World Health Organization

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

Part 1	**General information**
Manufacturers details	
Name of manufacturer	Universal Corporation Limited
Corporate address of manufacturer	Strides House, Bilekahalli, Bannerghatta Road, Bangalore-560 076, India
Inspected site	
Name & 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	11-14 October 2021
Type of inspection	Routine GMP Inspection
Introduction	
Brief description of the manufacturing activities	The company is authorized by the 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 product manufacturing is outsourced by the company. Some Quality Control activities and tests could be outsourced, if necessary, at approved laboratories. The list of external service providers is included as Annex 3 of the SMF.
General information about the company and site	Universal Corporation Limited (UCL) is a subsidiary of Strides Science Limited (formerly Strides Shasun Limited). 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. The first product was approved by WHO PQ in 2013. In 2016 Universal merged with Strides Pharma Care Limited.
History	This was the seventh WHO inspection. The last WHO inspection was carried out during 27-30 November 2018.

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	**Documents reviewed including but not limited** • 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 **Areas visited:** • Starting material and FPP warehouses • Tablet and ORS manufacturing operations • QC laboratories • Stability chambers and retained samples area.
Restrictions	The inspection was restricted to products approved by WHO PQ and UNICEF
Out of scope	Products not submitted to WHO or UNICEF
WHO and UNICEF products covered by the inspection	HA390 Efavirenz tabs film-coated 600mg HA490 Lamivudine/Zidovudine tabs film-coated 150mg/300mg HA524 Lamivudine/Nevirapine/Zidovudine tabs film-coated 150/200/300mg HA729 Dolutegravir (Sodium)/Lamivudine/Tenofovir disoproxil fumarate tabs Film-coated 50mg/300mg/300mg MA088 Artemether/Lumefantrine tabs 20/120mg MA166 Pyrimethamine/Sulfadoxine tab, dispersible 12.50mg/250mg (pending) MA163 Pyrimethamine/Sulfadoxine tab, dispersible 25mg/500mg (pending) MA169 Pyrimethamine/Sulfadoxine + Amodiaquine (hydrochloride) tab, dispersible 25mg/500mg + 150mg (pending)

	MA172 Pyrimethamine/Sulfadoxine + Amodiaquine (hydrochloride) Tablet, Dispersible 12.5mg/250mg + 75mg (pending) DI012 Zinc (sulfate) Tablet, Dispersible 20mg (pending) ORS low osm. Flavour 20.5g/1L CAR/100 CHX Gel 20gm (Chlorohexidine Di-Gluconate 7.1% w/w)
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
APS	Aseptic process simulation
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CFU	Colony-forming unit
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
DQ	Design qualification
EDI	Electronic deionization
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GMP	Good manufacturing practices
GPT	Growth promotion test
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography (or high performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
IQ	Installation qualification
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae
MFT	Media fill Test
MR	Management review
NC	Non conformity
NRA	National regulatory agency
OQ	Operational qualification
PHA	Process hazard analysis
PLC	Programmable logic controller
PM	Preventive maintenance

PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
RO	Reverse osmosis
SIP	Sterilization in place
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer
WFI	Water for injection

Part 2	**Summary of the findings and comments (where applicable)**

1. Pharmaceutical quality system

Since the merger of UCL with Strides Pharma Science Limited, UCL implemented a QMS following corporate quality practices which aim to harmonize quality principles and approaches across all Strides sites. The Quality Policy that governed the principles behind UCL QMS was designed by the Corporate Quality Team. There were two types of procedures available, namely Group Quality Procedures and Site-Specific Procedures. Quality Assurance had defined authority and responsibilities.

Product Quality Review (PQR)

PQRs were compiled based on a written procedure. The procedure adequately described the steps to verify consistency of existing processes, appropriateness of established specifications for starting materials, in process and finished products. This procedure also included description of statistical tools used to evaluate the control over manufacturing processes and product critical quality attributes. An annual plan was prepared at the end of December including target dates for completion for each product review. Each PQR had to be completed within 30 days of the target date.

The following PQRs were requested for review:

Lamivudine/Nevirapine/Zidovudine tabs film-coated 150/200/300mg

Efavirenz tabs film coated 600mg

Zinc Sulphate tabs dispersible 20mg

ORS low osm. Flavour 20.5g/1L CAR/100

CHX Gel 20gm (Chlorohexidine Di-Gluconate 7.1% w/w)

Change and deviation management

The company had in place procedures for change and deviation management. Trackwise software was used to register and manage deviations and changes. The 2020 deviation trend report was reviewed along with 12 registered deviations during 2019-2021

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. Several examples of OOS and OOT results registered during 2019-2021 were reviewed.

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. Required resources were available, including adequate premises, equipment and utilities. Appropriately qualified personnel were employed.

3. Sanitation and hygiene

Premises and equipment were generally maintained at an acceptable level of cleanliness and they were generally, 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. The document described and defined how validation and qualification activities were managed, different validation approaches, roles and responsibilities. It also provided clarity on cleaning validation, process validation and qualification of facilities, equipment, utilities and personnel. The VMP was reviewed every 3 years unless earlier revision was considered necessary. An annual validation/qualification plan was available and was spot-checked

Cleaning validation was reviewed in detail. A comprehensive risk assessment was performed and a toxicological assessment on the molecules used in production was made available along with the PDE calculations. Literature references were included in the toxicological assessment along with the CV's of the experts who performed these assessments.

5. Complaints

The company had in place a procedure on registering, investigating and monitoring complaints. Trackwise software 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 were 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 2020 and 2021 were reviewed

6. Product recalls

The company had in place a procedure describing actions and 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. Provisions for testing the effectiveness of recall measures were in place and the procedure suggested that a mock recall had to be performed annually. Documentation on recalls and mock recalls during 2019-2021 were reviewed in detail.

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 tested by a third party. The list of approved laboratories used for testing certain products is included as Annex 3 of the SMF. These laboratories had to be qualified and audited.

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

There was a procedure in place for qualifying vendors. Vendor requalification was performed every 3 years while there was an annual review. Due to COVID-19 pandemic certain vendor audits were postponed while others were carried out as distant assessments based on documentation review.

9. Personnel

Organization charts were available reflecting administrative structure as well as departmental hierarchy. Delegation of duties was in general included in job descriptions. Appropriate procedures for hiring personnel with the necessary qualifications were in place.

10. Training

Procedures for training were presented. Different training types were available (e.g. general training, classroom training, self-training etc.). An annual training plan was compiled at the end of each year for the following year considering different components of the PQS. Self-training was made available to employees by using an electronic platform. Evaluation of training was performed electronically by taking a test and training records were maintained in the database. The annual training program for 2021 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. Qualification criteria for personnel attending training sessions were established as well as a list of qualified trainers.

11. Personal hygiene

In general personnel followed good hygiene practices and extra measures like social distancing because of COVID-19 pandemic had been introduced. Additional training sessions on hygiene and COVID-19 had been implemented. Instructions on hygiene practices were described in SOPs. A procedure on monitoring medical examinations was available.

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. Some changes in the layout of the warehouse and sampling rooms had been introduced since the last WHO inspection. The new ORS area (had not been visited during the previous WHO inspection) was visited. 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 procedures in place for cleaning the facilities

13. Equipment

In general equipment was installed and adequately maintained to suit the requirements for the dosage forms manufactured. Cleaning and equipment maintenance logbooks were established. At large equipment was appropriately labelled. The procedure on use of punches and dies as well as their maintenance records were reviewed. A new compression machine was installed and the qualification and operation instructions were spot-checked.

14. Materials

There were procedures in place describing receipt, storage and management of raw materials. Incoming materials were purchased from approved vendors, 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 of raw and packaging material.

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. The majority of SOPs were of the Global Quality type and as indicated in the previous inspection report some of them were not fully applicable to UCL site operations

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 sampling rooms, dispensaries, the granulation area the punches and dies storage room, compression machines suites and coating rooms as well as the ORS unit. 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. Analytical equipment was installed in separate rooms and logbooks for use, maintenance and calibration of equipment were presented. Chromeleon 7.2 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. LIMS 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. There was a dedicated area where 4 stability chambers were installed. It is recommended that the company applies some rules on storage of liquid and solid dosage samples for stability in order to avoid potential contamination due to leakage in the chambers. Logbooks, for the chambers were available. Retained samples were stored in a dedicated room which had been mapped for temperature.

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, Past Kikuyu Post Office P.O. Box 1748-00902, Kikuyu Town, Kikuyu, 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 WHO 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 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

4. 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

5. 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

6. 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. 957, Annex 1***
http://www.who.int/medicines/publications/44threport/en/

7. 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 3. ***Short name: WHO TRS No. 957, Annex 3***
http://www.who.int/medicines/publications/44threport/en/

8. 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

9. 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

10. 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

11. 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

12. 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

13. 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/

14. 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/

15. 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

16. 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

17. 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

18. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10. ***Short name: WHO Multisource guidance*** or ***WHO TRS No. 996, Annex 10***
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

19. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8. **Short name: WHO TRS No. 1010, Annex 8**
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_1010/en/

20. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 10. ***Short name: WHO TRS No. 1010, Annex 10***
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

21. Production of water for injection by means other than distillation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 3. ***Short name: WHO TRS No. 1025, Annex 3***
https://www.who.int/publications-detail/978-92-4-000182-4

22. Good chromatography practice. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 4. ***Short name: WHO TRS No. 1025, Annex 4***
https://www.who.int/publications-detail/978-92-4-000182-4

23. Points to consider for manufacturers and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 6. ***Short name: WHO TRS No. 1025, Annex 6***
https://www.who.int/publications-detail/978-92-4-000182-4

24. Points to consider when including Health-Based Exposure Limits (HBELs) in cleaning validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 2. ***Short name: WHO TRS 1033, Annex 2***
https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations¨

25. WHO good manufacturing practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 3. ***Short name: WHO TRS 1033, Annex 3***
https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations

26. Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4. ***Short name: WHO TRS 1033, Annex 4***
https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations