services included:

- Testing of HEPA Filters and validation support of HVAC System
- Pressure gauge and thermal calibrations
- Cleaning of production and warehouse premises
- Pest control
- Washing and maintenance of production gowning

2.8 SELF INSPECTION AND QUALITY AUDIT

The company had procedures and a schedule for self-inspection. This covered the quality system, packaging and labelling, production system, facilities and equipment system, materials system and laboratory system plus any other areas as deemed necessary.

Corporate QA audits suppliers of their raw and packaging materials, either independently or jointly with Site QA. Extracts of selected reports reviewed indicated that the programme was well executed.

The observations raised from this section have been addressed adequately.

2.9 PERSONNEL

The site engaged adequate numbers of skilled personnel to conduct production and quality control procedures. There was an organizational chart and job description to guide personnel. These indicated independence of quality control from production. The responsibility for batch review and release was assigned to Quality Assurance.

2.10 TRAINING

The training needs were identified and training was organized as per the training SOP. In general, training initiated by the site following the last WHO GMP inspection found to be acceptable. It is recommended to provide training to the operators on a regular basis and also ensure to amend the relevant procedures accordingly.

The observations raised from this section have been addressed adequately.

2.11 PERSONAL HYGIENE

There were facilities and procedures for changing and entrance into production areas which required staff members to wash their hands and change into clean factory garments. The facilities were generally adequate.

Production staff were required to undergo health checks on recruitment and thereafter regularly as required.

2.12 PREMISES

In general the buildings and facilities used for manufacture and quality control were located, designed, and constructed to facilitate proper cleaning, maintenance and production operations. Premises were designed to ensure the logical flow of materials and personnel. In Process Laboratory was located in the production block. Quality control laboratories were separated from production areas.

Access to the warehouses, production premises and Quality control laboratories was controlled.

Premises were protected from entry by insects, birds and animals.

Premises were clean and well maintained.

The observations raised from this section have been addressed adequately.

2.13 EQUIPMENT

Balances and other measuring equipment with appropriate range and precision were available for production and control operations and were calibrated on a scheduled basis. Calibration due-date labels were attached to the equipment.

Calibrated standard weights used for in-house checking of balances were available.

The observations raised from this section have been addressed adequately.

2.14 MATERIALS

Deliveries of raw materials were checked against a purchase order and an authorised supplier list. There was a checklist for document review and physical inspection of the consignment before offloading into the warehouse. All starting and packaging materials were tested and approved before they could be accepted for use.

There was a system for development, qualification, dequalification and requalification of vendors of raw materials and packaging materials. A list of approved vendors existed and was followed in procurement and receiving of materials reviewed.

In general, the materials were arranged in the warehouse in a clean, tidy and orderly manner.

The observations raised from this section have been addressed adequately.

2.15 DOCUMENTATION

In general, documents were adequately designed, prepared, reviewed and distributed. Documents were approved, signed and dated by the appropriate responsible persons. Documents were laid out in an orderly fashion. There was a significant improvement seen in the control and clarity of documentation. In particular, various key SOPs were noted to have been revised to provide greater detail and much clearer instructions.

The observations raised from this section have been addressed adequately.

2.16 GOOD PRACTICES IN PRODUCTION

Handling of materials and products was done in accordance with written procedures and was recorded, checks on yields and reconciliation of quantities were carried out. During processing, materials, bulk containers, equipment, rooms and packaging lines being used were labelled. Access to production premises was restricted. In-process controls were performed within the production area.

The general design of the facilities was appropriate.

Processes were generally under good control. Blending, granulation, compression, coating, primary and secondary packaging areas were visited. Sifting, dry mixing, granulation, drying and sizing were carried out in one room.

The observations raised from this section have been addressed adequately.

2.17 GOOD PRACTICES IN QUALITY CONTROL

The quality control laboratory consisted of the analytical laboratory (wet chemistry and instrumental analysis), stability and microbiology laboratory. Its function were independent of the production and this was reflected in the organization charts and activities reviewed. There was an adequate number of staff with the necessary skills and competencies.

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

There were approved procedures and specifications to guide the testing of different samples. Records of testing were available which indicated that the procedures were followed.

The observations raised from this section have been addressed adequately.

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, **Ipca Labs Limited, Plot No.255/1, Village Athal, Silvassa, 396230 Union territory of Dadra & Nagar Haveli, 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.