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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Finished Product Manufacturer

Part 1	General information
Manufacturers details	
Company information	
Name of manufacturer	**Universal Corporation Limited**
Corporate address of manufacturer	Club Road, Past Kikuyu Post Office P.O. Box 1748-00902, Kikuyu Town, Kikuyu, Kenya
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, Kikuyu, Kenya GPS Coordinates 1°14' 26.64''S, 36°39'38.83''E
Inspection details	
Dates of inspection	27-30 August 2018
Type of inspection	Routine GMP Inspection
Introduction	
Brief summary of the manufacturing activities	The company is authorized by Poison & Pharmacy Board, Kenya to manufacture tablets, hard gelatin capsules, liquids, dry syrups, powders and semisolids. No hazardous products are manufactured on the site. No manufacturing activities are outsourced by the company. At the time of inspection the company had submitted or was in process of submitting variations for transfer of products from Strides to Universal.
General information about the company and site	Universal Corporation Limited (UCL) is a subsidiary of Strides Shasun Limited, India. The manufacturing site is located at Kikuyu Town, 21km from Nairobi and 37km from Jomo Kenyatta International Airport. The facilities cover an area of approximately 7,600m^2. The site started its operation in 2004. Manufacturing facilities were expanded during 2009-2010. In addition, new granulation, oral rehydration salt, coating, packaging and FPP warehouse areas were commissioned in 2018.
History	This was the sixth WHO inspection. The last WHO inspection was carried out on 29 May – 01 June 2017

Brief report of inspection activities undertaken - Scope and limitations	
Areas inspected	Production and QC laboratories including but not limited to: • Organization Chart • Job descriptions for key personnel • Personnel training and hygiene • Product Quality Review • Quality Risk Management • Responsibilities of the quality units and production • Complaints and Recalls • Deviation control and change control • CAPA procedure • OOS and investigation • Material release • Self-inspection and vendor qualification • Validation and qualification • Equipment calibration • Data integrity • Sampling and testing of materials • Batch processing records • Materials management system • HVAC system **Site visited:** • Starting material and FPP warehouses • Tablet manufacturing operations • QC laboratories including chemical and microbiological • Stability chambers and retained samples area.
Restrictions	The scope of the inspection was restricted to products submitted to WHO Prequalification
Out of scope	Products not submitted to WHO for Prequalification
WHO products covered by the inspection	The inspection focused on tablet manufacturing and quality control

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**

1. Pharmaceutical quality system

A pharmaceutical quality system (PQS) was established, with a Corporate Quality Manual, policies and written procedures covering essential GMP principles for the site. Categorization of the PQS documentation was not complete as the SMF was not classified as part of PQS documentation but this observation was appropriately addressed in the CAPA plan. A Quality System Review procedure was presented. The procedure described the system for monitoring, assessing and identifying opportunities for improving the effectiveness of PQS. Management review meetings were held monthly. Procedures were categorized in Group SOPs and Site Specific SOPs. Quality Assurance had defined authority and responsibilities. The Corporate Quality Manual was presented and was briefly reviewed during the inspection.

Product quality review (PQR)

A new Corporate PQR procedure was in place describing the steps to verify consistency of existing processes, appropriateness of established specifications for starting materials, in process and finished products. This procedure included description of statistical tools used to evaluate the control over manufacturing processes and product critical quality attributes. The annual PQR programme for 2018 was presented.

Change and deviation management

The company had in place procedures for change and deviation management. Corporate procedures were introduced to site through change control. A computerized system was used to register and manage deviations and changes. Handling of deviations was checked in detail during PQR review and changes in relation to introduction of new equipment and utilities in the new granulation area were reviewed.

CAPA management

A CAPA management procedure sufficiently described a system for conducting investigations and recording activities for remedial actions. A computerized system was used to record and manage CAPA.

Investigation of Out of Specification and Out of Trend Results

There was a procedure in place for handling OOS test results and its application was checked in detail during the laboratory visit. The company had also introduced a corporate procedure for trending and investigating OOT results. It was noted that OOT applied only to assay and related substances. Appropriate CAPA were applied

2. Good manufacturing practices for pharmaceutical products

Basic principles of good manufacturing practices were generally described, and implemented. Manufacturing processes were adequately defined and documented in BMRs and BPRs though there were cases where BMR instructions were not sufficiently clear. Required resources were available, including adequate premises, equipment and utilities. Appropriately qualified personnel were employed. The company should focus on improving processes and documentation in relation to receipt, quarantine and approval of starting materials.

3. Sanitation and hygiene

Premises and equipment were generally maintained at an acceptable level of cleanliness and they were appropriately labelled. There were cleaning procedures in place for facilities and equipment. In general facilities were found to be tidy. Pictorials of gowning instructions were posted on personnel entry rooms.

4. Qualification and validation

The key principles of qualification and validation program were defined and documented in the Validation Master Plan. A separate validation master plan for computerized systems was also available. Process validation of a product in tablet form was checked. A prospective validation approach was followed and three consecutive batches were manufactured between April and May 2017. A risk assessment was carried to determine critical process parameters. The qualification of the extension to the PW system (introduction of five new user points) was reviewed in detail. In addition, the HVAC system installed in the new granulation area was reviewed. Qualification of the new fluid bed dryer was checked. Special attention was paid to the qualification and verification of its PLC. With regards to laboratory equipment, calibration of pH meters was reviewed as well as operation and calibration of the dissolution apparatus

5. Complaints

The company had in place a procedure on registering, investigating and monitoring complaints. A computerized system was used to manage complaints. Received complaints were forwarded to QA and were classified as critical, major or minor. Primary investigation and root cause analysis was performed and timelines for the duration of complaint investigation according to their classification was foreseen. Investigations were extended to different product and batches where necessary. Records of complaints for 2017 and 2018 were reviewed

6. Product recalls

The company had in place a procedure describing measures for recalling products from the market. Different levels of recalls were foreseen. The recall decision was taken by the Corporate management team and was handled by the Recall implementation team. The recall had to be completed within 90 days. Provisions for testing the effectiveness of recall measures were in place and the procedure suggested that a mock recall had to be performed annually.

7. Contract production, analysis and other activities

The company did not contract out any manufacturing step or product. None of the WHO prequalified products were analysed by a third party.

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

Self-inspection was not covered in detail in this inspection due to time constraints. There was a procedure in place for qualifying vendors. However, it lacked clarity on the conditions for carrying out audits and using the observations as an input to the supplier requalification process. Appropriate CAPA were applied

9. Personnel

Organization charts were available reflecting administrative structure as well as departmental hierarchy. Some discrepancies regarding the organization charts were reported (see Part 3). Job descriptions were available. Appropriate procedures for hiring personnel with the necessary qualifications were in place.

10. Training

Procedures for training were presented. An annual training plan was compiled at the end of each year for the following year considering several components of the PQS. Each month the respective program was circulated to the concerned departments. The annual training program for 2018 was reviewed. The SOP described in detail training of newly employed personnel and the training of fixed term contract workers. A training module dedicated to hygiene practices was available and it was introduced on the annual plan every year. Relevant records were reviewed. Qualification criteria for personnel attending training sessions were established as well as a list of qualified trainers.

11. Personal hygiene

Instructions on hygiene practices were described in a procedure. Monitoring of medical examinations was performed and records were presented.

12. Premises

Generally, premises were maintained to suit the operations carried out. As noted in previous inspection reports there were some limitations in facility design in terms of minimizing accidental errors of mix ups and contamination. The layout and design of premises had changed since the last inspection. New granulation, packaging and FPP warehouse areas became operational in early August 2018. Granulation areas G2 and G3 were renovated. At the time of the inspection a new Oral Rehydration Salt area and a new coating room were about to be commissioned but they were not included in the scope of this inspection. The pressure cascade of the new granulation area was checked. The tableting facilities were equipped with single pass air circulation system. Adequate pressure cascade was implemented to ensure containment whereas in powder generation areas negative pressure was maintained. There were three dispensing rooms and a new one under commission at the time of inspection. There were general procedures in place for cleaning the facilities but these procedures did not include detailed instructions on cleaning the dispensaries and sampling booths. The company appropriately addressed these observations.

13. Equipment

The installed production equipment met minimum requirements for the dosage forms manufactured. Attention was paid to the installation and qualification of new equipment in the new granulation area. A new Rapid Mixer Granulator had recently been installed but its qualification had not been completed at the time

of inspection. Qualification of the new FBD was checked in detail. The new tablet counting and filling line was under installation at the time of inspection. Metal detectors were checked at the beginning of each shift. There was a procedure in place describing maintenance and use of punches and dies. Cleaning and equipment maintenance logbooks were established.

14. Materials

There were procedures in place describing receipt, storage and management of raw materials. Incoming materials were purchased from approved manufacturers, sampled and tested according to specifications and testing procedures. There was a procedure in place for handling damaged containers at receipt. There were procedures in place for sampling raw and packaging materials. Finished products were held in quarantine until their final release according to the procedure.

15. Documentation

A documentation system was in place. Procedures defined and supported manufacturing and quality control operations. In general documents were approved, signed and dated by appropriate responsible persons, reviewed and kept up to date. Since the last inspection more than 150 Corporate SOPs were identified as applicable to Universal. Most of these SOPs had been transponded to site but there were still pending a few procedures that required site adoption, training and implementation.

16. Good practices in production

A visit to production areas was made. At the time of inspection there were ongoing production operations. Areas inspected included the dispensaries, the new granulation area (granulation room 4, equipment washing room), the new tablet filling line (qualification had not been completed at the time of inspection), the punches and dies storage room, compression machines suites and coating rooms as well as primary and secondary packaging areas. In general, raw materials for manufacturing of tablets were dispensed, processed, packaged and distributed under appropriate conditions. Operating status of rooms was labelled with product names and batch numbers.

17. Good practices in quality control

Quality control laboratories were separated from production areas. The QC lab was well equipped. Efforts had been made since the last inspection to improve analytical work planning and monitoring. However, this inspection identified several areas that require attention and improvement including but not limited to completion of sampling and testing in a timely manner. The company proposed appropriate CAPA to rectify this observation. Analytical equipment was installed in separate rooms and logbooks for use, maintenance and calibration of equipment were presented. Calibration of pH meters was checked as well as the requalification of the dissolution apparatus. Laboratory software was used for data management of HPLCs and GCs. Procedures were in place for granting access rights. Different user profiles were defined and responsibilities were adequately described in procedures. Laboratory software was used for management and use of standards (reference standards, in-house standards), use of chromatographic columns, handling of volumetric solutions, raw material, semi-finished product, in-process and finished product samples.

Part 3	Conclusion – Inspection Outcome

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, **Universal Corporation Limited,** located at **Club Road**, **Kikuyu Town**, **Kenya** 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

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive

Part 4	List of GMP Guidelines referenced in the inspection report

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2.
   Short name: WHO TRS No. 986, Annex 2
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

2. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2.
   Short name: WHO TRS No. 957, Annex 2
   http://www.who.int/medicines/publications/44threport/en/

3. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth-sixth Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2
   Short name: WHO TRS No. 970, Annex 2
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/

4. WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4
   Short name: WHO TRS No. 929, Annex 4
   http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1

5. WHO guidelines on good manufacturing practices for heating, ventilation and air-conditioning systems for non-sterile pharmaceutical dosage forms. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 5
   Short name: WHO TRS No. 961, Annex 5
   http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

6. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4
   Short name: WHO TRS No. 937, Annex 4
   http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf?ua=1

7. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1
   Short name: WHO TRS No. 961, 957), Annex 1
   http://www.who.int/medicines/publications/44threport/en/

8. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2
   Short name: WHO TRS No. 957, Annex 2
   http://www.who.int/medicines/publications/44threport/en/

9. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 6
   Short name: WHO TRS No. 961, Annex 6
   http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7
    Short name: WHO TRS No. 961, Annex 7
    http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

11. Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 9
    Short name: WHO TRS No. 961, Annex 9
    http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

12. General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-first Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3
    Short name: WHO TRS No. 943, Annex 3
    http://whqlibdoc.who.int/trs/WHO_TRS_943_eng.pdf?ua=1

13. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2
Short name: WHO TRS No. 961, Annex 2
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

14. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2
Short name: WHO TRS No. 981, Annex 2
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

15. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3
Short name: WHO TRS No. 981, Annex 3
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

16. WHO guidelines for drafting a site master file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 14
Short name: WHO TRS No. 961, Annex 14
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

17. WHO Guidelines on good manufacturing practices: validation, Appendix 7: non-sterile process validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 3
Short name: WHO TRS No. 992, Annex 3
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

18. WHO General guidance on hold-time studies WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4
Short name: WHO TRS No. 992, Annex 4
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

19. WHO Technical supplements to Model Guidance for storage and transport of time – and temperature – sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 5
Short name: WHO TRS No. 992, Annex 5
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

20. WHO Recommendations for quality requirements when plant – derived artemisin is used as a starting material in the prosecution of antimalarial active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 6
Short name: WHO TRS No. 992, Annex 6
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

21. WHO good manufacturing practices for biological products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 3
Short name: WHO TRS No. 996, Annex 3
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex03.pdf

22. Guidance on good data and record management practices. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 5
Short name: WHO TRS No. 996, Annex 5
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf