



**WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Finished Product Manufacturer**

Part 1: General information

Name of Manufacturer	Sandoz SA (Pty) Ltd
Unit number	NA
Production Block	NA
Physical address	Sandoz SA (Pty) Ltd, 72 Steel Road, Spartan, Kempton Park, South Africa
Contact person and email address.	Mr. Peter Indinger (Director: Quality) Mobile: +27-82-449 7984 Tel: +27-11-929 9014, Fax: +27-11-394 3084 E-mail: peter.indinger@sandoz.com
Date of inspection	12, 13, 14 and 15 April 2010
Type of inspection	Routine inspection
Dosage forms(s) included in the inspection	Coated tablets
WHO product categories covered by the inspection	Finished Pharmaceutical Products (FPPs) used in the management of Tuberculosis (TB)
Summary of the activities performed by the manufacturer	Manufacturing, packaging, quality control and batch release of tablets and hard gelatine capsules.



Part 2: Summary

General information about the company and site

The facility inspected was **Sandoz SA (Pty) Ltd**, 72 Steel Road, Spartan, Kempton Park, **South Africa**, here after referred to as **Sandoz SA**. According to the Site Master File, Edition 08 effective 23 November 2009, Sandoz SA is fully owned by Sandoz AG. Sandoz AG is wholly owned subsidiary of Novartis AG, Basle, Switzerland. Sandoz SA was established in 1979 as Rolab, acquired by Ceiba Geigy in 1987 and subsequently by Novartis SA in 1997. In 2003 the name was changed from Rolab to Sandoz and in 2006 it was registered as a legal entity separate from Novartis SA, but still fully owned subsidiary of Novartis AG. The plant at the current Spartan site was established in 1995/6. Existing at the site are other business units of Novartis SA, namely Novartis Pharma, Novartis Consumer Health and Novartis Animal Health. However, these are separate facilities used for each of these business units. This inspection report is specific to the facilities used by Sandoz SA.

The factory of **Sandoz SA** is located in Spartan Industrial Area on a 51,023m² site and built up area of 19,791m² (13,136m² for technical operations, 2,1818m² for warehouses and 1,134m² for laboratories. It was involved in production of hard gelatin capsules and uncoated, film coated, sugar coated and chewable tablets (approximately 250 finished dosage forms). It was also involved in secondary packaging of tablets, capsules, nasal sprays, eye drops, suppositories plus ampoules and vials for injection (approximately 180 finished dosage forms). The QC laboratory had capacity to test approximately 130 batches per month.

According to the SMF, the company employed a total of 170 people distributed as follows:

- Quality assurance 12 (3 pharmacists)
- Production 84 (10 pharmacists)
- Quality control 36 (23 chemists/analysts)
- Logistics (planning, storage & distribution) 22 (1 pharmacist)
- Technical & Engineering support services 08
- Site Head 01
- Responsible Pharmacist 01
- Support staff (HSE, HR, PA, BPA) 06

History of WHO and/or regulatory agency inspections

This was the fifth inspection of this site by WHO Prequalification team; the previous have been conducted in 2003, February 2006, May 2008 and March 2009.

The above manufacturing facility was regularly inspected by and had a valid manufacturing license and GMP certificate from the Medicines Control Council (MCC) of South Africa.

According to the company presentation, the site had also been approved by the following regulatory agencies:

- Medicine & Healthcare Products Regulatory Agency (MHRA, UK, 2000)
- Ministry of Health Saudi Arabia (MOH, Saudi Arabia, 2002)
- ENVISA, Brazil (2003, 2005)

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- Danish Medicines Agency (2004, 2007, 2010)
- Ministry of Health, Sudan (2004)
- Ministry of Health, Botswana (2005)

Focus of the inspection

The inspection focused on the production and control of Anti-tuberculosis products. The inspection covered several sections of the WHO GMP text, including premises, equipment, documentation, materials, validation, sanitation and hygiene, production, quality control and utilities. Special focus was also given to the issues raised in the Notice of Concern.

Inspected Areas

Day 1

The inspection was opened with a meeting which was attended by the key personnel of Sandoz South Africa and representatives from Sandoz Corporate. Following introductions, the proposed inspection plan/schedule was confirmed. This was followed by a series of company presentations which covered the Company overview, site description, production and QC capacities, quality management and assurance systems, summary of manufacturing processes, major equipment and product range, inspection history, summary of changes and CAPAs since the last inspection. It highlighted that CAPAs for all the major observations had been closed and 2 of the minor observations (temperature mapping and hold time studies) were still ongoing. A copy of the presentations was obtained and will be placed in the company file.

The evaluation of the following areas of the quality management system followed:

- Personnel Policies: Organization charts, Job descriptions, Training. Job descriptions and training records of the following were reviewed in details:
 - Production Director.
 - Pharmaceutical Process Manager.
 - Production Manger (shift leader).
 - Production Manager (Packaging).
 - Quality Director.
 - QA Compliance Manager.
 - Responsible Pharmacist.
 - Several analysts from other sites
- List of products of TB products under the prequalification programme and the corresponding MCC registered versions.
- Batch numbering system. Batch/Lot numbers were generated by SAP:
 - Raw materials and Packaging materials: 9 digits starting from 100000001.
 - FPP and bulk: 6 digits starting from 500001.
 - Secondary packaged products: used supplier's batch/lot number and a suffix starting from A added for various secondary version of the same primary pack.
 - Reworked/repacked batches: Suffix "R" added to original batch/lot number.
 - Part release batches: only on exceptional request and formal approval.
- SOP and document preparation, review and control: The SOP provided for review after 36 months for all SOP and annually for those with names of individuals.

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- Change control + related SOPs and register for 2009: The SOP provided for changes to be completed within 30 days and only extended on QA approval. Emergency changes could be handled as deviations and documented with 24 hours. Selected changes were reviewed in detail:
 - Change in suppliers of selected APIs and excipients.
 - Change of item code for selected APIs and excipients.
 - Optimization of granulation steps for one FPP. Added overage of one API for granulation but weighed off the exact amount of granules for the next steps.
 - Change in LOD specification for one FPP from arrange to maximum value.
 - Installation of final filter 0.2µm on N₂ sampling pipeline.
 - Installation of heating device for HVAC for main warehouse to maintain temperature within 15⁰ - 25⁰C limits.
- SOP for Change Management of Computer Systems:
 - Change on implementation of SAP Plant maintenance Solution to cover the following:
 - Preventive maintenance/Calibration
 - Work order processing
 - Work order confirmation
 - Maintenance/ Calibration reports
- SOP on GMP audits of vendors and third part manufacturers.
- Deviations + related SOPs and registers for 2009: The SOP provided for deviations to be completed within 30 days and only extended on QA approval. Selected deviations were reviewed:
 - Deviation related to related to 4 batches of FPP which showed LOD of final granule below the limit. The batches also failed for assay of one API and were rejected for destruction.
 - Deviation on batches packed on quarantine - before release of the bulk.
- Reprocessing/Reworking policy:
- Self inspection (SOP, Plans and reports): The schedule and summary report showed that most audits in 2009 were done well beyond scheduled date and those for 2010 were so far on schedule.
- Complaints handling system + related SOP and register for 2009.

Other issues reviewed included:

- Sourcing, receiving and release procedures for Nitrogen gas (N₂)
- Hold time studies for locally produced bulk products: Protocol and report.

Because inspection ended late in the evening, the inspectors only outlined the outstanding issues from inspection and the feed back on the findings of the day was differed to the following morning.

Day 2

The inspectors gave feed back on the observations during the previous day and a revised schedule for the day. Then the evaluation of the outstanding issues from the previous day followed:

- Report of the investigation of a complaint related to red powder and marks inside the blisters of two batches of one FPP was reviewed in detail.
- Product recall system + related SOP and register for 2009. Selected cases were reviewed.

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- Evidence of disposal of the 4 rejected batches of One FPP: two batches had been destroyed but stock was still reflected in SAP while the other two were still in the warehouse. The SOP on waste disposal was reviewed.
- History of dispensing, compounding, compression, packaging, analysis and release of a batch of one FPP was reviewed.
- Upgrade of the HVAC system for the dispensing rooms: Dispensing 1 - AHU-M721 and Dispensing 2 - AHU-M722 and the corresponding risk assessment and qualification report.

The team proceeded with the inspection of receiving and storage areas plus related procedures and records.

- Vendor approval, qualification and maintenance system in relation to sampling and testing procedures:
 - An extract from the approved vendors' list showing approved vendors for APIs.
 - List of suppliers and codes of APIs used in TB products for the local market and export.
- Starting materials, packaging materials and components receiving, quarantine, sampling and storage areas +SOPs and log books:
 - SOP on sampling procedures
 - Form on the sampling plan
 - Selected batches of raw materials and packaging materials (e.g. Printed aluminium foil) were identified for more detailed evaluation of their sampling and testing.
- Testing of packaging materials and components: specifications, procedures, calibrations and maintenance records for testing instruments.
- Temperature + RH mapping and monitoring:
 - Records of monitoring conditions in the main warehouse. The temperature was around 25⁰C but relative humidity varied from 60% to 80%.
- Pest control procedures: Rodent bait stations were outside the ware house and there were insecticutors inside near the entrance of the warehouse.

The inspectors proceeded to review the records for monitoring the water generation and distribution systems for the year 2009.

The inspectors outlined the outstanding issues from inspection and the feed back on the findings of the day was differed to the following morning.

Day 3

The inspectors started by reviewing the areas inspected the previous day, gave feed back on the observations made and outlined a revised schedule for the day. Then the evaluation of the outstanding issues from the previous day followed:

- SOP on sampling procedures, pooling samples to make a composite and nitrogen purging procedures during sampling.
- Policy and records of cleaning sampling rooms.
- Procedures for gowning and entrance into the sampling room.
- Procedures for cleaning sampling tools.
- Procedures and records for cleaning the vacuum cleaner used in the sampling rooms.
- Preparation and handling of materials before and after sampling.
- SOP on testing aluminium foil.

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- Records of sampling and testing of a batch of printed aluminium foil.
- Sampling and testing records of selected batches on APIs.

The open area where the vacuum cleaner and plastic pallets were stored was inspected. This was followed by an inspection of the staging warehouse and cold rooms (8^o - 15^oC). Selected batches of an API that showed multiple sampling were identified for more detailed evaluation. The storage section for rejected material was inspected to confirm the presence of the rejected batches awaiting destruction.

Document review followed in the board room:

- Cleaning validation approach: the SOP provided for a matrix approach to determine the worst case and the parameters monitored during validation included: visually clean plus removal or reduction of detergent, active and microbial residues.
- A report of the discussion of the worst case and limit setting (*NMT 10ppm in the next product or NMT 0.1% of normal therapeutic dose in the maximum daily dose of next product*) based on solubility, therapeutic dose; surface area of the equipment chain was reviewed.
- Recovery studies were evaluated using studies done on one API and related products.

After lunch, the production area were inspected following the flow of materials from dispensary, mixing, granulation, drying, compression, coating, primary packaging and secondary packaging observing current practices and reviewing related SOPs, logbooks, BMRs and BPRs. Selected documents were reviewed in detail:

- SOP on cleaning of manufacturing areas.
- SOP on bulk processing.
- SOP and records of calibration and daily verification of dispensing scales.
- Records of in process control including metal detection.
- SOP on Storage, issue, cleaning and caring of punches and dies.
- SOP and records of operating, cleaning, requalification and maintenance of Glatt AG coating machine.

Inspectors visited the technical area and inspected the final filter (0.2µm) for compressed air. AHU M721 and AHU M722 supply the dispensaries and AHU supplying the Glatt AG coating machine.

At the end of the day, the inspectors outlined the outstanding issues.

Day 4

The inspectors started by giving feed back on the observations made the previous day and a revised schedule for the day. They outlined the outstanding issues that will be prioritized for review.

The team proceeded to inspect the main quality control laboratory:

- Sample receipt, storage and allocation.
- Wet chemistry laboratory:
 - Preparation and labelling of electrolyte and care for electrodes for the Karl fisher.

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- Cleaning and handling glassware (SOP) including cuvettes for UV-VIS spectrophotometer and polarimeter tubes.
- Instrumental laboratory: Qualification, calibration, preventive maintenance of:
 - SOP on calibration and operation of the Dissolution Apparatus in the QC laboratory. Certificates of USP calibrator standards of Prednisone and Salicylic acid.
 - HPLC apparatus (and chromatographic columns)
 - Polarimeter
- Laboratory materials management (Samples, Reagents, Stock Solutions, Reference and Working Standards).
- Starting materials and finished products specifications, testing and release.
 - Records of sampling and testing of the two batches of an API that had undergone multiple sampling.
- The use of LIMS in analysis and evaluation of the audit trail.

This was followed by inspection of the retention samples store and stability testing laboratory:

- Stability testing programme (SOP), stability specifications, records and raw data for selected batches were reviewed in detail including raw data on the HPLC.

The following outstanding issues were reviewed after lunch:

- Sensitivity setting of metal detectors.
- Record from LIMS on the status of a batch one FPP which was packed in buckets and stored in the hold area at the back of the main store.
- Annual product Review for selected FPPs for the period 22/11/2008 to 01/03/2010.
- Records of qualification of the FBD and calibration instruments used in the qualification.

At the end of the day, the team reviewed progress of the inspection, gave feed back on the activities of the day and a summary review of the entire inspection and received reactions from the management of the company. There was consensus on all the observations made. It was also noted that tremendous progress had been made in addressing the issues raised in the Notice of Concern (NOC) in the areas of HVAC system, premises, sampling area and measures to reduce cross-contamination. It was therefore found reasonable to recommend that both the NOC and Notice of Suspension (NOS) be lifted.

2.1 QUALITY ASSURANCE

Improvements in the quality assurance systems were noted since the previous inspection and the systems in place now generally enabled the manufacturer to assume responsibility for the quality of the products to ensure that they consistently complied with approved specifications. The management structure in place enabled senior management, through the Quality Assurance Department and other key personnel, to assume this responsibility and the job descriptions of staff at different levels and organograms facilitated their participation and commitment. Documentation of staff training and evaluation of its effectiveness required further strengthening.

GMP requirements were incorporated in the various quality assurance procedures and their implementation had greatly improved. Routine procedures were guided by written and approved

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procedures. Policies and schedules were in place to ensure that equipment and systems were qualified and procedures and processes validated. Systems were in place to control and ensure the quality of starting materials, intermediate products, finished goods and related data generated during production, quality testing, calibration and validation. Consistency and continuous improvement in the quality of systems, procedures and products were ensured through change and deviation control and were regularly reviewed and monitored through self inspection, annual product review and evaluation of trends.

The facilities in form of premises, equipment, and other facilities were generally adequate and suitable to support the quality assurance system.

2.2 GOOD MANUFACTURING PRACTICES (GMPs) FOR PHARMACEUTICAL PRODUCTS

The design and implementation of GMP adequately ensured minimization of the risk of cross contamination and mix ups. The necessary resources were provided in form of personnel; premises; equipment and services; materials, containers and labels; approved procedures and instructions; laboratories and equipment for in-process controls. The available facilities at the site, the manufacturing and quality control procedures were generally comprehensive and well executed and maintained by adequately qualified personnel to ensure products of consistent quality.

Nevertheless, there were some observations, like quality of air and nitrogen; comprehensiveness of and compliance with some procedures; monitoring storage conditions of some materials; testing of packaging materials and components; and others described in the sections that follow and summarized in the table of observations, that required attention to further improve the degree of GMP compliance.

2.3 SANITATION AND HYGIENE

The production and quality control facilities were maintained at high level of cleanliness. Cleaning procedures for the equipment and the premises were in place and were generally well executed, though weaknesses were noted with respect to cleaning of sampling tools and areas plus related documentation. Good waste collection and management procedures ensured a high level of hygiene of premises.

Personnel changing procedures and related gowning were appropriate but procedures and practices related to gowning for sampling need to be clarified and the staff appropriately trained.

2.4 QUALIFICATION AND VALIDATION

The policies and approaches to be followed in qualification of equipment and validation of systems and processes were outlined in a Validation Master Plans (VMP). Qualification included definition of user requirements and specifications (URS), Design Qualification (DQ), Installation Qualification (IQ), Operation Qualification (OQ) and Performance qualification (PQ). Validation and qualification were guided by approved protocols. There were schedules and frequencies for planned requalification, validation and revalidation. Reports reviewed showed that generally

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equipment was qualified and systems and process were validated. The need to improve the related documentation and calibration was noted.

2.5 COMPLAINTS

There was a system to record and investigate market complaints, give feed back promptly and take appropriate corrective and preventive action. Noted improvements in documentation of deviations will facilitate improvements in the investigation of complaints.

2.6 PRODUCT RECALLS

There was a recall procedure which had classified the deficiencies 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 to be informed while conducting a recall. The recall procedures for products already in the distribution chain were coordinated by the sales and distribution section located at Mahogany Ridge, Pinetown while recalls outside South Africa were coordinated by Sandoz Global QA.

It was noted that the backlog in stability testing previous experienced sometime caused delays in the initiation of recalls. Sometimes, delays in documentation procedures caused delays disposal of condemned products.

2.7 CONTRACT PRODUCTION AND ANALYSIS

The company packed bulk products manufactured by other sites or manufactures and also used some companies for packaging. Some analytical procedures were contracted out to outside laboratories. Where the contact giver or acceptor was a company outside the Sandoz Group, these arrangements were governed by technical agreements and there were provisions for auditing such vendors before entering into such agreements. Some of the agreements reviewed did not indicate all the required information.

2.8 SELF INSPECTION AND QUALITY AUDIT

There were procedures to conduct self inspection at least once a year for the purposes of monitoring the quality system and continuous improvement of the procedures. This procedure was comprehensive and covered all areas of production, quality control, quality assurance and engineering and its implementation was guided by a schedule with defined teams.

The schedule and summary report for 2009 showed that most audits were done well beyond scheduled dates but those for 2010 were so far on schedule.

There was a provision for conducting Vendor audits for API, excipients, packaging materials and component suppliers' manufacturing facilities as part of the vendor approval procedure. The procedure, however, did not provide for auditing suppliers of manufacturing aids like Nitrogen and other material used in sanitisation and cleaning.



2.9 PERSONNEL

The company had recruited a number of personnel, engaged a number of consultants and also engaged staff from other sister companies to help in reducing the backlog in analysis, execute specific remediation projects and train the newly recruited personnel.

There was an organization chart and job description to guide personnel. The responsibilities of the key personnel like responsible pharmacist, head of production, head of quality control and head of quality assurance were defined and there were personnel designated to deputise the key personnel in their absence.

The responsibility for batch review and release was assigned to pharmacists in the Quality Assurance Department who functionally report to the Responsible Pharmacist. Some deficiencies were noted in this area, mainly related to documentation, induction of new staff and compliance with procedures.

2.10 TRAINING

The company had training policy and program for all the employees. Training programs provided for induction training, basic cGMP training including health and hygiene, on the job training (SOPs Training), training on specific skills, and continuing training.

There was a provision for maintaining records of training and evaluation of effectiveness of the training although this was not effectively and consistently done. Review of records, observation of practices and interview of personnel revealed that more training of staff was needed to ensure full understanding of and compliance with several updated and new procedures.

2.11 PERSONAL HYGIENE

Personnel were trained in personal hygiene procedure and facilities were provided in form of change rooms, protective garments and disinfectants. The facilities were generally adequate and the procedures were generally well enforced. The health of the staff was checked on recruitment and thereafter every year. Medical check records were maintained for each staff.

2.12 PREMISES

The premises of Sandoz SA were suitably located in the middle of an industrial area and on a site that housed other Novartis Pharmaceutical production companies. The production areas were segregated from storage and quality control areas. The production premises were designed to facilitate cleaning, provide adequate segregation of different stages of production and a unidirectional flow of operations. Entrance into the production areas was through change rooms and toilets were effectively segregated from production areas, though not from the main warehouse. The design and operation of the HVAC system ensured that the production and storage areas were pressurized relative to the atmosphere and the corridors were pressurized relative to the production areas. The pressure cascade was regularly monitored. The system also provided controlled temperature to production and storage areas.

The areas of premises where dust was generated were provided with a centralized dust extraction system which was coupled to the HVAC system. This arrangement was adequate to reduce chance of cross-contamination.

The premises were supplied with purified water in all production areas. Its generation and distribution was regularly monitored and sanitised. Other utilities supplied to the production areas included nitrogen and compressed area. Issues were noted with their testing.

2.13 EQUIPMENT

Production and laboratory equipment were generally located, designed, and installed to suit the operations to be carried out. The layout and design of equipment could permit effective cleaning and maintenance in order to avoid cross-contamination, build-up of dust or dirt. In the tableting section, these included high speed granulators, tumble mixer, FBDs, mills and screens, rotary compression machines fitted with dedusters and metal detectors, sugar and film coating machines, thermoforming blistering machines, tablet counters for filling plastic containers. The surfaces of these machines in contact with the products were made of stainless steel.

Major laboratory equipment included HPLCs, GCs, UV spectrophotometers, FTIR spectrophotometer, dissolution testers, particle size testers, pH meters, polarimeter, Karl Fisher apparatus, disintegration apparatus and a various glassware.

The equipment reviewed had been qualified and were regularly maintained and calibrated according to approved schedules. In some cases, the level of calibration and maintenance was not comprehensive.

2.14 MATERIALS

Starting materials

Vendors of Raw Materials and Packaging Materials were approved mainly based on a questionnaire filled by the suppliers and full analysis of the first 3 batches. The audit of the suppliers' manufacturing facilities was only performed when deemed necessary. A list of approved vendors was available at the receiving area and was always followed in procurement and receiving of materials reviewed.

All containers of active pharmaceutical ingredients and excipients were sampled individually and tested for identity while full testing was done on a composite sample. Received materials were held in virtual quarantine (computer controlled) until when sampled and tested. Only approved materials were released for use. Materials were stored either in the main warehouse with controlled temperature (NMT 25⁰C) or cold rooms (8⁰ - 15⁰C). In these storage areas, relative humidity was monitored but not controlled.

Packaging materials

Packaging materials were purchased from approved vendors. Each consignment was quarantined, sampled and tested before release for use although the sample size was not in line with ISO2859 or BS6001.

Intermediate and bulk products

Granules were stored in intermediate bulk containers (IBCs) and could be held up to 30 days, though this was had not been validated.

Bulk tablets that were not packed immediately could be stored up to 12 months with retesting after every 3 months. Hold time studies were on going to generate data to support this hold time which was otherwise supported by data generated from other sites.

These were packed in double polythene bags and placed in plastic buckets. Imported bulk tablets were packed in aluminium foil and packed in paper cartons. These were also sampled and tested before being approved for packaging.

Finished products

Products were not released for distribution unless each batch was tested and its production, packaging and testing records reviewed and found in compliance with GMP and regulatory requirements.

2.15 DOCUMENTATION

The preparation, review, distribution and retrieval of Standard Operating Procedures were under the control of QA. SOPs were available or easily accessible at the points of use.

Validation and qualification activities were guided by approved protocols and corresponding reports were in place. The details in these protocols and reports could be improved.

Production and control of products was guided by master formulae, specifications of starting and packaging materials, production and packaging instructions, batch processing and packaging records, finished product specifications, standard testing procedures and corresponding records were maintained.

Weaknesses were observed in the comprehensiveness of some documents and records and compliance with some procedures. It was noted that most records were either new or recently revised and, although staff had been trained on them, this had to be done regularly and effectiveness of the training properly evaluated to improve compliance with the procedures.

2.16 GOOD PRACTICES IN PRODUCTION

Tablets production generally included sieving, pre-mixing, milling, wet granulation using a Rapid High-shear Mixer Granulator, drying in an FBD, resizing or screening of granules, blending, compression, coating and packaging. Compression machines had an on line deduster and metal detector.

Packaging was done either in plastic containers or in blisters and was accompanied by pre and post line clearance. Blisters were tested for proper sealing. There was online automatic inspection for correct label coding.

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All handling of materials and products, such as receipt and cleaning, quarantine, sampling, storage, labelling, dispensing, processing, packaging and distribution, was generally done in accordance with written procedures or instructions and records were maintained. This was supported by BMRs and BPRs.

There were provisions for conducting in-process checks (mass variation, hardness, friability, disintegration and tablet dimensions) and calculation of yield at various stages of production. Yield reconciliation was carried out and any out of limits yields were documented and investigated.

Improvements were noted in the documentation, evaluation and approval of deviations from instructions or procedures.

2.17 GOOD PRACTICES IN QUALITY CONTROL

The quality control and quality assurance departments were independent of production and were located in a separate building from production. It had adequate facilities in the form of space, equipment, reagents and chemicals to test all starting materials, packaging materials, intermediates and finished products before release for use or distribution.

Retention samples from each batch of starting materials and finished products were kept to facilitate any future investigation, if necessary.

There was a stability testing programme supported by stability chambers set at 40⁰C/75%RH, 30⁰C/65%RH, 25⁰C/60%RH and 5⁰ ± 3⁰C. Records showed that the backlog in stability testing had been greatly reduced but not totally eliminated, as some records reviewed that some analysis was completed beyond the stipulated 30 days from date of withdrawal.

General and wet chemistry laboratory

The laboratory had a fume hood for safe handling of volatile chemicals. The laboratory had the basic apparatus like pH meters, polarimeter, Karl Fisher apparatus, and various glassware. There were procedures and records for preparation of reagents, calibration of equipment and handling of glassware, though weaknesses in this area were noted.

Instrumentation

The instrument laboratory was stocked with HPLCs, GCs, UV-Visible spectrophotometers FTIR spectrophotometer, dissolution testers, and disintegration apparatus instruments. They were routinely maintained and calibrated and the performance of the HPLC columns was monitored.

The calibration and maintenance programme of the QC equipment was evaluated using the dissolution testing equipment which was found to have been calibrated by regularly checking the temperature probe, RPM and paddle clearance, wobble of the paddle and basket, performance checks using the standard USP tablets (Prednisone and Salicylic Acid).

Reference standards

Primary reference standards were used to standardize Working standards. There was a standard method of preparation of working standards.

Microbiology

There was a microbiology laboratory for testing water samples and other materials for microbial limit test. This was however not inspected.

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, **Sandoz SA (Pty) Ltd, 72 Steel Road, Spartan, Kempton Park, South Africa**, 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

The WHOPIR is valid for a maximum of 3 years, unless the site is found to be non-compliant in another inspection before the 3 years had lapsed.