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Prequalification Team Inspection services
WHO INSPECTION REPORT
of the FPP manufacturer

Part 1	**General information**
Manufacturers Details	
Company information	
Name of manufacturer	Universal Corporation Limited
Corporate address of manufacturer	Strides Shasun Limited Opp. IIM-B, Bilekahalli, Bannerghatta road, Bangalore -560 076, India
Contact person	Dr George Mugi Muriithi Email: george.muriithi@ucl.co.ke
Inspected site	
Address of inspected manufacturing site if different from that given above	Club Road, Past Kikuyu Post Office P.O Box: 1748-00902, Kikuyu Town, Kenya.
Inspection details	
Dates of inspection	29 May - 1 June 2017
Type of inspection	Follow up inspection
Representative from the National Regulatory Authority	Poison and Pharmacy Board (PPB), Kenya was informed and attended this inspection
Introduction	
Brief summary of the manufacturing activities	The company is currently manufacturing tablets, hard gelatin capsules, liquid orals, dry syrups, powders and topical dosage forms. The product types include cardiology, dermatology, pediatrics, orthopedics, gastro-enterology, dental hygiene, obstetrics and gynecology, antibiotics, antimalarial and ant-retroviral products. No WHO prequalified products were manufactured since 2015. No hazardous products are manufactured on the site. No manufacturing activities are outsourced by the company.
History	This was the fifth WHO/Unicef inspection with the last being in 6 to 9 September 2016. The site has been certified by PPB, Kenya and had a valid GMP certificate at the time of inspection.

Brief report of inspection activities undertaken	
Scope and limitations	
Areas inspected	Quality management system Production operations with particular focus on tablet line and oral liquid line Packaging Operations QC Laboratories and control system Materials management system including warehouses for starting material and finished products Facilities management and engineering support systems including HVAC, water etc.
Restrictions	The scope of the inspection was restricted to the WHO prequalified products and products supplied to UNICEF. The production lines were partially in operation throughout the inspection.
Out of scope	Products that were not WHO prequalified or were not supplied to UNICEF were not included in the scope of this inspection
WHO/UNICEF product numbers covered by the inspection	Dosage forms inspected include: tablets, capsules, powder for suspension and solution, liquids for internal use and gels for topical use.

Abbreviations

AHU	air handling unit
ALCOA	attributable, legible, contemporaneous, original and accurate
API	active pharmaceutical ingredient
APQR	annual product quality review
BDL	below detection limit
BMR	batch manufacturing record
BPR	batch packaging record
CAPA	corrective actions and preventive actions
CC	change control
CFU	colony-forming unit
CoA	certificate of analysis
CpK	process capability index
DQ	design qualification
EM	environmental monitoring
FAT	factory acceptance test
FBD	fluid bed dryer
FMEA	failure modes and effects analysis
FPP	finished pharmaceutical product

FTA	fault tree analysis
FTIR	Fourier transform infrared spectrometer
GC	gas chromatograph
GMP	good manufacturing practice
HACCP	hazard analysis and critical control points
HPLC	high-performance liquid chromatograph
HVAC	heating, ventilation and air conditioning
IR	infrared spectrophotometer
IQ	installation qualification
KF	Karl Fisher
LAF	laminar air flow
LIMS	laboratory information management system
LoD	limit of detection
LOD	loss on drying
MB	Microbiology
MBL	microbiology laboratory
MF	master formulae
MR	management review
NMR	nuclear magnetic resonance spectroscopy
NRA	national regulatory agency
OQ	operational qualification
PHA	process hazard analysis
PM	preventive maintenance
PpK	process performance index
PQ	performance qualification
PQR	product quality review
PQS	pharmaceutical quality system
QA	quality assurance
QC	quality control
QCL	quality control laboratory
QRM	quality risk management
RA	risk assessment
RCA	root cause analysis
SOP	standard operating procedure
TAMC	total aerobic microbial count
TFC	total fungi count
TLC	thin layer chromatography
URS	user requirements specifications
UV	ultraviolet-visible spectrophotometer

Part 2	Brief summary of the findings and comments (where applicable)

1. Pharmaceutical quality system

Since the last inspection the company made an effort to address all deficiencies regarding the quality system. It was however determined that there were still a number of gaps to be attended to, especially pertaining to the computerized systems.

Product Quality Review (PQR)

PQR was managed through a recently revised procedure; however, some of the PQRs that were completed at the beginning of 2017 followed the previous procedure. PQRs were appropriately compiled by the quality assurance team and reviewed by several cross functional departments. The SOP stated that all products were to be reviewed every 12 months, but it was not necessarily required to be within a calendar year. The reports had to be completed and reviewed within a two-month period from the scheduled date. The PQR schedule was available and adequately approved and indicated the required completion date for each product. The PQR included review of starting materials and packaging materials, critical in-process controls and finished product results. Results were trended and depicted as graphical presentations. Other aspects reviewed, were inclusive of batches that failed to meet established specifications, deviations, stability monitoring programme, quality related returns, complaints and recalls, post marketing commitments, qualification statuses of relevant equipment and utilities and a review of technical agreements. A number of PQRs were reviewed and some observations were raised.

Deviations

A procedure on handling deviations was available for review. This was a corporate procedure that was implemented without any risk assessment or impact assessment on site operations and it indicated that deviations had to be reported within 24 hours of occurrence. The company should improve contemporaneous registration of deviations.

Quality Risk Management (QRM)

The company's procedures on "Quality risk management" were reviewed. This SOP discussed various risk assessment tools including failure modes and effects analysis (FMEA). There were a number of documented assessments in place however procedures need further enhancement in this area.

Management review

Management review was performed according to a corporate procedure implemented on site. The procedure specified that periodic management meetings should be scheduled to review action plan to the previous meeting decisions, deviations, complaints etc.

Change control (CC)

The relevant procedure and records were reviewed.

2. Good manufacturing practices for pharmaceutical products

Good manufacturing practices were generally implemented. Necessary human and physical resources were provided, including adequate premises, suitable equipment and services, appropriate materials, containers, approved procedures and instructions, laboratories and equipment for in-process and other controls. Since the last inspection airlocks were installed for dispensaries and sampling areas with

separate entries and exits for personnel and material. Personnel airlocks for the oral solid dosage, liquid and creams and ointment facilities were separate. However, there were limitations because of the facilities' design since personnel and material flows were similar in the production corridor and appropriate instructions were not always available to personnel. It was noted that equipment specifications in the liquid filling facilities were not readily available. Manufacturing steps were recorded in batch manufacturing and packaging records. Manufacturing processes were defined and reviewed. Products were released by the authorized persons.

3. Sanitation and hygiene

Sanitation and hygiene in terms of personnel, premises, equipment and apparatus etc. were generally found to be adequate. However, the company should improve cleaning methods and application cleanliness status labels.

4. Qualification and validation

The company's approach to validation was described in the Corporate Validation Mater Plan (VMP). Computer system validation (CSV) was handled separately. Several computerized systems were being introduced at the time of inspection or had recently been implemented

Process validation procedure was reviewed and discussed.

The company's cleaning validation approach was documented in the Cleaning Validation Master Plan. At least three consecutive applications of the cleaning procedure had to be successfully performed to render the cleaning process validated. Furthermore, a new full cleaning validation would be conducted when a new worst case product, equipment or cleaning detergents were introduced or when there was a change in the cleaning procedure. Products were grouped according to their equipment train and other criteria used were inclusive of permitted daily exposure (PDE), potency, clean ability, water solubility, characteristics and toxicology. A bracketing approach was also taken addressing critical equipment. However it was noted that there was room for improving certain aspects of cleaning validation .

5. Complaints

A corporate procedure on handling complaints was implemented. 2016 complaint log was reviewed. The company should improve their root cause investigation process

6. Product recalls

A recall procedure was available for review. The product recall performed in 2016 was reviewed.

7. Contract production, analysis and other activities

Technical agreements for API suppliers were requested for review and for certain suppliers they were not readily available.

8. Self-inspection, quality audits and suppliers' audits and approval

Self-inspection was not covered in detail in this inspection.

9. Personnel

At the time of the inspection, the company employed an adequate number of personnel in various departments. The company's organogram was available and it was noted that production and quality assurance were independent from each other.

Analysis, Approval and Release of Raw Materials, Intermediate, Semi-finished Goods and Finished Products, were performed in accordance with an established procedure. Checklists were used to appropriately review all aspects of the manufacturing and packaging processes as well as testing and related results. The quality assurance pharmacists were responsible for the production part and a QA person for the QC part. The checklist was inclusive of all processes and was improved since the last inspection.

The job descriptions of key personnel were reviewed and found adequate.

10. Training

Spot checks on training records due to implementation of new procedures were made. It was noted that in some occasions the date of approval and the date a procedure became operational were identical indicating that training was not always carried out before a procedure came into force. Periodic re-qualification of analysts was performed.

11. Personal hygiene

Gowning procedure has not been changed since the previous inspection and remains appropriate for personnel and visitors.

12. Premises

Storage areas

The storage areas were of sufficient capacity to allow orderly storage of various categories of materials such as starting and packaging materials, finished products, products in quarantine, released products, rejected and returned products. Receiving and dispatch bays were separated and protected materials and products from the weather. Printed packaging material were stored in accessed control areas; however, it was observed during the inspection that leaflets in quarantine were stored in a non-demarcated non-quarantine area. The storage areas were monitored for temperature and humidity.

Production areas

Generally, premises were located, designed, constructed and maintained to suit the operations to be carried out. The layout and design of premises have not been changed since last inspection It was confirmed that HEPA filters were installed in all areas in the facility. Adequate pressure cascade was implemented to ensure containment whereas in powder generation areas negative pressure was maintained.

13. Equipment

The equipment installed to manufacture tablets was not dedicated. Some of the equipment of tablet production line was in operation at the time of inspection. New metal detectors were procured and installed since last inspection.

14. Materials

Incoming raw materials for production purposes were purchased from approved suppliers, sampled and tested in accordance with testing procedures and specifications. Raw materials were received in accordance with an established procedure. At the time of inspection, a hybrid system was in place, consisting of a manual system as well as a computerized system. Each consignment and the containers were checked for integrity and placed in quarantine until sampled, tested and released for use.

15. Documentation

In general, improvement was made in terms of documentation practices and the company is in the process to implement an electronic documentation system which would improve documentation practices observed during the inspection.

16. Good practices in production

The oral solid dosage, liquid and packaging areas were inspected. At the time of inspection there was some production of tablets on going. Access to production areas were accessed controlled and was restricted to authorized personnel only. Batch manufacturing and packaging records were in general adequate and cleaning and equipment logs were available. Adequate steps were in place to ensure that work areas and equipment were clean and free from any starting materials, products, labels etc. In process controls were performed by production and IPQC personnel alternatively. Major items of equipment, bulk containers, rooms and packaging lines were in general adequately labeled for status identification with some minor issues observed during the inspection. Practices in the liquid preparation area should be improved.

Improvements in relation to access control on equipment through passwords were made. The set-up of blister packing was performed in accordance with written procedures inclusive of tests to be performed during the start, change of shifts and at the end of operations.

Water System

There was one purified water generation system which was connected to two distribution loops. Purified water was generated by processing bore well water through double ROs and EDI systems and stored in the distribution tank. The PW was supplied at ambient temperature to user points through pipework before returning to the tank. The conductivity and flow rate were monitored online. pH was tested offline. The in-house specification of purified water produced met BP standard.

Reprocessing and reworking

Reprocessing and reworking procedure was checked and discussed.

17. Good practices in quality control

Sample receiving and distribution

There was a procedure in place describing receipt and allocation of samples in the laboratory. However, it did not provide sufficient details on controls during receipt. Registration of samples and monitoring of analyses completion requires further improvement.

Microbiology

The microbiology laboratory conducted water testing, environmental monitoring testing, microbial load test for raw and finished and biossay.

Media preparation procedure and log book as well as purified water (PW) microbiology testing procedure and records were reviewed during the inspection. Media and culture receipt and management were also reviewed.

OOS

Procedure on OOS and the relevant log books of 2016 and 2017 were available for review. The investigation of microbial OOS were discussed.

Part 3: Conclusion

Based on the areas inspected, the personnel met and the documents reviewed, and considering the findings of the inspection, including the deficiencies listed in the Inspection Report, as well as the Corrective Actions taken and planned, Universal Corporation Ltd. was considered to be operating at an acceptable level for compliance with WHO GMP guidelines.

All the non-conformances observed during the inspection that were listed in the full inspection report as well as those reflected in the WHO Public Inspection Report (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.