



WHO PUBLIC INSPECTION REPORT

(WHOPIR)

Finished Product Manufacturer

Part 1: General information

Name of Manufacturer	Ajanta Pharma Ltd
Unit number	Paithan
Production Block	N/A
Physical address	b-4/5/6, MIDC Industrial Area Paithan District 431128. Aurangabad Maharashtra India
Contact address	Same as above
Date of inspection	27 - 30 June 2011
Type of inspection	Routine
Dosage form included in the inspection	Tablets
WHO product categories covered by the inspection	Malaria
Summary of the activities performed by the manufacturer	Production and quality control



Part 2: Summary

General information about the company and site

Ajanta is a 67% privately owned Indian generics manufacturer, with headquarters in Mumbai. The Aurangabad site is the company's main Indian manufacturing site, and was established in 1983. The site underwent significant expansion in 2009, with the provision of a new packaging area and dispensary. The site is relatively large, employing 220 regular staff plus around 150 casual workers. The site is engaged in the manufacture of a large number of non-sterile solid dosage forms, including ORS powder, capsules and tablets.

History of WHO and/or regulatory agency inspections

The site was inspected three times before by WHO in 2007, January 2009 and August 2009. The site was also previously inspected by various Drug Regulatory Authorities. This inspection was performed jointly with MHRA.

Focus of the inspection

The inspection focused on the production and control of tablets with specific focus on WHO PQ product. It was a routine inspection.

Inspected Areas

- Overview of activities at site
 - Anticipated future changes
- Inspection of the Quality Management System
- Product Quality Reviews
 - Deviations
 - Customer complaints
 - Recall system
 - Out of Specification investigations
 - Change Control
 - Artwork control
 - Distribution of products from the site
 - Technical agreements
 - New product introduction/technology transfer processes
- Inspection of Production Operations & Facilities
- Warehousing and storage
 - Changing Facilities
 - Dispensaries
 - Powder blending
 - Tablet manufacture
 - Capsule manufacture
 - Wash room, day stores e.t.c
- Packaging operations



- Component testing
- Primary packaging
- Secondary packaging
- In-process controls

Quality Control

- Specifications, sampling & testing
- QC Labs
- Microbiology lab
- Method Validation
- Retention Samples
- Stability chambers

Utilities

- Purified Water
- HVAC, Extraction Systems, Building Management Systems

Environmental monitoring

- Environmental monitoring results
 - Purified water, monitoring of production areas

Stability results for selected products

- Bulk tablets, finished product

Validation

- Process validation for Sildenafil / WHO products
- Validation Master plan, programme, protocols
- Facility & equipment qualification
- Cleaning validation
- Equipment validation

Materials Management

- Transport & Distribution
- Supplier approval and supplier complaints
- Supplier audit program
- TSE compliance
- Sampling, testing & raw material release

Review of batch documents

- Example batch record review
- Batch Release systems

Review of procedures from facility tour

- Production / cleaning procedures

PPM & Calibration procedures & Programmes

Staff training programme & records

Self-inspection records and procedures

Pest control

Post inspection summary meeting



2.1 QUALITY ASSURANCE

The company had quality management system in place to attempt to ensure the quality of products manufactured. There was a designed system of quality assurance incorporating GMP and quality control. QA is independent from production department. The system at site was broadly satisfactory.

The company generated Product Quality Reviews (PQRs) on an annual basis for each product it manufactured at the site. The procedure for generating PQRs together with the PQRs for the inspected products was inspected.

2.2 GOOD MANUFACTURING PRACTICES (GMPs) FOR PHARMACEUTICAL PRODUCTS

Good manufacturing practices were implemented and generally maintained.

Necessary resources were generally provided, including adequate premises and space, suitable equipment and services, appropriate materials, approved procedures and instructions, suitable storage, personnel, laboratories and equipment for in-process controls.

Manufacturing steps were recorded in batch manufacturing and packaging records; records were made during manufacture.

2.3 SANITATION AND HYGIENE

The topic was covered during the inspection; an acceptable level was observed in inspection.

2.4 QUALIFICATION AND VALIDATION

The key elements of the qualification and validation program were defined and documented in Validation Master Plan (VMP).

The inspected products were produced in a multi-products manufacturing facility. The protocol and reports of process validation and cleaning validation were inspected.

2.5 COMPLAINTS

The company's system for dealing with customer complaints, together with example customer complaints reports was inspected. Customer complaints records were adequately maintained, the identification and follow-up on actions to prevent reoccurrence was a re-occurring weakness at the site. Corrective actions have been made.

2.6 PRODUCT RECALLS

SOP on product recall was reviewed during inspection.



2.7 CONTRACT PRODUCTION AND ANALYSIS

The company contract out some analytical tests to outside laboratories, however, the number of contract tests was limited to those requiring specialist instrumentation. The list of contracted out tests was reviewed during the inspection. An example technical agreement and audit report was inspected and was found to be satisfactory.

2.8 SELF INSPECTION AND QUALITY AUDIT

The self-inspection approach and schedule for 2011 were inspected and found to be satisfactory.

2.9 PERSONNEL

In general, the personnel met and interviewed during the inspection were experienced and skilled.

The company made significant use of casual workers. There was no overall company policy for the use of casual workers, and controls around ensuring that only trained staff were allowed on site, corrective actions have been made.

2.10 TRAINING

Training documents, files and related information for personnel were inspected. Training records were generally kept.

Basic training records were in place for casual staff, and a number of spot checks indicated that these covered all casuals on site. Training involved generally hygiene awareness, health checks and some basic procedural training to local language. Specific GMP training was absent from the casual's training program, corrective actions have been made.

2.11 PERSONAL HYGIENE

An acceptable level of personal hygiene was observed. Direct contact was avoided between the operator's hands and starting materials, primary packaging materials and intermediate or bulk product. Personnel were wearing clean body coverings appropriate to the duties they performed,



2.12 PREMISES

The premises was located, designed, constructed, adapted, and maintained to suit the operations carried out. The HVAC system was in general acceptable in terms of its design.

The building was medium size and consisted mainly of bricks with plastered walls. Since the last inspection, the new extended area for production was completed and operational. The new area was spacious and of good design and finishing. Personnel and material flow was acceptable. Additional plans were mentioned for further expansion of dispensing, storage and packaging areas.

Warehousing

The site was furnished with separate raw materials and finished product storage areas. These were a mixture of non-air conditioned stores, <30°C & <25°C storage areas with provision for refrigerated storage. The controls around the use of the correct area for material storage was lacking in that a raw material requiring <25°C storage was noted stored in the <30°C storage area.

Generally the storage areas were well maintained and controlled. The system used was validated in 2007. Its validation was not explored in detail, but is an area which should be further examined in future inspections.

Dispensary

A dedicated dispensary was in use. This was a well laid out area, being a new addition to the site in 2009. A series of separate rooms with down-flow booths were present for dispensing on a batch-wise basis. Observation was made during the inspection, and the company stated their intent to implement these.

Primary manufacturing areas

The primary manufacturing areas consisted of standard granulation, drying, compression, encapsulation and coating areas which were suitably controlled segregated and maintained. Separate air handling systems were in use for each manufacturing cubicle, which contained terminal HEPA filters. The air in these rooms was classified on an annual basis. The policy in relation to this activity was inspected, and found to contain suitable controls over this practice.

Packaging

The packaging at site consisted of a newly constructed secondary packaging hall with several lines, which were well segregated. The packaging methodology itself was very basic. Offline over-coding of cartons was in general use, and secondary packaging was a manual process with no on-line verification of the correctness of components.

Utilities

Purified water was generated using a double Reverse Osmosis system from the municipal supply. Water was stored in a stainless steel tank which fed a 316L steel distribution loop, sanitised by heat on a regular basis. The system was well maintained



and controlled. Air handling units were present on the mezzanine area of the facility, which were inspected. The area was found to be generally satisfactory.

2.12 EQUIPMENT

Equipment was located, designed, constructed, adapted, qualified and maintained to suit the operations to be carried out. Production equipment was in good condition.

2.13 MATERIALS

The company had developed a suitably controlled approved supplier's list, which was supported by a program of audits and supplier questionnaires. The item code system for raw materials was weak and to be improved.

2.14 DOCUMENTATION

In general, the documentation system was established and maintained; documents were approved, signed and dated by appropriate responsible persons, regularly reviewed and kept up to date. Specifications and testing procedures were available.

2.15 GOOD PRACTICES IN PRODUCTION

The site was essentially a multi-product facility which handled a large number of APIs. Production operations followed defined procedures. Materials, bulk containers, major items of equipment, and where appropriate, the rooms and packaging lines being used were labelled with an indication of the product or material being processed. The company's policy or procedure for the introduction of new products to the facility were inspected and discussed.

2.16 GOOD PRACTICES IN QUALITY CONTROL

The quality control laboratories were inspected. These were housed in a separate block, and comprised separate chemistry, microbiology and stability storage areas. The company maintained a range of standard analytical equipment (HPLC, HP-TLC, GC, UV-spectroscopy, TIR spectroscopy, dissolution testing). The labs were found to be generally well controlled.

A small microbiology laboratory was also present where raw material, water samples and environmental monitoring samples were processed. The area was generally found to be fit for purpose for a non-sterile solid dose facility.

Example equipment validation reports for dissolution apparatus, and Malvern particle size apparatus were inspected, with no significant issues identified.



The company had a defined process for investigating out of specification (OOS) results, but the system was noted to be weak. Corrective actions have been made.

A stability storage area was present with a series of stability cabinets covering standard ICH stability conditions on UPS back-up. Temperatures and humidities were continuously recorded. Example records for the 30°C 60%RH cabinet were inspected and were found to be satisfactory.

Environmental monitoring of the production areas was comprehensive. Data indicated that the areas were suitable for their intended purpose, conforming to the WHO Grade D requirements.

Microbiological testing on the purified water system was carried out. Total viable Aerobic count, tests for specific pathogens and a wide variety of chemical tests (covering a number of pharmacopeial requirements) were carried out on a daily basis. Data were well within both action and alert levels for the system.



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, Ajanta Pharma Ltd, b-4/5/6, MIDC Industrial Area, Paithan District, 431128, Aurangabad, Maharashtra, 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 three years, provided that the outcome of any inspection conducted during this period is positive.