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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
of the Quality Control laboratory

Part 1	**General information**
Laboratory details	
Laboratory information	
Name of the laboratory	United States Pharmacopeia - Ghana
Corporate address of Laboratory	No. 3, Park Avenue, Motorway Extension, North Dzorwulu, Accra, GHANA Longitude -0.188617, Latitude 5.620431; GPS Coordinates: 5˚ 37’ 13.552” N 0˚ 11’ 19.021” W; UTM Coordinates: Zone 30N E: 811466.02 N: 621995.31
Inspected Laboratory	
Address of inspected Laboratory if different from that given above	Same as above
Summary of activities performed at the laboratory	

Type of Analysis	**Finished products**	**Active pharmaceutical Ingredients**
Physico-Chemical analysis	pH, Loss on drying, Water content (Karl Fischer), Disintegration, Dissolution, Uniformity of dosage units (by mass or content)	pH, Loss on drying, sulphated ash, Acid insoluble ash, Water content (Karl Fischer), Residual solvents, Limit tests
Identification	HPLC (UV-Vis, Fluorescence and Refractive index detection), GC with headspace (FID, TCD), UV- Vis spectrophotometry, FT-IR, Basic tests	HPLC (UV-Vis, Fluorescence and Refractive index detection), GC with headspace (FID, TCD), UV- Vis spectrophotometry, FT-IR, Basic tests
Assay, impurities and related substances	HPLC (UV-Vis, Fluorescence and Refractive index detection), GC with headspace (FID, TCD), UV- Vis spectrophotometry, Volumetric titrations, Potentiometric titrations	HPLC (UV-Vis, Fluorescence and Refractive index detection), GC with headspace (FID, TCD), UV- Vis spectrophotometry, Volumetric titrations, Potentiometric titrations.

Inspection details	
Dates of inspection	11 – 13 June 2017
Type of inspection	Routine
Introduction	
General information	The United States Pharmacopoeia - Ghana (USP Ghana) was initially set up as Center for Pharmaceutical Advancement and Training (CePAT) by the United States Pharmacopial Convention (USP), a scientific not-for-profit organization *in the United States of America* that sets standards for the identity, strength, quality and purity of medicines, dietary supplements and food. USP Ghana was formally incorporated in Ghana on November 13, 2012 as Center for Pharmaceutical Advancement and Training with registration No. G-39,902 and registered as an NGO with the Department of Social Welfare on January 22, 2013 with registration No. 5658. The testing laboratories are on the 5th floor (Wet chemistry and Instrumentation) and 3rd floor (Microbiology) of the Taylor & Taylor Building located at No. 3 Park Avenue; Off Motorway Extension (Route N1), North Dzorwulu, Accra, Ghana; West Africa. The cold storage room and sample store room were on the 4th floor. USP Ghana (formerly CePAT) was established by the United States Pharmacopeia Convention (USP) to help build the capacity of Sub-Saharan Africa's human resource in pharmaceutical quality assurance and quality control by training and developing local professionals to be experts. USP Ghana has access to USP resources (e.g. personnel, equipment, USP reference standards and library, etc.) to support all its operations in Sub-Saharan Africa. The USP site is set up to deliver an integrated platform of training and consulting services as well as laboratory testing services to support a sustainable approach to medicines quality assurance.
History	The laboratory was inspected by WHO in December 2015. The Center has been assessed for ISO 9001:2008 certification by BSI and for ISO/IEC 17025:2005 accreditation by ANSI-ASQ National Accreditation Board ANAB. The latest assessments were carried out on February 15th & 16th, 2017 and May 2nd & 3rd, 2017 and certification / accreditation were maintained.

Scope and limitations		
Areas inspected	See Part 2 below	
Restrictions	N/A	
Out of scope	Microbiological laboratory, stability studies	
Abbreviations	AHU	air handling unit
	ALCOA	attributable, legible, contemporaneous, original and accurate
	API	active pharmaceutical ingredient
	BDL	below detection limit
	CAPA	corrective actions and preventive actions
	CC	change control
	CFU	colony-forming unit
	CoA	certificate of analysis
	DQ	design qualification
	EM	environmental monitoring
	FAT	factory acceptance test
	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
	MR	management review
	NMR	nuclear magnetic resonance spectroscopy
	NRA	national regulatory agency
	OQ	operational qualification
	PHA	process hazard analysis
	PM	preventive maintenance
	PQ	performance qualification
	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 recommendations**

1. Organization and management

The organization of the laboratory was defined in the Organogram. The organogram named the technical and quality assurance staff under each of their functions. Responsibilities were specified.

The laboratory maintained a registry for receiving, distributing and supervising the consignment of the samples to the specific laboratories; and keeping records on all incoming samples.

2. Quality management system (QMS)

Generally, the QMS covered aspects according to good practices for pharmaceutical quality control laboratories. The document Laboratory Quality Manual was reviewed. Scope of the documents was:

- Organisation
- Roles and responsibilities
- Quality policy
- Quality objectives
- Quality planning
- Responsibility for quality
- Document control
- Customer service
- Complaints
- Improvements
- Non-nonconforming testing
- Corrective actions (CA)
- Preventive Actions (PA)
- Control of records
- Internal audits
- Management review
- Personnel
- Environmental conditions
- Test methods and method validation
- Equipment

- Sampling,
- Reporting test results.

Change controls (CC) and deviations were not covered by the QM, however separate SOPs for CC and deviations were available.

The SOP "Management review (MR)" was discussed. According to the SOP MR should be held at least twice a year, a standard agenda was included. It was noted that there were four MR meetings held in 2014 and 2015 and three in 2017. The SOP and meetings covered, but not limited e.g. OOS, deviations, CAPAs, previous minutes, policy and procedures, objectives, customer feedback, quality plan.

The last MR meeting was held on January 2017. Attendance list and MR minutes were discussed.

The list of SOPs was presented to the inspectors. Laboratory implemented lecturing documentation system in November 2016.

The SOP "Document control" was discussed. There were the several documents levels specified:
- Quality manuals
- Quality system SOPs and Work instructions
- Quality system Forms and records

The SOP "Deviation Management" was discussed. The document was applicable to the deviations related to consultancy and training services, materials management, testing and data reporting.
Deviations were classified as:
- Critical
- Major
- Minor

The SOP "CAPA" was discussed. The SOP was applicable to:
- Internal and external audits
- QMS related processes

CAPA forms were maintained electronically as well as CAPA tracker (register).

The SOP "Records control" along with the SOP "Control of laboratory notebooks" were discussed. Analysts were using individual controlled laboratory note books. Issuance/return of note books was QA controlled. According to the procedures returned notebooks should be stored by QA for at least one year after the date of the last analytical data entry.

The SOP "Customer complaints" was discussed. QA was responsible for dealing with customer complaints. Complaints register was maintained electronically. Complaint No XX and related CAPA form were checked.

The SOP "Change control (CC)" was discussed. CCs were classified as:

- Critical
- Major
- Minor

CC were evaluated by QA and approved by Manager of operations.

The SOP "Internal audits" and check list was discussed.

The SOP "SOP for investigation of questionable results", its flow chart and OOS investigation form were discussed. OOS investigation of the pH out of specification for Kanamycin sulphate powder for injection was discussed.

3. Control of documentation

Generally, documented procedures were in place to control the documents. Documents had a unique identifier, version number and date of implementation. A system of change control was in place to inform staff of new and revised procedures.

4. Records

Original observations, calculations and derived data, calibration, validation and verification records and final results, were retained. The records included the data recorded in analytical note books. The records included the identity of the personnel involved in the sampling, preparation and testing of the samples.

5. Data processing equipment

HPLCs, FT-IR and GC were located in the new separate Instruments Laboratory. Log in to the HPLC, GC and FT-IR was by individual passwords and their use was governed by defined access levels and user rights that were set in the equipment, ranging from user to administrator. Date, time and time zone were blocked on all HPLCs; they were all displaying the same time in the same format.

In the case of HPLCs, sequence audit trail, method audit trail and activity log trail were verified and found to be permanently enabled. Manual integration was only done for impurity tests and not for assay test. Bracketing standards were appropriately used.

In-house verification of the FT-IR was done every three months using Polystyrene film. Records were reviewed and showed that they included all the seven wave numbers as per the BP.

Backup of data was done on Symantec.

6. Personnel

Staff members undergoing training were supervised and were assessed on completion of the training. Personnel performing specific tasks were appropriately qualified in terms of their education, training and experience, as required. Current job descriptions were maintained.

The SOP "Avoiding conflict of interests" was discussed. All staff members had to sign conflict of interest form and update in case of arising conflict of interests.

The following job descriptions were discussed:

- Dossier evaluation specialist
- Senior microbiologist
- Consultant (contract analyst), responsible for receiving samples and completing test request forms, control of laboratory reagents, and supervision of inventory Management officer
- Associate chemist, responsible for performing analysis and sample management
- Chemist I, responsible for performing analysis and sample management; was said to be responsible for reference standards management, but this was not specified in his job description.
- Chemist III, responsible for performing analysis and sample management and equipment management.

The SOP "Personnel competency testing" and competency evaluation form were discussed. The SOP was applicable to establishing analyst competency to perform tests assigned to them. According to the SOP analyst performance was to be observed by the supervisor. Testing involved inter-laboratory testing and proficiency testing of samples (experienced analysts) and blank samples for new analysts.

7. Premises

Generally, laboratory facilities were of a suitable size and construction. Rest and refreshment rooms were separate from laboratory areas. Access to the laboratory premises was controlled by biometric system. Laboratory had storage facilities for storage of samples, reagents and glassware.

Microbiological laboratory was installed in February 2017. The microbiology laboratory was not inspected because its quality system was not yet fully functional.

8. Equipment, instrument and other devices

Generally, the laboratory had test equipment, instruments and other devices for the performance of the tests and/or calibrations, validations and verifications. Calibration status labels were attached to each instrument.

9. Contracts

Laboratory had a procedure for the selection and purchasing of services and supplies. The SOP-QA-013-01 "Subcontractor evaluation" was discussed. It was said that till the date of inspection no test had been subcontracted / outsourced.

The SOP "Supplier evaluation", Supplier Assessment Form and approved suppliers list were discussed. Reagents were supplied by local brokers. Supplier's paper based evaluation/ approval was carried out regularly. Initial approval was for 6 months, then for 1 year. In case there was no problem with supplier, approval was valid for 3 years. In case brokers had stock in place, facility audits were carried out.

Suppliers were divided in 4 groups. Suppliers of reagents, chemicals and reference standards were evaluated by questionnaire every 3 years. Approved suppliers list was presented to the inspectors.

10. Reagents

Generally, reagents and chemicals were purchased from approved suppliers and were accompanied by the certificate of analysis, and material safety data sheets, as appropriate. Approved suppliers/vendors list was presented to the inspectors. Expiry dates for purchased reagents were specified in separate register.

11. Reference substances and reference materials

Reference substances and reference materials were stored in transparent desiccator boxes and fridge under controlled conditions. Reference substances and reference materials usage registers were maintained and presented for inspectors. ID numbers of used standards were specified in analytical raw data sheets. There was an assigned person in charge for reference substances and reference materials.

The validity of the available stock of USP RS was said to be regularly checked on the USP website, but there was no evidence (record) to prove this.

12. Calibration, verification of performance and qualification of equipment, instruments and other devices

Dissolution apparatus I, ID No XX mechanical calibration report was discussed. The following parameters were calibrated:

- Shaft wobble
- Shaft verticality
- Basket wobble
- Shaft cantering
- Vessel verticality
- Basket height
- Rotational speed
- Vessel plate level
- Temperature

Kit ID No YY calibration certificate was presented to the inspectors.

Analytical balances were verified daily using 3 standard weights; and every 6 months. The following parameters were verified every six months:

- Linearity
- Accuracy
- Eccentricity
- Repeatability

13. Traceability

The results of an analysis were traceable to reference substances, equipment and instruments used for analysis; and the weights traceable to OIML. All traceability records about a sample that was tested were maintained in the Laboratory notebook for each analyst, including reagent preparation records.

14. Incoming samples

When samples are received at the USP Ghana Laboratory, the Analysis Request Form is printed (indicates date and time of printing) and filled in, sample identification number assigned and samples taken for storage in the sample storage room (T 20 – 30 °C) or in the refrigerator (2 – 8°C). Sample management was paper based, using a hardcover logbook.

The SOP “Sample management” and Analysis Request Form were discussed. The SOP explained sample receiving procedures, handling of retention samples, destruction or disposition of samples.

15. Analytical worksheet

Instead of analytical worksheets laboratory used Laboratory Notebooks, which were used by analysts for recording all information about the sample, the reagents preparation, the test procedure, calculations and the results of testing. It was complemented by the raw data obtained in the analysis. Laboratory logbooks were signed by the responsible analysts, verified and approved and signed by the QC supervisor.

The following sample information was recorded in laboratory notebooks:

- Description of materials
- Label claim/composite
- Lot/batch number
- Manufacturing date
- Expiry date
- Source/manufacturer
- Quantity received
- Analysis start date
- Analysis end date
- Packing
- Project code
- Sample code

16. Validation of analytical procedures

The SOP “Verification of validated and/or compendial procedures” was discussed.

According to the SOP for method verification the following tests should be carried out:

- Specificity
- System suitability
- System precision
- Method precision
- Accuracy
- Linearity
- LOD & LOQ (only for impurities)

17. Testing

Testing was done in accordance with the compendial methods and in some cases according to the client's in-house specifications.

18. Evaluation of test results

Test results were reviewed and evaluated before issuance of the CoA. Test results were reviewed by Head of QC or his designee.

19. Certificate of analysis

The SOP “Reporting of tests” was discussed. SOP explained reviewing and reporting of test results. Soft copies of CoAs in PDF were kept for 5 years.

20. Retained samples

The SOP "Sample management" section 4 explained that retained samples were retained for period of shelf-life or for a specific period mutually agreed with the client.

21. Safety

Safety data sheets were available to staff before testing was carried out; smoking, eating and drinking in the laboratory was prohibited. Staff wore laboratory coats and used eye protection. Safety showers were installed.

PART 3 CONCLUSION

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, as well as the corrective actions taken The United States Pharmacopoeia - Ghana (USP Ghana) formerly known as Center for Pharmaceutical Advancement and Training (CePAT), located at No. 3, Park Avenue, Motorway Extension, North Dzowulu, Accra, GHANA was considered to be operating at an acceptable level of compliance with WHO Good Practices for Pharmaceutical Quality Control Laboratories for the following expertise:

Type of Analysis	Finished products	Active pharmaceutical Ingredients
Physico-Chemical analysis	pH, Loss on drying, Water content (Karl Fischer), Disintegration, Dissolution, Uniformity of dosage units (by mass or content)	pH, Loss on drying, sulphated ash, Acid insoluble ash, Water content (Karl Fischer), Residual solvents, Limit tests
Identification	HPLC (UV-Vis, Fluorescence and Refractive index detection), GC with headspace (FID, TCD), UV- Vis spectrophotometry, FT-IR, Basic tests	HPLC (UV-Vis, Fluorescence and Refractive index detection), GC with headspace (FID, TCD), UV- Vis spectrophotometry, FT-IR, Basic tests
Assay, impurities and related substances	HPLC (UV-Vis, Fluorescence and Refractive index detection), GC with headspace (FID, TCD), UV- Vis spectrophotometry, Volumetric titrations, Potentiometric titrations	HPLC (UV-Vis, Fluorescence and Refractive index detection), GC with headspace (FID, TCD), UV- Vis spectrophotometry, Volumetric titrations, Potentiometric titrations.

PART 4
List of GMP guidelines referenced in the inspection

1. 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/

2. 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/

3. 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

4. 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/

5. 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

6. 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

7. 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

8. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert 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 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 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

15. 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