Administration of
Dadra & Nagar Haveli, UT.,
Office of the Asstt.Drugs Controller
Shri Vinoba Bhave Civil Hospital

WHO-GMP Certificate

Certificate No: **DMHS/ADC/WHOGMP/Ipca/2015/8815**

On the basis of the inspection carried out on **21.07.2015** we certify that the site indicated on this certificate complies with Good Manufacturing Practices for the dosage forms, categories and activities listed in Table 1.

1. Name and address of site: **M/s.Ipca Laboratories Limited,Plot No.255/1, Athal, U.T of Dadra & Nagar Haveli,Silvassa.**

2. Manufacturer's licence number: **NH/34 and NH/35**

3. Table 1:

Dosage form(s)	Category (ies)	Activity(ies)
Tablets (coated and uncoated) and Capsules	General	Manufacturing and Selling

The responsibility for the quality of the individual batches of the pharmaceutical products manufactured through this process lies with the manufacturer.

This certificate remains valid until **06/06/2018**.It becomes invalid if the activities and/or categories certified herewith are changed or if the site is no longer considered to be in compliance with GMP.

Address of certifying authority: **At Shri Vinoba Bhave Civil Hospital, Silvassa, UT of Dadra and Nagar Haveli.**

Name and function of responsible person: **Dr. V. K. DAS, Assistant Drug Controller, UT of Dadra and Nagar Haveli, Silvassa.**

Email:vkdas511@gmail.com
Telephone.No.0260-2642961,
Fax No.:0260 -2642961.

Signature:
Stamp and date: 7/6/2016

सहायक औषधि नियंत्रक और लाईसेंस प्राधिकारी
Assistant Drug Controller and Licencing Authority
दादरा एवं नगर हवेली, सिलवासा
Dadra & Nagar Haveli, Silvassa

सहायक औषधि नियंत्रक और लाईसेंस प्राधिकारी Assistant Drug Controller and Licencing Authority D&NH, Silvassa दा.न.ह., सिलवासा

The Ministry of External Affairs accepts no responsibility for the contents of the above documents.

भारत सरकार GOVERNMENT OF INDIA
अपोस्टिल / APOSTILLE
(Convention de La Haye du 5 octobre 1961)

Country: INDIA

This public document of the type
COMMERCIAL DOCUMENT

is issued to IPCA LABORATORIES LIMITED

has been signed by R. VENKATESH

with the seal / stamp of THE ALL INDIA EXPORTERS CHAMBER,
MUMBAI-INDIA

Certified by
Section Officer(OI) MINISTRY OF EXTERNAL AFFAIRS

on 21-Jun-2016 at NEW DELHI, INDIA

With reference no. MHMC0021332216

Seal / Stamp: Ministry of External Affairs, Govt. of India, New Delhi 10568

Signature

(कल्पना हुमपाल)
(KALPNA HUMPAL)
अ. भाग अधिकारी (ओ.आई.)
Section Officer (O.I.)
सी.पी.वी. प्रभाग/C.P.V. Division
विदेश मंत्रालय, नई दिल्ली
Ministry of External Affairs
New Delhi

THE ALL INDIA EXPORTERS' CHAMBER
DT. 14 JUN 2016
MUMBAI - INDIA

ATTESTED BY

R. Venkatesh
Jt. Executive Director
THE ALL INDIA EXPORTERS' CHAMBER

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WHO PUBLIC INSPECTION REPORT (WHOPIR) of the Finished Pharmaceutical Product manufacturer

The report is the property of the organization responsible for performing the inspection.

Part 1: General information about the inspection

Name of manufacturer	**IPCA Laboratories Limited, Athal**
Physical address	Plot No.255/1, Village Athal, Silvassa, 396230 Union territory of Dadra & Nagar Haveli, India
Postal address (Head Office)	142 - AB Kandivli Industrial estate, Kandivli (west), Mumbai - 400067, India
Telephone number (Corporate Office)	+91 22 66474747 / 66474400
Fax number (Corporate Office)	+91 22 28686613
Summary of all the activities performed by the manufacturer Dosage forms and type of products	Manufacture and distribution of : Non sterile final pharmaceutical product manufacturing: tablets and hard gelatine capsules
Focus of inspection - products in WHO PQ program covered in the scope at the time of inspection with the WHO reference number	**Prequalified products:** **MA038** Artesunate 50 mg tablets **Products under assessment:** **MA001** Amodiaquine HCl tablets 153.1 mg + Artesunate Tablets 50 mg **MA062** Artemether/Lumefantrine 20 mg / 120 mg tablets
Dates of inspection	28, 29, 30 January 2008
Programme	Prequalification Programme of Essential Medicines

Part 2: Summary

Background information

IPCA Laboratories Limited, located in Athal, Silvassa, India was inspected by a WHO prequalification team on the above mentioned dates.

IPCA Laboratories Limited was established in 1949.

IPCA Laboratories Limited manufactures Finished Pharmaceutical dosage forms, Active Pharmaceutical Ingredients and Intermediates.

IPCA Laboratories Limited had ten manufacturing facilities in India:

- Athal (formulations)
- Kandla (formulations)
- Piparia (formulations)
- Ratlam (formulations, API's and intermediates)
- Dehradun (formulations)
- Indore (API's and intermediates)
- Pithampur (formulations)
- Aurangabad (API's and intermediates)
- Dombivali (API's and intermediates)
- Mahad (API's and intermediates)

IPCA Laboratories Limited Research and Development Centers were located at Mumbai, Ratlam and Indore. Corporate Quality division was located in Mumbai.

Focus of the inspection

The purpose of the inspection was to ascertain the level of GMP compliance for the manufacture of tablets what are provided for the treatment of Malaria and is in the WHO prequalification list. Two products were under assessment in the WHO prequalification.

History of WHO or regulatory agencies inspections

The site was previously inspected by WHO team on 20 - 23 June 2006.

2.1. Quality Assurance (QA)

A quality assurance system was implemented and maintained.

The QA unit and QC unit were independent from production.

Product release was the responsibility of the Vice President Quality, who was also the Authorized person, hierarchically independent from production. QA personnel were involved in all the production and quality control activities.

Managerial responsibilities were specified in job descriptions.

Formal system for change control was described in a written procedure.

Formal system for deviation management was described in writing. Major deviations were sent for discussion to the corporate level. Categorization major/minor was done by the site.

Annual product review included all batches..

2.2. Good manufacturing Practices for Pharmaceutical products

Good manufacturing practices were implemented and maintained.

Manufacturing processes were clearly defined and reviewed. Manufacturing steps were recorded in Batch Manufacturing Documentation. The storage and distribution of products ensured batch traceability. Records were made during manufacture.

Necessary resources were provided.

Instructions and procedures were written in clear and unambiguous language.

2.3 Sanitation and Hygiene

The site's hygiene program covered personnel, equipment, materials and premises. The hygiene measures in place at the time of the inspection were generally found to be sufficient to assure the prevention of contamination of the premises and product.

2.4 Qualification and Validation

The key elements of a qualification and validation programme were clearly defined and documented in the Validation Master Plan. VMP was a comprehensive document, it included the worst case principle and specified re-qualifications of the systems.

Generally validations were considered to be appropriately performed.

2.5. Complaints

Complaints and other information concerning potentially defective products were reviewed according to written procedure and the corrective actions were taken.

Overseas / local complaints were received by corporate office and then forwarded to the Athal site. Local complaints were received directly at Athal site were forwarded to regulatory for information. Complaints were classified as quality related, packaging related, transpiration related and others. Complaints were categorized as critical, major and minor. Complaints were reviewed every 6 months. Complaints and their investigation reports were kept together with Batch Manufacturing Documentation.

2.6 Product Recalls

Recalls were handled in accordance with written procedure. Recall procedure was regularly reviewed and updated.

Recalls were classified in 4 categories. Mock recall for local market was done.

2.7 Contract production and analysis

No manufacturing was contracted out.

Analytical technical assistance was contracted out to four analytical laboratories. The contracts permuted the contract giver to audit the facilities of the contract accepter. The responsibilities of contract giver and contract acceptor were clearly defined.

2.8 Self inspection and Quality Audits

Self-inspection was performed in accordance with written procedure. Procedure included questionnaires on GMP requirements and main GMP items were covered. After completion of self inspection the self inspection report was drawn up and necessary CAPA's were initiated. Implementation of CAPA's were monitored. Self inspection schedule was available for

inspection. Self inspection team was properly trained. Self inspection trends were evaluated annually.

Vendors audits and approval procedure was implemented and followed.

2.9 Personnel

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

An organization chart was available. Key personnel responsibilities were specified in job descriptions. The production and quality control responsibilities were independent, in line with cGMP requirements.

2.10 Training

Training issues were covered in written SOP. Company provided initial training at the time of recruitment, specific training relevant to area of deployment and regular continuous SOP training. Comprehension of training content was assessed by discussions and observation of performed activities. The training plan and programme for the year 2008 was availed to the inspectors. Training records were maintained.

2.11 Personal Hygiene

All personnel prior and during employment passed medical examinations. Persons with illness and open lesions were not allowed to work in areas where open products were exposed to the environment.

All changing rooms were provided with photos describing the gowning procedures.

2.12 Premises

Buildings and facilities used for manufacture and quality control were located, designed, and constructed to facilitate proper cleaning, maintenance, and production operations. Facilities were designed to minimize potential contamination, production area had adequate space for the placement of equipment and materials to prevent mix-ups and contamination. There was also sufficient space for the movement of materials and personnel. There were separate personnel and material entrances. Temperature, relative humidity and pressure differentials were regularly monitored and recorded.

In general the buildings were well maintained and clean.

Storage areas

The receiving and dispatch areas protected materials and products from the weather.

Quarantined, rejected, recalled and returned materials and products were stored separately and secured.

Temperature mapping of storage areas was done and reports were available for inspection.

Sampling areas

There were two sampling rooms. A separate sampling booth was designed for sampling of API and other raw materials and a separate sampling booth was designed for sampling of solvents. Primary packaging materials were sampled in RLAF booths.

Weighing and dispensing areas

Weighing was done in two RLAF booths.

Qualification of the room and booths and related validations were not inspected due to lack of time.

Production spare parts room

Punches, dies and other production equipment spare parts were stored in the separate room outside the clean production facilities.

Production areas

In general facilities were smooth, free from cracks and open joints and permitted effective cleaning. Facilities were designed and maintained to minimize the risk of cross–contamination and contamination. Production areas were effectively ventilated with supply air grills located higher than return air grills, such that there was a downward flow of clean air from above and extracted lower down. Air flow pattern tests were performed in all production rooms where open products were exposed to the environment.

Quality control (QC) areas

QC laboratories were separated from the production areas. Adequate space was provided for storage of samples, laboratory reagents and reference standards, solvents, reagents and records. Separate rooms were provided for instruments such as analytical balances, HPLC, IR and GC.

Microbiological laboratory was separated from the chemical laboratory, the laboratory was clean and procedures could be conducted in different rooms with appropriate separation.

2.13 Equipment

Process equipment was installed and maintained in a way that minimizes risk of error and contamination.

Preventive Maintenance program was in place and was followed. The program was spot-checked in terms of the compressed air system. No remarks.

Cleaning SOP's and records were available. Production and quality control equipments were identified as to content and cleanliness status and appropriately indicated by labels.

Equipment calibration schedule was established on annual basis.

2.14 Materials

The procedures describing the receipt, identification, quarantine, storage, handling, sampling, testing and approval or rejection of materials were available.

Incoming goods and finished products were quarantined until tested and released by QC. Materials and products were generally stored in a proper manner.

Damage to containers was reported to QA. Containers under quarantine and approved containers were appropriately indicated.

The lists of the approved vendors of the raw materials and packaging materials were available in the warehouse.

Culture media were prepared and controlled according to written procedures. Liquid media was freshly prepared. pH of media was checked before and after sterilization.

Positive and negative controls were used. Use of in-house isolates in addition to ATCC strains was planned for growth promotion tests on prepared media.

Autoclave for media sterilization was regularly checked and sterilisations processes validated.

Reference and working standards were stored appropriately.

Usage of reference and working standards was recorded; log books on use of standards were available.

Lubricants, paste for polishing punches and dies and disinfectants were approved by QA.

2.15 Documentation

In general documentation system was well established and maintained.

Documents were designed, prepared, reviewed and distributed with care. Documents were approved, signed and dated by the appropriate responsible persons.

Documents had unambiguous contents were laid out in an orderly fashion and were easy to check.

Documents were regularly reviewed and kept up to date.

2.16 Good practices in production

Production operations were done following clearly defined procedures.

Deviations from instructions or procedures were done in accordance with an approved procedure.

Necessary checks on yields and reconciliation of quantities were carried out.

Operations on different products were not carried out simultaneously or consecutively in the same room.

During processing, materials, bulk containers, major items of equipment, and the rooms and used packaging lines were labelled and indicated the products being processed, its strength and the batch number.

Access to production premises was restricted.

Special precautions were taken to prevent the generation and dissemination of dust.

Environmental monitoring programme was established and followed. Air sampling results could be traced back to activities conducted at the time of sampling.

Line clearance was performed and recorded before processing operations were started.

Necessary in-process controls were carried out and recorded.

During the inspection attention was paid only to the production rooms and equipment where pre-qualified and products under assessment were manufactured and will be manufactured in the future, respectively:

- Granulation I
- Granulation II
- Granulation VII
- Granulation IP
- Granulation IIP
- Compression IP
- Compression I
- Compression VI
- Compression VII
- Compression VIII
- Compression IX
- Compression X
- Scale up auto coater
- Strip blister bulk packaging
- Blister packaging 6
- Blister packaging 7

2.17 Good practice in Quality Control

In general Good Practice in Quality Control was implemented and maintained.

The quality control functions were independent of other departments.

Adequate facilities, trained personnel and approved procedures were available for all relevant activities.

Batches of products were released for sale or supply only after certification by the authorized person or designated persons.

Sufficient samples of starting materials and products were retained to permit future examination of the product.

Quality control personnel had access to production areas.

Analyst competency list and training files were available.

OOS were evaluated and investigated in accordance with written procedure.

Utilities

The HVAC system

HVAC system was designed to avoid possible contamination and cross contamination.

HVAC system was designed in a way that production corridors were in positive pressure with respect to production rooms. HVAC system was controlled and monitored by the BMS system. During the inspection attention was not paid to the BMS system.

Purified water system

PW was produced by two methods: reverse osmosis and demineralisation. Utilities were located in a separate building. Water was kept in circulation on ambient temp.

Chemical methods were used to sanitise certain sections of the PW production system. Loops were regularly sanitized.

Sampling plan was established for routine monitoring of PW; final user points were monitored with suitable frequency.

Compressed air

Compressed air generation system was located in a separate utilities building, oil-free compressors were used. Air was dried and collected in the production building, on the technical floor. Incoming air was filtered via several pre-filters and dried. 0.01 µm filters were installed at the used points. Compressed air samples were taken and analysed on regular basis.

Part 3: Conclusion

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, reflected in the observations listed in the inspection report, *IPCA Laboratories Limited, Athal* Plot No.255/1, Village Athal, Silvassa, 396230 Union territory of Dadra & Nagar Haveli, India was considered be operating at an acceptable level of compliance with WHO GMP.

However the observations (non-compliances with the WHO guidelines) listed below need to be addressed by the manufacturer and verified through evaluation of the documentation of the corrective actions (planned and implemented) submitted by the manufacturer.