

Prequalification of Medicines Programme
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Finished Product Manufacturer

Part 1: General information

Name of Manufacturer	Meditab Specialities Pvt Ltd
Unit number	N/A
Production Block	N/A
Physical address	352, Kundaim Industrial Estate, Kundaim, Goa. 403115, India
Postal Address	As above
Telephone number	+91 832 239 5058, +91 832 239 5193
Fax number	+91 080 222 56323
Summary of all activities performed by the manufacturer Indicate dosage forms and type of products	Manufacturer and packer of tablets
Scope and type of inspection	Routine GMP inspection
Focus of inspection - products in WHO PQ program covered in the scope at the time of inspection	Tablets (coated and uncoated)
Date of inspection	27 -30 January 2009
Program	Prequalification Programme: Priority Essential Medicines

Part 2: Summary

The manufacturing site of Meditab Specialities Pvt Ltd located in Goa, India, was inspected by a WHO prequalification inspection team on the abovementioned dates.

General information about the company and site

Meditab Specialities Pvt Ltd was established in 1998. Tablets (coated and uncoated) and hard gelatine capsules were manufactured on site. The company employed about 130 members of staff. It manufactured products under contract from other manufacturers.

History of WHO and/or regulatory agency inspections

This was the first inspection of the site by WHO. The site was previously inspected by agencies from Nepal, Namibia, Ukraine and Zambia.

Focus of the inspection

The inspection focused on the production and control of coated tablets. The inspection covered various sections of the WHO GMP text, including premises, equipment, documentation, materials, validation, sanitation and hygiene, production, quality control and utilities.

Inspected Areas

On the first day after arrival at the site, the company welcomed the inspectors. Business cards were exchanged followed by an introduction of responsible persons (unit head and QA Head) as well as two representatives from the contract giver. The company made a brief presentation of its activities and systems, after which the inspectors introduced themselves. There was then agreement on the tentative inspection plan for the week.

The inspection was started by reviewing the following documents:

- Product List (05.01.2009)
- Organization chart (January 2009)
- Job description (Quality Assurance Head and Unit Head - January 2009)
- Product Quality Review report for a selected product, and SOP
- SOP for complaints handling and complaints register for 2007 and 2008
- SOP for change control and register / list of changes
- Change control reports (change in API specification and increase in batch size of a product)
- List of tests and materials tested at contracted quality control laboratories
- Agreement between Meditab and the contract giver
- Agreement between Meditab and a Contract Research Organisation
- List of contract workers
- SOP for handling deviations, including the trends for 2008 and deviation list/register
- Corrective action and preventive action list
- Approved Supplier List

- Master formula for a selected product submitted in prequalification
- Site layout including process flow, personnel and material flow, area cleanliness classification, specifications, list of AHUs

After lunch, the inspection continued by reviewing areas, activities and documentation on site. These included the receiving bay, receiving and dusting area of starting materials, warehouse, sampling and dispensing. Operators were interviewed and documents were inspected. These included SOPs and records relating to environmental monitoring (temperature), sampling, dispensing, cleaning, use of areas and components, status of materials, transfer of materials (codes), and bin locations. In general, areas, records and activities were considered acceptable excluding some minor findings as listed below.

On the second day, the findings of day one were presented to the company. The inspection then continued as the inspectors reviewed documents and source data including:

- Validation Master Plan
- Process validation protocol and report
- Source data including chromatograms
- Batch manufacturing records for a selected batch of product

Three batches of product were included in the process validation. However, at the mixing stage, each batch is subdivided into three sub-lots. Only one of the sub lots in a batch was subjected to validation (sampling). The sub lots were then mixed and blended with the lubricant (step included in the validation. Drying was not included in the validation as it was considered to have been done by the contract giver and not verified as part of the concurrent validation.

The production areas were then inspected including the sifting area, granulation, blending, compression, coating, washing, tools and components and bulk storage areas as well as primary packaging (III and IV). In general, areas, records and activities were considered acceptable excluding some minor findings as listed in the full inspection report.

After lunch, documentation related to the HVAC system and FBD was inspected and the service areas for the selected AHUs and the purified water system. Documents inspected included:

- Protocols and reports for the qualification of selected AHUs including raw data and calculations
- Qualification protocols and reports for the FBE
- Schematic drawing of the newly installed purified water system

On the third day, the findings of day two were presented to the company. The inspection then continued by inspecting the secondary packaging area where packaging line III was inspected. Documents were reviewed and the leak test was observed. Then the inspectors inspected the receiving, storage and control of packaging materials. This included sampling of primary and secondary packaging materials as well as the quality control laboratory for packaging materials. The inspection then continued in the quality control laboratory. The inspection of the laboratory included the retention sample storage area, stability testing, chemicals and reagents, instrument use and calibration and related activities. The purified water system

documentation was then reviewed late in the afternoon. Document inspected during the day included:

- SOP for sampling of materials
- Batch Packaging records
- SOP for training, schedule and records
- Leak test SOP
- Temperature monitoring records
- Analytical reports and specifications for selected packaging materials including Al foil, carton and leaflets
- Specifications and analytical reports for selected starting materials
- Source data including calculations, mobile phases preparation records, chromatograms
- Procedures and records for selected equipment (calibration, maintenance)
- Incubators
- Stability schedules and test reports
- Retention samples and records
- Temperature mapping
- Selected documentation for the purified water system including schematic drawing and qualification documentation

On the fourth day, the inspectors reviewed cleaning validation documentation, out-of-specification (OOS) investigation and selected results for the testing of water samples (microbiology). The documents inspected included:

- Selected documents for cleaning validation (analytical method validation, matrix / bracketing, worst case product selection, equipment chains, recovery study and summary for cleaning validation for mebendazole)
- SOP for OOS and OOS register, as well as two OOS investigations identified from the records
- Purified water testing results (source data) for selected sampling points for identified dates, records for media preparation and sterilization as well as positive and negative controls.

2.1 QUALITY ASSURANCE

There was a quality assurance system in place that covered all the relevant aspects of the WHO GMP guidelines. Production and control operations were specified in written form, deviations were reported, investigated and recorded, changes were approved before implementation and responsibilities of key personnel were described in job descriptions. Annual product quality review was done according to an SOP, however, some aspects were not covered fully such as materials and trending of results / data. This was addressed by the company in the corrective action plan.

2.2 GOOD MANUFACTURING PRACTICES (GMPs) FOR PHARMACEUTICAL PRODUCTS

In general, principles of Good Manufacturing Practices were implemented and followed.

2.3 SANITATION AND HYGIENE

A high level of sanitation and hygiene was practised. There were systems implemented to minimize the risk of contamination and cross-contamination to an acceptable level. Cleaning procedures and records for premises and equipment were available. Cleaning validation was performed, but some equipment was left out of the chain identified (e.g. chain 1) and recovery studies were not performed on all non SS surfaces. This was addressed by the company in the corrective action plan.

2.4 QUALIFICATION AND VALIDATION

The validation policy of the company was documented in a validation master plan. The validation master plan also covered cleaning procedures, analytical methods and computerized systems. Protocols and reports for the qualification and validation were available for the premises, utilities, equipment and processes checked during inspection. Although validation and qualification was in general considered acceptable, some aspects lacking included appropriate qualification of all parameters of the FBD and newly installed AHUs.

2.5 COMPLAINTS

Complaints were handled, investigated and reviewed according to the established procedure and considered acceptable.

2.6 PRODUCT RECALLS

Not inspected.

2.7 CONTRACT PRODUCTION AND ANALYSIS

The arrangements for production and analysis of the product were clearly defined in a contract. Special analytical tests were contracted out to other laboratories. The responsibilities of both parties were also defined in a contract. The contract checked during inspection did, however, not cover all necessary aspects as e.g. handling of out of specification results or storing of retention samples. This was addressed by the company in the corrective action plan.

2.8 SELF INSPECTION AND QUALITY AUDIT

Not inspected.

2.9 PERSONNEL

An organizational chart was available. Individual responsibilities of key personnel were defined in job descriptions. Quality assurance and quality control departments were independent from production. The head of quality assurance was responsible for the release of the product to be shipped to the contract giver.

2.10 TRAINING

The procedure for training listed the introductory training for new employees as well as the on-going training of existing staff. On-going training was carried out according to a training schedule. The system did not ensure that all employees got the needed training in the relevant areas of their work. Though the procedure did not specify any exemptions, contract workers received a "reduced" training, which was not described in the SOP.

2.11 PERSONAL HYGIENE

Acceptable - see also 2.3 above. Employees had to undergo a health examination prior to employment. The initial training also included aspects to personal hygiene and gowning.

2.12 PREMISES

In general, the premises were found to be designed, constructed, maintained and cleaned to suit the operations carried out and facilitate sanitation. An exception was the change room and corridor leading to the production rooms - these were not of the same classification as the production rooms. The logical flow of materials and personnel was ensured. The HVAC system was suitably designed, installed and maintained (with the exception of the observations listed below which include balancing of the total system). A new purified water system was installed about three months prior to the inspection and was still under validation (Phase III was on-going).

2.13 EQUIPMENT

In general, the equipment was found to be designed, constructed, maintained and cleaned to suit the operations carried out. In some cases, there was lack of traceability to instruments used in the calibration of equipment / instruments. This was addressed by the company in the corrective action plan.

2.14 MATERIALS

Materials were generally procured, received, stored, sampled, dispensed and used in an appropriate manner according the GMP recommendations. Material management linked to production planning required attention. The handling of reference materials, in particular re-testing / stability of bulk from which individual vials were prepared, required attention. This was addressed by the company in the corrective action plan.

2.15 DOCUMENTATION

The company had an elaborate documentation system with SOPs, specifications, protocols and reports as well as other related documents. These were in general acceptable (clearly designed, completed, controlled and authorized).

2.16 GOOD PRACTICES IN PRODUCTION

In general, production activities were performed in accordance with SOPs and batch documentation as well as principles of GMP.

2.17 GOOD PRACTICES IN QUALITY CONTROL

In general, quality control activities were performed in accordance with SOPs, specifications and standard test methods as well as principles of GMP.

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, Meditab Specialities Pvt Ltd, Goa, India was considered to be operating at an acceptable level of compliance with WHO GMP guidelines.

The manufacturer's response to all observations included a description of the corrective action implemented or planned to be implemented, and the date of completion or target date for completion. The corrective actions were evaluated, found acceptable and will be followed up during the next inspection.