

WHO PUBLIC INSPECTION REPORT

(WHOPIR)

Finished Product Manufacturer

Part 1: General information about the inspection

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| Name of manufacturer | Quality Chemical Industries Ltd (QCIL) |
| Physical address | Plot 1-7 Luzira Industrial Park, P.O BOX 34871, Kampala, Uganda |
| Postal address | P.O.BOX 34871 Kampala, Uganda |
| Telephone number | + 256-312341100 + 256-772727262 |
| Fax number | + 256-414221319 |
| Summary of all the activities performed by the manufacturer (e.g. manufacturing, packing). Indicate dosage forms and type of products (e.g. tablets; penicillin or cephalosporin containing products) | Manufacturer and packer of oral solid dosage forms - anti Retroviral and Anti Malarial tablets Uncoated and film-coated tablets |
| Scope of inspection | General and Product Specific GMP inspection with data verification. |
| Date of inspection | 25 - 28 January, 2010 |
| Programme | Prequalification of Medicines Programme |

Part 2: Summary

The manufacturing site of Quality Chemical Industries Ltd (hereafter referred to as QCIL) which is located at Luzira Industrial park, Uganda, was inspected by a WHO prequalification inspection team on the above mentioned days.

General information about the company and the site, History of WHO or regulatory agencies inspections

QCIL was established in 2007. QCIL is a joint venture company of Quality Chemical Ltd, Uganda and Cipla Ltd., India.

Inspection of QCIL was requested by Cipla Ltd., India as variations and product transfer.

QCIL got a manufacturing License from National Drug Authority (NDA) in 2008 and commenced Production of Anti Retroviral and Anti Malarials in February 2009.

QCIL is additional manufacturing site for Cipla Ltd., India. The site is located at Luzira Industrial park about 2 km from Luzira city and about 10 km from Kampala.

In total there were approximately 150 employees working at the site of which 18 were involved in QA/QC activities and 13 in production activities.

Manufacturing was campaign based and was depending on market requests.

Focus of the inspection

The focus of this inspection was to verify production and quality control activities and to assess compliance with WHO GMP.

2.1. Quality Assurance (QA)

A quality assurance system was implemented and maintained

The Quality Assurance (QA) department and Quality Control (QC) department were independent from production with the QA Manager reporting to the Chief Executive Officer. The QA Manager was also the Authorized person and his duties were delegated to the QA Pharmacist.

Change Controls

Change controls covered all changes including documentation, processes and equipment and were defined in SOP "Change control" and flow chart. Time limits for closing of Change controls were specified. The impact of change was assessed by appropriate departments. Changes were classified as:

- Major (has direct impact on product quality, stability and efficacy)
- Minor (has no direct impact on product quality, stability and efficacy)

Change Control Log book was reviewed and found to be satisfactory. Change control impact investigation was performed using check list.

Deviations

Deviations were classified into two categories major and minor in SOP "Deviation handling" and flow chart. Time limits for closing of Deviations were specified. Deviations were recorded in Batch Manufacturing records (BMR) and Batch Packaging Records (BPR).

Trending of deviations was carried out every six months. Deviation trends and Log book were reviewed and found to be satisfactory.

Annual product review

The Annual product review (APR) was prepared in accordance with the revised SOP "Annual product review". APR from January 2009 to December 2009 was reviewed and found to be satisfactory. All required information regarding starting materials, packaging materials and product quality was collected and presented.

Quality risk management

A quality risk management procedure had been implemented. SOP "Risk management (Failure mode effect analysis)" and flow chart were reviewed and found to be satisfactory. Critical control points were specified. According with SOP risks should be re-evaluated after 3 years.

Batch release

Batch release for WHO market was performed by Cipla. Batch release agreement for WHO commercial batches between Cipla LTD the principal (contract giver) and QCIL manufacturer (contract acceptor) was reviewed and found to be satisfactory.

2.2. Good manufacturing Practices for Pharmaceutical products

Good manufacturing practices were implemented and generally maintained.

The manufacturing steps were recorded in the Batch Manufacturing Records (BMR) Batch Packaging Records (BPR), records were made during manufacture.

Instructions and procedures were generally written in clear and unambiguous language.

Qualification and validation were performed.

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

2.3 Sanitation and Hygiene

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Quality Chemical Industries Ltd (QCIL), Uganda
25-28 January 2010

The topic was not specifically covered during the inspection; however no notable concerns were identified during the inspection. The hygiene measures in place at the time of the inspection were generally found to be sufficient to assure the prevention of contamination of the premises and product.

2.4 Qualification and Validation

The key elements of the qualification and validation program were defined and documented in the Validation Master Plan (VMP). VMP was reviewed and found to be satisfactory.

Re-qualification and re-validation:

Critical equipment and systems were re-qualified every 3 years, non-critical every 5 years. Production process was re-validated every 2 years (one batch), HVAC system was re-validated every year. Cleaning process should be re-validated only if there will be changes in the cleaning process, method, formulation, SOP or storage conditions. Compressed air system was re-validated every year.

Validation teams consisted of officers from QA, QC, production and engineering departments. Protocols and Reports were approved by QA manager and authorized by Chief Operating Officer (COO).

Responsibilities were defined. Validation/Calibration Master schedules were available for process, cleaning, method transfer and hold time studies and were presented to inspectors.

Capacity planning was also covered by the VMP.

Purified water (PW) system validation

PW was produced by Reverse Osmosis and was in continuous recirculation at ambient temperature. PW validation was performed in three phases, all phases were completed. PW validation protocols/reports were reviewed and found to be satisfactory.

Phase 1 validation

Validation was carried out, samples were taken daily from all user points for duration of 28 days according with sampling SOP. There were no OOS results obtained during the 1st phase validation. PW sanitization SOP was developed after this phase. System was sanitized once per month.

Phase 2 validation

Validation was carried out, samples were taken daily from all user points for duration of 28 days. The same tests as per phase 1st were carried out. There were no OOS results obtained during the 2nd phase validation.

Phase 3 validation

Validation was carried out, samples were taken as per monthly sampling schedule. All sampling points were sampled on weekly basis. Microbiological and chemical analysis were performed on every sample. There were no OOS results obtained during the 3rd phase validation.

PW system was continuously monitored by weekly sampling and MB & chemical analysis. Sampling schedule indicating sampling points were available.

URS, DQ, IQ, OQ and PQ protocol/reports were available. Water storage tank and loops were made from SS 316L. Orbital welding technique was used for the joints, welding quality was checked by boroscopy. Four boroscopy photographs were available and were presented. Welding reports, welding clearance format and welder's certificate were available.

SOP "Water sampling technique for MB analysis and chemical analysis" was reviewed and found to be satisfactory.

HVAC system validation

During inspection attention was paid to the validation of AHU No 12. HAVAC system validation was carried out by an external party. Initial validation was performed by the company who installed the system. Re-validation was contracted out to another company. AHU 12 validation protocol/report was reviewed and found to be satisfactory. Filter integrity test certificates, HEPA and EU filters certificates and instrument calibration certificates were available.

Cleaning validation

Cleaning validation was performed in accordance with validation protocol/report "Cleaning of equipment validation report". Validation approach was cleaning after each product. Cleaning validation was performed for 3 batches.

Cleaning procedure was performed manually, report did not contain the name of the operator who performed the cleaning, however it was possible to trace it back from the cleaning Log and BMR. Samples were taken by QA personnel. Equipment drawings were attached to the report; sampling points were not indicated on the equipment drawings.

SOP "Cleaning validation and establishment of worst case product" as well as above mentioned validation protocols/reports were reviewed and found to be satisfactory. Cleaning was checked "visually clean" and rinse and swab samples were taken for validation studies. Acceptance criteria for daily dose and 10 ppm was set up, which ever is lower.

Swab recovery studies and related analytical method validation studies were performed at CIPLA site. There was no evidence that results are reproducible at QCIL as well as that the same swab material was used in the both companies. Swab material used in Cipla for

cleaning validation studies was not identified at the presented and reviewed validation report.

Cleaning effectiveness was not periodically monitored.

Compressed air system validation

Compressed air validation was performed in accordance with validation protocol/report "Compressed air validation report". Samples were collected during 7 days. Re-validation was performed once per year, all above mentioned tests were carried out.

Process validation

Process validation was carried out.

Holding time validation for granules and tablets

According with validation report the holding time for granules was specified 45 days and for coated tablets 90 days.

Holding time studies of cleaned equipment

Validation report was reviewed. Holding time studies for the sifter was evaluated. According with validation protocol/report samples were taken every day for duration of 9 days. Samples were taken using swab method. MB analysis was performed. Acceptance limit for microorganisms was specified. According with the results established holding time for cleaned equipment was specified 7 days.

2.5. Complaints

Complaints SOP "Handling of product complaints" was available for inspectors. There were no complaints received till the date of the inspection. Complaints were classified and categorized. Complaint trending will be done once per year.

2.6 Product Recalls

SOP "Recall procedure" was available for inspection. There were no recalls initiated till the date of the inspection.

- Three levels of recall were specified.

Dummy recall was carried out. Dummy recall Validation protocol/report "Dummy recall validation" was available for inspection and was found to be satisfactory. According with SOP Dummy recall should be re-validation once in two years if there was no recalls.

2.7 Contract production and analysis

Manufacturing activities were not contracted out.

Two contract laboratories in India were used for some tests. The same laboratories were used also by Cipla. Laboratories audits were carried out by Cipla every year and reports were available for inspections. GMP agreement with laboratories was reviewed and found to be satisfactory.

Washing of garments used on site was carried out by an external party. GMP agreement between QCIL and laundry was reviewed and found to be satisfactory. Agreement specified that the laundry should not pass to a third party laundry work entrusted. Laundry was audited once per year. Audit check list was available for inspection.

Systems, instruments and gauges calibrations and autoclave validation were carried out by an external party every year. Technical and GMP agreements with QCIL and organization were available for inspection.

2.8 Self inspection and Quality Audits

SOP "Self inspection" was reviewed and found to be satisfactory. Self inspection team consisted minimum of two experienced, knowledgeable, independent and free of conflict of interest inspectors. One person always was from QA. All departments were inspected every 6 months according with schedule. Intimation about inspection was given to the departments one day before inspection. Inspection was carried out according to check list for every department. After inspection report listing critical/major/minor non conformance were drawn up, CAPA's were proposed. Implementation of CAPA's were checked by the team.

Suppliers' audits and approval

SOP "Evaluation and approval of manufacturer" and approved manufacturers /suppliers list for WHO - Raw materials and packaging materials was available for inspection, was reviewed and documents were found to be satisfactory. Manufacturer's approval was based on manufacturing site inspection. QA, QC and production officers were part of the audit team. Audit was carried out using check lists, separate for Active Pharmaceutical Ingredients (API) and packaging materials. Audit findings were listed in the audit report. Findings were classified as:

- Critical
- Major
- Others,

CA received from the audited company were reviewed, final decision to approve/reject the manufacturer was taken by QA department.

Till the date of the inspection, audits have been carried out by Cipla personnel. This was covered under the Technical Agreement between CIPLA and QCIL. Audit reports were available for inspectors. According with SOP API manufacturer's audits should be carried out every 3 years and for packaging materials - every 4 years.

2.9 Personnel

The personnel met during the inspection were experienced, skilled and conscientious. For all responsible staff their specific duties were recorded in the Job responsibilities The following Job responsibilities were reviewed:

- Quality assurance department - manager
- Quality control department - manager

- Quality assurance pharmacist
- Production department - production pharmacist
- Production department - manager

Reviewed Job responsibilities were comprehensive, however a clear explanation as to who is responsible for packaging and starting materials receipt, rejection and release and approval of CoA was missing.

2.10 Training

Training was explained in SOP "Training" and relevant flow chart. Schedule for 2010 and attendance sheets for training sessions were available. Training effectiveness was evaluated through the questionnaire (objective and descriptive). Training certificates were issued after successful completion of training. If training was not successful, personnel had to be re-trained and re-evaluation had to be carried out.

SOP "Training" was reviewed and found to be satisfactory.

2.11 Personal Hygiene

The topic was not specifically covered during the inspection but no notable concerns were identified during the inspection of the production areas and the level of hygiene observed was considered satisfactory. All changing rooms were provided with photographs which described the gowning procedures.

2.12 Premises

The buildings and facilities used for manufacture and quality control were located, designed, and constructed to facilitate proper cleaning, maintenance, and production operations. The production areas had adequate space around equipment and good material flow to prevent mix-ups and contamination with separate personnel and material entrances. Premises used for the manufacture of finished products were suitably designed and constructed to facilitate good sanitation. Premises were carefully maintained and cleaned, cleaning records were maintained. Premises were protected against the entry of insects, birds or animals. The rodent and pest control procedure was in place.

Storage areas

The receiving and dispatch areas had protection of materials and products from adverse weather conditions. Storage areas were of sufficient capacity to allow orderly storage of the various materials and products with proper separation and segregation.

Entrance to the storage area was via change room No. I. Stores were located on the ground floor. There were separate receiving and dispatch areas for starting materials and packaging materials.

Separate movable racks were provided for quarantine storage for starting materials as well as for packaging materials. Rejected materials were stored in separate locked rooms - one for starting materials, one for packaging materials.

A separate, locked room was provided for storage of recalled or returned materials in the finished goods warehouse.

Production areas

Production premises were laid out in such a way as to allow the production to take place in areas connected in a logical order corresponding to the sequence of the operations and to the requisite cleanliness levels.

Quality control (QC) areas

Quality control laboratories were separated from production areas. Sufficient space was given to avoid mix-ups and cross-contamination. Sufficient space was provided for samples, reference standards solvents, reagents and records storage.

2.13 Equipment

Process equipment was installed and maintained in a manner that minimized the risk of error and contamination. Balances and other measuring equipment with appropriate range and precision were available for production and control operations and were calibrated on a scheduled basis. Calibrations due date labels were attached to the equipment.

Production equipment was thoroughly cleaned on a scheduled basis.

Laboratory equipment and instruments were suited to the testing procedures undertaken.

Calibration schedule and preventive maintenance program was in place and was followed.

2.14 Materials

All materials were stored in locked metal mobile racks. Racks were properly labeled. Materials were placed on SS pallets.

Materials upon receiving were checked against purchase order and delivery note. Afterwards materials were moved to the quarantine area and GRN was prepared and intimation was sent to the QCL. Materials management in the stores was done manually.

Temperature and relative humidity were monitored and recorded daily.

Temperature mapping was done for all storage rooms. Report "Temperature and relative humidity distribution study in critical and non critical areas" was reviewed and found to be satisfactory. Study was carried out following ISO standard.

There were 2 sampling rooms - one for active materials and one for inactive materials sampling. Entrance to the sampling rooms was via airlocks, separate for personnel and materials. Sampling was done under RLAF. RLAF operational procedure was available. Line clearance was checked by QA officer before sampling operations. The line clearance was carried out according with checklist. Sampling tools were stored and

cleaned in QCL. Sampling tools cleaning procedure was validated. SS sampling tools were used.

Appropriate procedure was in place to ensure the identity of the contents of each container of starting material. 100% sampling were carried out for the starting materials used for the WHO product.

All materials including packaging materials were received from Cipla together with CoA. All tests, according with product specifications were carried out also at QCIL.

Starting materials have different Item codes for different markets. Verbal explanation was given that starting materials "item code transfer" was not done, however this was not specified in the SOP.

There were 2 dispensing rooms - one for active materials and one for inactive materials dispensing. Entrance to the dispensing rooms was via airlocks, separate for personnel and materials. Dispensing was done under RLAF. After dispensing materials were passed through material pass box and delivered to the production floor by the lift. Lift shaft was ventilated with filtered air.

Dispensed materials were stored in double poly bags, placed in the SS containers. One label was placed between poly bags and other stacked to the outer bag.

Each dispensed material and its weight was independently checked and the checks were recorded. Balances were calibrated daily, standard weights were stored in SS container and calibration certificates were available for each individual weight. 3 balances were located in the both dispensing rooms. Balance and operator location positions were identified during RLAF qualification studies. The line clearance was carried out according with check list.

If materials after dispensing were taken back to the store, those were properly identified with "loose" label.

All materials in stores and production areas were placed in SS containers or drums.

Dispensing tools and SS containers were cleaned in the separate washing room. PW was used for final rinse. After rinsing tools and containers were dried by filtered compressed air.

Cleaned dispensing tools were wrapped in poly bags and stored in locked SS cabinet. All cleaned tolls, drums or containers were properly labeled and "due to clean date" indicated. If the cleaned tools, drums or containers in stores or in production have not been used within the specified date (7 days) red color stamp "clean before used" were put on the labels.

Samples of the primary packaging materials were taken in the store. Sampling area was identified, but did not protect the materials from the environment.

SOP "Sampling" was reviewed and found to be satisfactory. Sampling plan was drawn up in accordance with AQL.

Primary and printed materials were dispensed in the stores. Dispensing places were identified. After dispensing materials were placed in locked SS trolleys and transported to the production department.

Printed packaging materials were securely stored in double locked mobile racks. One key was with store officer and one with QA officer. Roll sticker labels were used for the labeling. Labels indicating manufactures batch numbers and amount were stacked on the inside part of the roll. Labels had Pharma code. Pharma code reader was not installed on the packaging line. Company was planning to install the reader in the future. Joints on the roll labels were indicated with red color. First and last label from the roll were stacked to the BPR as well as the label after the joints.

2.15 Documentation

In general the documentation system was established and maintained, documents were approved, signed and dated by the appropriate responsible officers, regularly reviewed and kept up to date.

Documents reviewed:

- SOP "Batch numbering system"
- SOP "Batch split up"
- SOP "Receipt and storage of expired and recalled/withdrawn products"
- SOP "Reprocessing and reworking"
- SOP "Testing of samples and reporting of results"
- SOP "Handling of returned/rejected goods"
- SOP "Password system for computers"
- SOP "Batch release system of formulations"
- SOP "Pest control":
- SOP "Personal hygiene"
- SOP "Batch failure investigation":

Product related documents were stored in QA archive for 6 years.

2.16 Good practices in production

Production department was located on the first floor. Entrance to the production department was via two changing rooms. Changing room I was located on the ground floor (the same changing room was used for the entrance to the stores and laboratories). After Changing room I (where garments were changed to the production garments) workers and visitors had to use stairs (controlled area) to get to the first floor. Entrance to the production was via Change room II (class ISO 8), located on the first floor. Change to other garments was not required, only footwear was changed.

Pressure differentials from the corridors to the processing rooms were monitored and recorded two times per day. Pressure differentials from the corridors to the processing rooms were set up from 10 to 40 PA. Corridors were maintained positive to the processing rooms.

There was separate material entrance to the production department. Materials were entered via air lock.

The FBE 500 schematic diagram, tablet compression cycle for double rotary compression machine explanation as well as pictorial demonstration "How to wear snood and gloves" were stacked to the walls.

Production operations were carried out following defined procedures and line clearance was carried out and recorded before processing operations were started. During change over from the same product different batches, line clearance was carried out and recorded by two production officers. During product change over line clearance was carried out and recorded by two production officers and QA officer.

Temperature and relative humidity in the production rooms were monitored and recorded daily.

Production facilities were inspected in detail. The general design of the facility was appropriate and well was maintained. Some small damage to walls was seen in some areas but this was not considered significant enough to be listed as a deficiency.

General processes were under good control and blending, granulation, compression, and coating areas were visited. Also viewed was the bulk packing of tablets into HDPE containers and the compression tooling storage area where punch controls were satisfactory carried out. Food grade lubricants and Emery paste, QC approved, were used for punches and dies. Punches cleaning and polishing procedures were in place. Punches drawings and certificates were available for inspectors. Punches were numbered and rotation was insured. Punches usage was recorded in the punch stock card. Punches were inspected before and after use. Punches were dedicated for each product and were stored in locked SS cabinets.

Other production tools as sieves, finger bags and engineering tools were also stored in the locked rooms in SS cabinets.

In the sifting room there was Dynascan illuminator fixed to the wall. Metal sieves integrity was checked before and after sifting of each product.

Materials after sifting and granulation were transferred to the next processing room via double doors pass box.

The wash areas were connected to the production rooms (sifting and granulation). To avoid production room's contamination, air was 100% exhausted from the washing rooms.

Filter bags were dedicated for each product. After use bags were cleaned and dried in the FBE.

Vacuum cleaners were dedicated for each production room.

There was a central IPQC room containing the usual equipment for controlling compression parameters where the calibration status of equipment was checked. The following tests were carried out in the laboratory:

- Disintegration (calibration was carried out every month)
- Weight (balance verification was carried out every day)
- Friability (calibration was carried out every 6 months)
- Hardness & thickness & diameter (calibration was carried out every month)

Primary packaging

HDPE containers and caps were cleaned on the line using filtered compressed air. Filling performance was checked every hour. 5 containers from both nozzles were taken for the tablet count. Tablets were counted manually, using SS tablet counter. After counting tablets were taken back to the production line. Containers integrity was checked manually every hour. 5 containers were taken for the checks.

Data to the labels were printed by the inch printer.

2.17 Good practice in Quality Control

In general Good Practice in Quality Control was implemented and maintained and there was adequate facilities, trained personnel and approved procedures available. Records of analysis were 100% checked by QA staff and the C of A was signed by the technician who carried out analysis, checked by the QC manager and approved by QA manager.

There were separate instrumentation room and weighing scale section as well as wet chemistry room.

Samples receiving flow chart was available for starting materials, packaging materials, finished products and bulk finished products.

Separate sampling check lists for line clearance were available for starting, primary packaging and secondary packaging materials.

After sample receipt QC manager assigned work to technicians using "Daily work output report".

Analyst competency and signature specimen lists were available.

SOP "Quality control of raw materials (API and excipient)" and SOP "Sampling and analysis of raw materials for WHO" were reviewed and found to be satisfactory. Composite sample preparation was explained.

Retention samples from finished products and API's were kept for one year after the expiry date.

OOS

OOS results were evaluated and investigated in accordance with SOP "OOS investigation for raw material, finished product & stability study". OOS investigation flow chart and check list were available. Time limit for closing out of OOS was specified - 30 calendar days. Till the date of inspection there was no OOS.

IQ, OQ, PQ initially was carried out by the equipment manufactures. Regular equipment calibration was carried out by the delegated officer.

The calibration report of HPLC No. 17 was reviewed and found to be satisfactory. Log books were available for each column, columns were managed satisfactory. Glass vials were used for analysis. Vials after RS tests were discharged. HPLC grade water was used for the analysis.

All instruments in the laboratory had Log books and were properly labeled, calibration status and due to date were indentified. Instruments were unique numbered.

KBr used for the identification tests before analysis was dried at 105 °C from 1 to 2 hours, after drying substance was kept in the dry box.

There was separate glassware washing room. PW was used for the final rinse. Automatic glassware machine was used for the washing. After washing glassware was dried in 60 °C.

Analytical balances were properly located on the special vibration proof tables. Daily calibration of analytical balance No. 54 was reviewed and found to be satisfactory.

Reagents were stored in the titration room. Expiry dates for test solutions and reagents were set up.

Reagent solutions and titration solutions were properly labeled and manufacturer's batch numbers were traceable from the solution preparation sheets.

Primary reference and working standards were stored in the fridge and in the freezer according with storage conditions. Working standards (WS) were dispensed under the LAF, and were transferred to the amber glass bottles for single use .WS were qualified against primary reference standards in accordance with SOP "Laboratory reference

standards". Temperature mapping in the fridge and in the freezer was carried out by an external party. "Temperature distribution study of refrigerator along with door" report was reviewed and found to be satisfactory. USP primary standards were available.

WS preparation and qualification records were evaluated and found to be satisfactory as the analysis was carried out in triplicate.

Usage of primary reference and WS was recorded; the standards usage log books were available for inspection.

Retention samples

Retention samples were properly stored and maintained in sample storage room which was temperature mapped. Temperature was monitored and recorded two times per day.

Microbiology

The laboratory conducted water, environmental monitoring, starting material, finished product and stability testing.

The preparation of media was investigated and growth promotion testing which appeared to be satisfactory. There was a separate autoclave for media sterilization and for destruction. Autoclave validation using thermocouples was carried out by an external party and the results were satisfactory however there was a risk of media being overcooked because sterilization time was specified 20 minutes. Autoclave yearly re-validation was contracted out to Indian company. Validation report was reviewed and found to be satisfactory.

SOP "Preparation and disposal of microbial culture media" was reviewed and found to be satisfactory.

pH meter was calibrated daily, calibration records and Log book was available for inspection.

Sub culturing record was reviewed and found to be satisfactory. 4 sub culturing passages were allowed. Master cultures and sub cultures were properly stored.

Incubators were equipped with alarm and temperature was monitored and recorded twice per day.

SOP "MB monitoring of environment in production area" was reviewed and found to be satisfactory. MB monitoring was carried out monthly for ISO 8 areas and quarterly for controlled areas. Action and alert limits were set up. Sampling point layout for air sample and settle plates was available for inspection. Separate schedule was available for production, stores, MBL and other control areas. Trends were available for all sampling points, there was no OOS.

SOP "Investigation of OOS test results" - applicable for MBL was reviewed and found to be satisfactory. There was no OOS reported.

Stability studies

There were two walk in stability chambers, one for accelerated and one for long term stability studies. Stability chambers were equipped with alarm which was connected to the QC and security. Temperature was software controlled. Chambers were connected to the diesel power generators.

Stability protocol was reviewed and found to be satisfactory.

SOP "Stability studies" was reviewed and found to be satisfactory. Time point windows were specified. After withdrawal of the samples analysis should be initiated within 15 days. Acceptance criteria for the tests results were specified.

Utilities

HVAC system

The pressure differentials between corridors and processing rooms were specified as ++++ (corridors) and +++ (processing rooms). Such a classification is not in accordance with WHO Supplementary guidelines on good manufacturing practices for heating, ventilation and air-conditioning systems for non-sterile pharmaceutical dosage forms.

The inspection of the air handling system entailed a visual inspection of the equipment in the plant room, checks against drawings and qualification which was carried out by an external party.

During inspection attention was focused AHU 12 which supplied air to the granulation II and Blending room II.

Condensate drains were cleaned by the compressed air every month during the PM.

The HVAC system was equipped with sound alarm. Alarm would be indicated on the displays located in all processing rooms.

PM schedules and logs were available for each individual AHU. Check list for planned PM of AHU 12 was checked and found to be satisfactory.

Damper positions were marked for every AHU.

Ducts were cleaned following SOP "AHU duct cleaning". Ducts were dismantled and cleaned once per year.

Separate room, connected to the service floor, was provided for the filters cleaning.

Spare filters were stored in the separate room. Two spare filters of each size were available.

Exhaust from the FBE was passed through cartridge filter, powder remains were collected, water was added and mixture was discharged at Effluent Treatment Plant.

There was a "walkable ceiling" in between the service floor and processing rooms. HEPA filters and lights were changed from this floor.

Purified water system

The Purified Water (PW) was produced by the Septron line 30 VAL. The PW system appeared to be well maintained. PW was produced by RO and associated pretreatment by softeners and filtration. PW was continuously circulated at ambient temperature which was controlled by a flow meter and temperature. Conductivity, flow rate and temperature were controlled on line after the recirculation loop on return to the tank. Flow limit was established NLT 5000l/hour. UV lamp working hours and intensity was controlled continuously. Hardness was checked on line before and after softener. Brine solution was used for the regeneration of softener. Regeneration was carried out every two months. Back flush was carried out automatically every two hours. The system was sanitized monthly. Sanitization and maintenance was recorded. Recirculation of the PW was through SS pipe work.

Hydrophobic water storage tank filter integrity checks were carried out every month.

PW trends up to January 15.2010. for each sampling point were available for inspection, the following tests were performed. All results were within the specifications.

Compressed air system

Atlas Copco equipment was used to process oil free compressed air. There were two units. One was in operation, another was stand by. Compressed air after receiving tank was transferred to the service floor and was passed through 25 µm, 1 µm and 0.01 µm filters.

Part 3: Conclusion

Based on the facilities inspected, the personnel met and the documents reviewed, and considering the inspection observations listed in the inspection report, Quality Chemical Industries Ltd (QCIL) located Plot 1-7 Luzira Industrial Park, Kampala, Uganda, was considered to be operating at an acceptable level of compliance with WHO GMP.

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 3 years, provided that the outcome of any inspection conducted during this period is positive.