



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

Part 1: General information

Name of Manufacturer	Aspen Port Elizabeth (Pty) Ltd
Unit number	Unit 1, Unit 2 (and QC lab attached to Unit 3)
Production Block	Unit 1 and Unit 2
Physical address	Aspen Port Elizabeth (Pty) Ltd, Cnr Fairclough Road and Gibaud Road, Korsten, Port Elizabeth 6020, Republic of South Africa
Contact person and email address.	Dr. Chris Stubbs, Quality Executive: SA Operations <ul style="list-style-type: none">• E-mail: cStubbs@aspenpharma.com• Switchboard Tel No: +27 (0) 41 407 2111• Direct Tel No: +27 (0) 41 407 2236
Date of inspection	8, 9, 10 and 11 March 2010
Type of inspection	Routine inspection and Data verification
Dosage forms(s) included in the inspection.	Tablets (coated and uncoated) and hard gelatine capsules.
WHO product categories covered by the inspection	Finished Pharmaceutical Products (FPPs) used in the management of HIV/AIDS (HA)
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 **Aspen Port Elizabeth (Pty) Ltd, located in an industrial area at the corner of Fairclough Road and Gibaud Road, Korsten, Port Elizabeth 6020, Republic of South Africa**, here after referred to as **Aspen OSD**. Aspen is a South African company listed on the South African Stock exchange. According to the company presentation at the beginning of the inspection and the Site Master File No. A0407 (Doc. No. OSD_PR_QSA_0564, ver. 4.0, effective 08 Feb. 2010), Aspen had direct ownership in 15 pharmaceutical manufacturing facilities on 11 sites on 3 continents (South Africa 4, India 2, East Africa 2 and Latin America 3). It also had strategic agreements with Boehringer Ingelheim, GSK, Iroko, Eli Lilly, BMS, Gilead Sciences and Merck to supply anti-infective molecules to South Africa and other developing countries. Other sites in South Africa included Aspen Pharmacare (East London, RSA) which manufactured mainly OTC products and Fine Chemicals Corporation (Cape Town, RSA) which produced APIs.

The Port Elizabeth facility was established in 1939 by Lennon Limited and later was owned by South African Druggists (SAD). It was purchased by Aspen in 1999 and named Aspen Pharmacare Ltd - General facility. This facility was now called **Aspen Port Elizabeth Unit 3**. In 2004, a second facility was built at this site and named **Aspen Pharmacare Ltd - OSD facility**. Its packaging capacity was expanded and warehouse modified in 2008/9. This was now called **Aspen Port Elizabeth Unit 1**. In 2008/9, a new OSD unit focussing on medium volume products was constructed and was now called **Aspen Port Elizabeth Unit 2**. This unit had no packing facilities and was being expanded to focus on oven drying and low volume products (*target: Q3 of 2010*). In 2008/9, a new facility, known as **Aspen Small Volume Parenterals**, for the manufacture of small volume parenterals was commissioned. **An off-site warehouse** for raw materials and packaging components was commissioned in 2008. These units share a number of systems including IT, procurement, QC laboratory (*located within Unit 3*), selected engineering services, stability laboratory and staff canteen.

Unit 1 and Unit 2 were operated under one name **Aspen Port Elizabeth (Pty) Ltd** and **license No. 0000001018** (*expiry date: 22 Dec. 2013*) issued by MCC of South Africa. This was the facility under inspection. According to the SMF, Aspen OSD employed **362 people** distributed as follows:

	Function	No. of employees Unit 1 & 2
1	Quality Assurance (QA)	24
2	Production	152 + 100
3	Quality Control (QC)	43
4	Storage and Distribution	24
5	Technical and Engineering Support Services	19
6	Total Employees	362

History of WHO and/or regulatory agency inspections

This was the 3rd inspection by WHO Prequalification team. The first was carried out jointly with MHRA on 4 - 6 April 2005 and the second was on 23 - 25 April 2007. At the time of inspection, several products manufactured at the site were either already prequalified or under evaluation.

The site had also been inspected by the following agencies:



- MHRA of UK on 21 - 23 April 2008 focusing on two none ARV/AIDS FPPs - one tablet and one capsule.
- ANVISA of Brazil on 16 - 20 February 2009 focusing on 13 FPP capsules and tablets (coated and uncoated), 6 of which were for the management of HIV/AIDS similar to the some under WHO-PQM.

Focus of the inspection

The inspection focused on the production and control of products (either already prequalified or under evaluation) in **Aspen OSD (Units 1 and 2)**. The inspection covered most of the sections of the WHO GMP text, including premises, equipment, documentation, materials, validation, sanitation and hygiene, production, quality control and utilities. Data verification relating to sources of APIs used in various products was also conducted.

Inspected Areas

Day 1

Opening meeting

On arrival, the inspectors were directed into the conference room, introduced themselves and exchanged business cards with the key staff of Aspen. The inspectors explained the procedure for WHO Prequalification Programme, the procedures and standards used for inspection and timelines for the processing the report and company responses to the inspection observations. The procedures for closing the inspection including the WHO public inspection report (WHOPIR), Notice of Concern (NOC) were explained. The tentative inspection plan was discussed and confirmed. The company made a presentation about the company and the site to be inspected. The presentation highlighted the company overview, site description, production and QC capacities, quality management and assurance systems, summary of manufacturing processes, major equipment, product range, inspection history and changes and CAPAs since the last WHO inspection. A copy of the presentation was obtained and will be filed in the company file.

This was followed by document review for the following areas:

Quality Management System review:

- Personnel Policies: *Organization charts, Job descriptions, Training. The following areas and documents were reviewed in detail:*
 - SOP on organization charts and organization charts of various departments.
 - SOP on competence, training, and development. Job descriptions of the Operations Manager (head of production), QA Manager, Responsible Pharmacist, QC Manger (Operational), QC Manager (Head of Quality), several letters of delegation of authority.
 - Competence matrix of analysts in QC laboratory for raw materials and finished goods
 - Training records of analysts involved in HPLC and particle size tests.
- Batch numbering system:
 - SOP on lot numbering system parameters. The format of the batch/lot number was PDNNNNN, where:
 - P = Prefix letter based on the Unit and whether it was purchased or manufactured.



Unit	BAAN number	Prefix for purchased lots	Prefix for manufactured lots
Unit 1	441	S	S
	442	B	A
	443	P	A-M
Unit 2	444	X	E
	555	H	Blank

- D = Digit depending on whether it was a bulk product batch (3) or finished packs batch (7).
- NNNNN = a 5-digit serial production order number generated from BAAN.
- For example, the lot number of the first bulk batch from Unit 1 would be B300001 while that for the first finished pack from Unit 2 would be E700001.
- Production plan for the 4 days of inspection
- SOP and document preparation, review and control:
 - SOP on control of SOPs and forms.
- Deviations/OOS + related SOPs and registers for 2009:
 - SOP on GMP deviations.
- Reprocessing/Reworking policy + SOPs:
 - SOP on reworking of bottled rejects from primary and secondary packaging line.
- Finished product release procedure
- Self inspection (SOP, Plans, reports)
- Complaints handling system
- Product recall system
- Product Quality Review (PQR) for the products in focus for 2009. The relevant SOP was reviewed.
 - All PQRs covered periods starting from June 2009 to specified date in the schedule. PQRs of the selected products were reviewed.

The inspection ended late in the evening so the review of the progress of the activities of the day, and giving the day's feed back were deferred to the next day.

Day 2

The inspectors started by reviewing the areas inspected the previous day and gave feed back on the observations made. The inspectors proceeded to review the current differences of the products registered with MCC and those prequalified or presented for prequalification by WHO. It was noted that whereas the products presented to PQ were equivalent to those registered with MCC at the time of submission, a number of amendments had since been made to the later and not the former. The codes of the products and API used there in were reviewed and compared.

The vendor qualification system and the approved list of manufactures for raw materials were reviewed. Selected APIs from a manufacturer in China were particularly noted. The inventory of batches released in the computer database, Enterprise Resource Programme (ERP) was reviewed and the list of batches under the certain codes and the current inventory were selected and a print out obtained. A batch under each code was randomly selected and the batches of FPPs in which it was used were identified and a print out obtained.



Starting materials, packaging materials and components receiving, quarantine, sampling and storage areas were inspected. The following SOPs in the sampling area were reviewed in detail:

- SOP on cleaning of the sampling area and equipment
- SOP on Sampling of Raw Materials.
- SOP on Sampling plan and vendor classification plan.

The procedure for sampling of packaging materials and components was reviewed. Selected examples were reviewed in detail (like PILs), corresponding specifications and test results. The sampling plan was in accordance with ISO2859/BS6001. Standard samples, positive and negative films and pantone colours were available to facilitate testing of packaging materials and components.

- Finished goods warehouse and dispatch procedures were reviewed briefly.

Inspection of Production activities:

- Dispensing
 - SOP on cleaning of the dispensary room.
 - SOP on cleaning of the dispensary equipment
 - SOP on dispensing of Raw Materials for a batch.
 - Dispensing was in progress. It involved a concession (planned deviation) to use an API under a different code instead of the code in the approved BMR.
 - SOP on cleaning procedure for mobile equipment parts in wash up area. This SOP was out of the review date.
- Production, packaging, in process controls and related records and SOPs:
 - SOP on issue, control and completion of environmental log books.
 - Process validation for selected products.

Review of BMRs

- SOP on batch review and batch release.
- Review of BMRs/BPRs/Testing records for selected batches.

The inspection ended late in the evening so the review of the progress of the activities of the day, and giving the day's feed back were deferred to the next day.

Day 3

The inspectors started by reviewing the areas inspected the previous day and gave feed back on the observations made. The inspection of the bottle packing area followed and packing was in progress in room G35-4, in room G34-4 and in extension S20. In process tests including leak test procedures (SOP) were evaluated.

The following areas were reviewed:

- Pest control procedures:
 - SOP on pest control.
- Temperature + RH mapping and monitoring:
 - Protocol for temperature and relative humidity mapping and monitoring of the warehouse. The warehouse was sectioned into section 1 to 4. Raw materials were located in Section 1 of the warehouse.
- Change control procedures and register for 2009:



- SOP on management of the change control system.
- SOP on concessions (Temporary deviations).
- Selected changes were reviewed:
 - Change in the description of one API and creation of a separate code.
 - To update the specification of one API to the current monograph and correct some typographical errors.
 - Add new items on the list of approved suppliers and removing others.
- Vendor approval, qualification and maintenance system:
 - SOP on vendor management. This required provision of manufacturing licence, GMP certificate, BSE/TSE declaration and questionnaire and filled audit questionnaire before a decision on whether to conduct a site audit was made.
 - SOP on vendor classification. The class of vendor was used to determine the level of testing the supplied raw materials. A validated vendor was a single product manufacturer who has been regularly audited.

	Vendor classification	Testing to be performed
(a)	Vendor not well known	All tests specified in the monograph
(b)	Vendor well known	Appearance, ID, Assay + one test
(c)	Validated vendor	Appearance, ID, full testing of 1 batch/year

- SOP on monitoring of vendor performance.
- The classification of vendors for all the APIs (and their codes) within the PQ process were selected from the ERP (*copy available in the file*). All were classified either as well known or as validated. The most recent audit report for the supplier one item classified as validated was reviewed.

Validation

- Validation Master Plan (including status and planned)
- Process validation and revalidation for the product in focus
- Validation of Analytical methods

The inspection ended late in the evening so the review of the progress of the activities of the day, and giving the day's feed back were deferred to the next day.

Day 4

The inspectors started by reviewing the areas inspected the previous day and gave feed back on the observations made. The following areas were reviewed:

- Block layout, area classification, AHU distribution and material and personnel flow.
- Qualification/Requalification/Monitoring the HVAC + Dust Control System
 - The OSD Unit 1 used only single pass air without recirculation.
 - Production areas, passages, stairs and lift were designed to ISO class 8 (Grade D).
 - 2nd and 3rd floor were supplied by AHU No. 5 with a variable speed fan.
 - There was a centralized dust extraction system, coupled to the AHU. It was fitted with goose neck traps and motorized damper to prevent back drop of dust. A trial had been done for risk assessment.
 - The AHU had G4 (ΔP 30 - 250Pa), F8 (ΔP 50 - 450Pa) and H12 (ΔP 150 - 500Pa) in the plenum.



- The last periodical requalification report (addendum of 15.08.2009 and protocol) of AHU 5 was reviewed.
- Equipment qualification/Requalification (DQ, IQ, OQ and PQ for major equipment), calibration and preventive maintenance:
 - Report on calibration of the High Shear Mixer - top drive was reviewed and the mixed granules were compressed in compression room 3 (G52).
 - Qualification of the compression machine in G52.
 - Calibration of metal detector, ref. Certificate No. AT201001/25.

The inspection of the following aspects of the Quality control laboratory followed:

- Analyst competencies and specimen signatures
- Sample receipt, storage and allocation:
- Wet chemistry laboratory
- Instrumental laboratory
 - Qualification, calibration, preventive maintenance
- Laboratory materials management (Samples, Reagents, Stock Solutions, Reference and Working Standards)
- Starting materials and finished products specifications, testing and release.
- Testing of Packaging Materials and Components
- Microbiological laboratory
 - Room and equipment
 - Media preparation and product testing
 - PW monitoring
 - Environmental monitoring
- Validation of Analytical methods
- Cleaning validation:
 - The cleaning validation protocol and report for one the IBC was evaluated during inspection. The time lapse between the use of equipment and cleaning, as well as time between cleaning and use (holding time), cleaning during campaign production was included in the validation studies. However, after the validation studies the criteria used to assess the cleanliness of the equipment was visually cleaning.
- Data in the ERP was evaluated to establish the bulk codes of all the products similar to the ones in the PQ process. Print out are available on file. Some codes did not appear on the summaries earlier provided by the company.
- Stability testing programme (*Protocols, programme, records and data*)
 - Stability chambers: two of 25⁰C/60%RH; one of 40⁰C/75%RH; one of 30⁰C/75%RH; one of 30⁰C/65%RH and one of 5⁰±3⁰C/Ambient.
 - SOP on stability trial storage and control. It provided for picking samples within ±5 days of due date.
 - SOP on stability testing. It provided for testing within 14 days of withdraw for 0 - 12m period and within 45 days for 18 - 60m period.
 - Records of charging and withdrawing samples from chamber plus testing of selected batches. The raw data of various test points was evaluated in the analysis books and the analytical equipment like HPLC.

At the end of the day, the team reviewed progress of the activities of the day and the entire inspection, gave feed back and wrap up for the inspection and received reactions from the management of the company. It was agreed that the evaluation of the information downloaded from the ERP will continue and if necessary, the inspector may require more information from the company.

The evaluation of some of the batches produced by Aspen and supplied to programmes funded by the global fund was done:

- Despite repeated requests during and after the inspection, the inspectors did not get some of the details of bulk and/or packed batches, codes and suppliers of the APIs batches used.
- It was noted that all supplies to South Africa under Global Fund were based on the MCC registered products whose specifications and some sources of APIs were different from those prequalified by WHO. It was noted that the adverts for the tenders (copies available on file) required MCC registration and did not mention that the tenders were funded by Global Fund.

2.1 QUALITY ASSURANCE

The responsibility for quality assurance systems of the sites was under the Responsible Pharmacist assisted by several pharmacists. These measures were also executed by the quality assurance department. The quality management system of the company included organization charts and job descriptions; written and approved procedures; systems to control and ensure the quality of starting materials, intermediate products and finished goods; procedures for equipment qualification, processes validation, change and deviation control; a self inspection and annual product review. Although these measures were found sufficient to ensure the quality of the products, there robustness could be improved by strengthening areas exemplified by the observation made in the report. It was particularly noted that special efforts had to be put in to ensure changes were consistently and promptly updated for all product submitted for WHO prequalification.

2.2 GOOD MANUFACTURING PRACTICES (GMPs) FOR PHARMACEUTICAL PRODUCTS

The facilities and procedures for the production and quality control of the products in focus were generally adequate. The level of execution and/or maintenance was generally adequate to ensure products of consistent quality.

Never-the-less, the observations described in the report required attention to ensure continuous improvement.

2.3 SANITATION AND HYGIENE

The site had adequate facilities and procedures for sanitation and hygiene. The premises, equipment and apparatus were cleaned adequately and regularly. Materials for production, containers and products for cleaning were handled in a manner to minimize their chances of becoming a source of contamination to the product.



2.4 QUALIFICATION AND VALIDATION

Aspen had established a system to ensure that equipment and systems were adequately qualified and regularly requalified as necessary. Processes and method were also validated and revalidated as appropriate. These activities were guided by a validation master plan and specific protocols. Reports were available to support the qualification and validation status of the various equipment, systems and processes. Care had to be taken in the design, compilation and review of some of the protocols and reports to strengthen trust in the evidence they provide.

2.5 COMPLAINTS

A system was in place although it was not evaluated in detail.

2.6 PRODUCT RECALLS

A system was in place although it was not evaluated in detail. No recall had been recorded in the previous year.

2.7 CONTRACT PRODUCTION AND ANALYSIS

It was stated that all production and analysis were done in house but the site was capable of producing and packaging for other parties on contract. This area was not evaluated.

2.8 SELF INSPECTION AND QUALITY AUDIT

There was a procedure and schedule for self inspection which ensured that all sections were inspected at least one a year. The system provided for reports, CAPAs with timelines and evaluation by relevant members of management. The reports were not available to inspectors and so it was not possible to evaluate how robust the system was.

The vendor approval process provided for the company to conduct site audits of suppliers of raw materials and packaging materials and other service providers if it was deemed necessary from other evaluations. Selected audit reports were reviewed and they had covered the essential elements.

2.9 PERSONNEL

There company engaged adequate numbers of skilled personnel to conduct production and quality control procedures. They were guided by organization charts and job descriptions. The responsibilities of the key personnel like Responsible Pharmacist, Head of Production, Head of Quality Control and Head of Quality Assurance were well defined and some of their authority had been delegated to staff with appropriate skills through letters of delegation. The responsibility for batch review and release was assigned to head of QA and the Responsible Pharmacist plus their delegated assistants.

It was observed that the staff involved in document design, review and execution needed close supervision to eliminate some of the lapses noted.



2.10 TRAINING

There was a system to ensure that all newly recruited staff members received basic GMP training. This was evaluated through a questionnaire with a pass mark of 70%. The QA department also coordinated training in specialized skills and work related requirements. A performance management process was used to assess staff performance, competence and training needs. Records of training were maintained.

2.11 PERSONAL HYGIENE

Personnel hygiene was part of the basic training received by all personal during induction and basic GMP training. Procedures for entrance into production areas required staff members to wash their hands and change into clean factory garments. The facilities were generally adequate and the procedures were well enforced.

Production staff were required to undergo health checks on recruitment and thereafter regularly as required. The company had a healthcare centre on site manned by a nursing sister and assistants to provide primary and occupational health care services.

2.12 PREMISES

Premises were designed to utilize gravity feed as much as possible during production (dispensary, milling, granulation, blending, compression, capsulation and primary packaging) spread over three floors. The floor in the production areas was smoothed with epoxy aggregate and the joints were coved. Doors were self-closing against the air flow and doors to airlocks were interlocked. The design and space available provided for adequate segregation of activities and materials at different stages of processing.

All operational areas were under negative pressure relative to the surrounding corridors with ΔP of 4 - 30Pa (*please note that the lower limit is below the WHO recommended lower limit of 5Pa*). In Unit 1, air to production areas was single pass without recirculation while in Unit 2 air was recirculated with $\geq 10\%$ make up air. The final filter was either H12 or H13. The environmental conditions (ΔP , T^0 and RH) were monitored and controlled using a BMS. The production areas were served by a centralized dust extraction system coupled to the AHU and fitted with goose neck traps and motorized damper to prevent back drop of dust.

The water used on site is obtained from the town water supply. It was chlorinated by sodium hypochlorite dosing, filtered with green sand multimedia and dechlorinated by activated charcoal filter. It was then polished by 5 μ m filter then softened and further polished through a 1 μ m cartridge filter before collection in a head tank. It was filtered by RO and then passed through the CEDI and CDI units for deionization and the sterilized with UV before collecting the purified water in holding tanks. The purified water was circulated through hot (>80 $^{\circ}$ C) and cold (>12 $^{\circ}$ C) SS 316L loops. The water was sampled and tested daily to the following specifications: Conductivity NMT1.3 μ S cm^{-1} , TOC NMT500ppb, Micro <100cfu/ml, E. Coli absent/ml, and Pseudomonas absent/ml.

2.13 EQUIPMENT

The design and installation of production equipment was mainly of closed systems utilizing gravity feed thus reducing human touch. The most of the machine parts that came into contact with the products was made of SS 316L. Most were PLC controlled and were adequately labelled. Records reviewed indicated that the equipment had been adequately qualified and were appropriately cleaned and regularly maintained.

2.14 MATERIALS

Starting materials

All materials were sourced from approved suppliers. They were quarantined, sampled and tested before approval for use according to the classification of the suppliers. A list of approved vendors was available at the receiving area (plus in the ERP) and was always followed in procurement and receiving of materials reviewed. All containers of active pharmaceutical ingredients were sampled individually and tested for identity while full testing was done on a composite sample. Materials were indentified by a unique number and tracked using ERP which was also used for material control (virtual quarantine and release). The conditions of storage were all controlled and monitored and were found to be appropriate for the materials held.

Rejected materials were separated and disposed off either by return to the supplier or destruction as waste through an external contractor.

Packaging materials

Packaging materials were purchased from approved vendors. Each consignment was quarantined, sampled and tested before release for use and the sample size was in line with ISO2859 or BS6001.

Intermediate and bulk products

Granules could be kept up to 14 days in intermediate bulk containers (IBCs) and this holding time had been validated though not systematically monitored.

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

Documentation system was under the control of QA. Production and control of products was guided by an elaborate documentation system including: production order with a batch formula, specifications of starting, packaging materials and packaging components, production and packaging instructions, batch processing and packaging records, finished product specifications, standard testing procedures and various standard operating procedures and protocols. There were corresponding records in form of reports, forms, checklists, logbooks, registers maintained as

evidence of compliance with the procedures and specifications. Soft copies of these documents were also maintained in ERP/BaaN. Deviations and changes were to these standard procedures were controlled, though the review was not always within the stipulated period.

2.16 GOOD PRACTICES IN PRODUCTION

The production equipment in Unit 1 was mainly closed in design and installed to utilize gravity feed with minimal human touch. Production was conducted over three floors utilizing integrated systems and gravity feed. Temporary storage of starting materials and dispensing was done on the third floor using floor scaled into IBCs on the second floor, milling and granulation was done on the second floor, while blending, compression, encapsulation, in process control, and primary packaging took place on the first floor.

In Unit 2, dispensing was conducted on the ground floor into IBCs on lower ground floor. Granulation took place on first floor while compression, coating and capsule filling took place on the lower ground floor.

There had been a new packaging facility constructed adjacent to Unit 1 to serve both Unit 1 and 2 and some of the packaging still took place in unit 3. Line clearance was done before and after packaging activities.

Production activities were recorded in the batch manufacturing record (BMR) and critical steps had to be witnessed and signed of by a pharmacist. In-process checks and determination of yield were done at appropriate intervals. The BMR and results of testing of the FPP were review by the QA Pharmacist/Manager before release for distribution.

2.17 GOOD PRACTICES IN QUALITY CONTROL

The quality control laboratory was shared with and located in Unit 3. It consisted of the analytical laboratory (wet chemistry and instrumental analysis), stability and validation samples testing laboratory and microbiology laboratory. Its function were independent of the production and this was reflected in the organization charts and activities reviewed. There was an adequate number of staff with the necessary skills and competencies.

The QC laboratory had adequate facilities in the form of equipment, reagents and chemicals to test all starting materials, packaging materials, packaging components, intermediates and finished products before release for use or distribution. The instrumental analysis laboratory was found to be congested.

There were approved procedures and specifications to guide the testing of different samples. Records of testing were available which indicated that the procedures were followed in the majority of cases except a few cases sites in the observations at the end of this report.

General and wet chemistry laboratory

The laboratory was generally in a good state of repair and cleanliness. It had safety facilities like a fume hood for safe handling of volatile chemicals and eye shower in case of accidental splashing in the eyes.



There was a calibration and maintenance programme for balances, Karl Fisher Moisture apparatus, pH meter, dissolution tester disintegration apparatus and other QC equipment. There were SOP and records for the preparation of reagents and standard solutions.

Instrumentation

The instrumental analytical laboratory was equipped with HPLCs, GCs, UV-Visible spectrophotometers, AA Spectrophotometer and IR Spectrophotometer instruments. They were routinely maintained and calibrated and the performance of the HPLC columns was monitored.

Reference standards

Primary reference standards were used to standardize working standards. There was a standard method of preparation of working standards (WS). One vial of WS was prepared at a time and used till the WS was finished. The company had already decided to make several vials so that each vial could be used not longer than one month. The freezer used for storage of reference standards was not frost free and the procedure did not prompt the analyst to equilibrate such WS to room temperature before use.

Microbiology

This was not inspected.

Retention samples and stability testing

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: two of 25⁰C/60%RH; one of 40⁰C/75%RH; one of 30⁰C/75%RH; one of 30⁰C/65%RH and one of 5⁰±3⁰C/Ambient. There were records to support traceability of stability samples from charging, withdrawing and testing. Records reviewed showed that the stability programme was generally well managed.



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, **Aspen Port Elizabeth (Pty) Ltd, Units 1 and 2, located at corner of Fairclough Road and Gibaud Road, Korsten, Port Elizabeth 6020, Republic of 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.