

Prequalification of Medicines Programme
WHO PUBLIC INSPECTION REPORT
Finished Product Manufacturer

Part 1: General information

Name of Manufacturer	Ranbaxy Laboratories Ltd
Unit number	Paonta Sahib
Physical address	District Sirmour 173025 Himachal Pradesh India
Date of inspection	18, 19, 20 and 21 November 2008
Type of inspection	Special
Dosage forms(s) included in the inspection	Tablets and capsules
Summary of the activities performed by the manufacturer	Production and quality control

1. Scope of the inspection.

A special inspection of Ranbaxy, Paonta Sahib was performed by a team of six inspectors from the World Health Organization (Geneva, Switzerland), Therapeutic Goods Administration (Australia), Medicinal Health Products Regulatory Agency (United Kingdom) and Health Canada, (Canada) on 18 to 21 November 2008.

The inspection focused on verification of data, to establish the reliability of data, and to assess compliance with Good Manufacturing Practices as part of the extension of the previous inspection performed at this site. (See also WHOPIRs on www.who.int/prequal). Various documents were reviewed and inspected for production and control activities.

2. Summary of the main steps/history of the inspection.

Following previous inspections by the different agencies and WHO, as well as the recent inspection by the USA FDA and an "import alert", FDA 483 and warning letters from the

This inspection report is the property of the WHO
Contact: prequalinspection@who.int

USA FDA, various inspections were planned at Ranbaxy sites. As an extension of the October routine GMP inspection lead by MHRA, a special inspection was further planned to inspect and verify the reliability and accuracy of data at Ranbaxy Paonta Sahib for selected products.

During the opening meeting, the company informed the inspection team on the key changes since the FDA and October MHRA inspection. These included changes in quality control and production, changes in some staff positions (including increased QA & QC staff) and quality meetings.

The Inspection plan was as reflected below:

Day 1	
08:30 OPENING MEETING	Introduction (Inspectors and company staff members) Objectives and scope of the inspection Confirmation of the proposed programme
Morning	Meeting and discussion with responsible persons for Production activities and archiving of documentation <u>Documentation review (Production activities):</u> Annual product Review Complaints Deviations Change control API Specifications Approved Supplier List Visit to the archive section Batch Manufacturing Documents (masters) and Batch Manufacturing Records for selected batches Material management (SAP)
Afternoon	Continue with documentation review (Production activities)
	Closed meeting of inspectors
Day 2	
Morning	Documentation review continued (Production activities)
Afternoon	Documentation review continued (Production activities)
	Closed meeting of inspectors
Day 3	
09:00	Meeting and discussion with responsible persons for quality control activities and archiving of documentation in the laboratory <u>Documentation review (Quality Control)</u> Specifications (Selected APIs and Finished Products) Standard Test Procedures Stability program, protocol, procedure OOS SOP and records
Afternoon	Retention sample storage Documentation review continued (Quality control)
	Closed meeting of inspectors
Day 4	

Morning	Documentation review continued (Quality control)
Afternoon	Documentation review continued (Quality control)
	Closed meeting of inspectors
16:00	Closing / exit meeting with company representatives

The inspectors worked in three teams and reviewed documents and data. This included - for selected products including but not limited to anti-retrovirals, anti-bacterials, anti-cholesterol product(s)- review of data and information on production and quality control, stability testing etc. (*Note: Details of products and batch numbers, codes etc are removed for confidentiality purposes*).

Below is a summary of documents reviewed and found to be acceptable during the inspection, or through corrective actions taken by the company in response to the inspection report.

- Annual Product Quality Review Reports for selected products for WHO markets, selected products for the Canadian market, selected products for the European market and selected products for the Australian market
- Lists of products and batches supplied to Australia, Canada, the United Kingdom and the World Health Organization in the last 2 years
- API and FP specifications for selected products for the markets referred to above
- Batch manufacturing records for selected products for the markets referred to above
- Various SOPs
- Standard test procedures
- Material transfer records

SAP: Various reports were run from SAP and materials and products were checked on SAP for their source, inventory, status, codes and transfers. SAP data and information inspected included

- All codes for selected APIs
- Report for API transfers (including several transactions)
- List of API transfers and stock transfer for the period of January 2007 to November 2008
- Reports on grouping of transfers by selected APIs
- Verification of suppliers / manufacturers listed for selected APIs
- Recipes for selected products
- "locked" API sources for selected products in recipes for batch manufacturing documents / manufacturing instructions

- whether the recipes were ensuring that the only the correct APIs could be issued for use in products
- Audit trail for transfers
- APIs sourced from all suppliers for selected APIs including the use in products by batch to verify in which batches these were used
- Verification of the use of batches of selected APIs in products prequalified to ensure that only APIs from approved sources were used in the period January 2007 to November 2008
- Material document list
- Material inventory list
- Process orders
- List of approved external vendors for procurement
- Approved Suppliers List (ASL), (January 2008 edition)
- Verification of the raw data for the testing of samples taken when a selected API was changed from one code to another for use for different markets
- Specifications for selected products for the markets referred to above, including
 - APIs and Finished product specifications
 - Product release specifications
- Method validation report for ID tests and raw data
- Master formulae
- Batch Manufacturing records and analytical reports including source data
- Update report into the investigation into discrepancies within validation data
- Selected OOS investigations and reports
 - Records of analysis for several batches of products
 - TSE/BSE Data: Certificates were requested and examined for selected materials
 - Approved Supplier List and materials codes

Inspection of quality control activities, documents and data included (but not limited to):

- Selected OOS investigations and reports
- CoA and records of analysis for the several batches
- Stability study raw data including verification of data presented in product dossiers (tabulated) against raw / source data
- Calculations were made and verified against original calculations by analysts during the inspection including for dissolution data, assay and LOD - at selected packaging presentations, stability storage conditions and time intervals (for various products)
- Analyst records, work sheets, calculations, chromatograms, weight slips and related reports
- Selected chromatograms including those of reference standards used were checked on the computers

- Specifications for APIs and Finished products were reviewed and verified against analytical reports and source data (including review of electronically stored data) for selected batches and selected parameters including spectra and chromatograms.

Complaints

Complaint files for 2007 and 2008 were reviewed.

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 - *Ranbaxy Laboratories Ltd Paonta Sahib, India*, was considered to be operating at an acceptable level of compliance with WHO GMP guidelines.

The observations (non-compliances with guidelines) listed in the full inspection report were addressed in a timely manner. The manufacturer responded to all observations and for each 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 assessed by all the inspectors and were considered acceptable.