World Health Organization

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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
Desk Assessment of Quality Control Laboratory (QCL)

Part 1	**General information**
Laboratory information	
Name and address of QCL	University of Liège Faculty of Medicine - Department of Pharmacy, Building B36, Tour de Pharmacie, Niveau +2, Quartier Hôpital, Avenue Hippocrate 15, 4000 Liège Belgique
Laboratory units/divisions	Department of Pharmacy
Desk assessment details	
Start and end dates of review	06 March 2019

Tests covered by this desk assessment

Type of Analysis	**Finished Products**	**Active pharmaceutical ingredients**
Physical/Chemical analysis	pH, density, optical rotation, refractive index, viscosity, water content, conductivity, residual solvents, limit tests, tablet hardness, friability, disintegration, dissolution, uniformity of dosage units (mass, content), tapped density, particles size, molarity,	pH, optical rotation, refractive index, viscosity, melting point, loss on drying, water content, osmolarity, conductivity, heavy metals, residual solvents, limit tests, acid value, iodine value, peroxide value, ester value, hydroxyl value, saponification value, tapped density, particles size, molarity,
Identification tests	UV-Vis, PDA, refractive index, LC-UV-ELSD-, UHPLC-UV-MS, MS, GC-FID, TLC, UV-VIS spectrophotometry, FT-IR spectroscopy, spectroscopy NIR, NMR, Raman spectroscopy, CEDAD, basic tests	UV-Vis, PDA, refractive index, LC-UV-ELSD-, UHPLC-UV-MS, MS, GC-FID, TLC, UV-VIS, spectrophotometry, FTIR spectroscopy, spectroscopy NIR, NMR, Raman spectroscopy, CEDAD, basic tests
Assay, impurities and related	HPLC (UV-Vis, PDA), LC/MS, GC (FID), UHPLC-UV-	HPLC (UV-Vis, PDA), LC/MS, GC (FID), UHPLCUV- MS, LC-

	substances	MS, LC-UVELSD, Spectrophotometry UV-Vis, AAS, FTIR, NIR, LC-NMR, CE-DAD	UV-ELSD, Spectrophotometry UV-Vis, AAS, FTIR, NIR, LC-NMR, CE-DAD Volumetric titrations
	Microbiological analysis	-	-
	Stability testing	Under ICH conditions	Under ICH conditions

List of documents submitted	• AFMPS 2017 rapport inspection.pdf • Annexe_PTS Results_2015_2018.pdf • Annexe_2_QualityManual CQ-01CQ-01.pdf • Annexe_3_Laboratory Plan.pdf • Document_1_GMP Certificate.pdf • Document_2_LIF ULg Pharmacy Department 2019.pdf • Document_3_Test to prequalify.pdf • Document_4_Equipment List.pdf • Document_5A_GMP_inspection report.pdf • Document_5B_IMP_inspection report.pdf • Document_6A_CAPA related to last GMP inspection of AFMPS.pdf • Document_6B_Proof of CAPA implementation for GMP inspection.pdf • Document_6C_CAPA related to last IMP inspection of AFMPS.pdf • Document_6D_Proof of CAPA implementation for IMP inspection • Document_7_Full set-inspection.pdf	
Any documents missing?	None	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last)**	
afmps – agence fédérale des médicaments et des produits de santé	Dates of inspection:	4 September 2018
	Type of inspection:	New activity
	Unit/Division inspected:	Department of Pharmacy
	Tests covered:	Laboratory analysis and IMP capsules
afmps – agence fédérale des médicaments et des produits de santé	Dates of inspection:	29-30 May 2017
	Type of inspection:	Routine
	Unit/Division inspected:	Pharmacy department
	Tests covered:	Floors 2, 3 and 5 are used for analytical testing (GMP) and related activities (storage, preparation, weighing, cleaning), and testing of Medicines
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	The last WHO Desk inspection was conducted on 11-15th August and on 3rd November 2016 INSP-2016-0095.	

Brief summary of activities	The laboratory belongs to the Pharmacy Department of the University of Liège in Belgium. It comprises the following 5 laboratories: a. Laboratory of Analytical Pharmaceutical Chemistry (LAPC), b. Laboratory of Pharmaceutical Technology and Biopharmacy (LPTB), c. Laboratory for Analysis of Medicines (LAM), d. Laboratory of Pharmacognosy (LPG), e. Laboratory of Pharmaceutical Chemistry (LPC), There is also an additional entity: Cell Activities of Department (CAD)
General information about the QCL	According to the LIF, the facility is part of the University of Liège, Belgium within the Pharmacy department, consisting of 5 laboratories with a total number of 13 staff. The facility is involved in the following activities: 1) Drug development and analysis including a. the development, robust optimization and validation of analytical and bioanalytical methods according to ICH/FDA guidelines b. Characterization of solid dosage forms and c. physical characterization of materials 2) Drug formulation including a. formulation of dosage forms (solid, liquid and semi-solid formulations) and b. consulting and expertise reports. 3) Other activities include organic synthesis, hemisynthetic drugs from natural products, clinical resolution of racemic compounds, full structural characterisation of organic compounds, a chemical library for biological screening and malaria-based research involving the evaluation of the antiplasmodial activity of potential drugs in vitro and in vivo. Customers include: • Drug manufacturers in Europe, spinoff and small pharmaceutical enterprises • Pharmacy Department of Health Ministries in Europe and low incomes countries • Nongovernmental organisation (NGO) around the world • Central of purchasing and distribution of medicines in low income countries
Focus of the last WHO inspection	The previous WHO inspection was a desk review. The site has not previously physically been inspected by WHO.
Out of scope and restrictions (last WHO inspection)	None recorded.

WHO Prequalified tests covered by the last WHO inspection	

Type of Analysis	Finished Products	Active pharmaceutical ingredients
Physical/Chemical analysis	pH, density, optical rotation, refractive index, viscosity, water content, conductivity, residual solvents, limit tests, tablet hardness, friability, disintegration, dissolution, uniformity of dosage units (mass, content), tapped density, particles size, molarity,	pH, optical rotation, refractive index, viscosity, melting point, loss on drying, water content, osmolarity, conductivity, heavy metals, residual solvents, limit tests, acid value, iodine value, peroxide value, ester value, hydroxyl value, saponification value, tapped density, particles size, molarity,
Identification tests	UV-Vis, PDA, réfractive index, LC-UV-ELSD, UHPLC-UV-MS, MS, GC-FID, TLC, UV-VIS spectrophotometry, FT-IR spectroscopy, spectroscopy NIR, NMR, Raman spectroscopy, CEDAD, basic tests	UV-Vis, PDA, refractive index, LC-UV-ELSD, UHPLC-UV-MS, MS, GC-FID, TLC, UV-VIS spectrophotometry, FT-IR spectroscopy, spectroscopy NIR, NMR, Raman spectroscopy, CEDAD, basic tests
Assay, impurities and related substances	HPLC (UV-Vis, PDA), LC/MS, GC (FID,), UHPLC-UV-MS, LC-UV-ELSD, Spectrophotometry UV-Vis, AAS, FT-IR, NIR, LC-NMR, CE-DAD	HPLC (UV-Vis, PDA), LC/MS, GC (FID,), UHPLC-UV-MS, LC-UV-ELSD, Spectrophotometry UV-Vis, AAS, FT-IR, NIR, LC-NMR, CE-DAD volumetric titrations
Stability testing	As per ICH requirements	As per ICH requirements

Additional tests covered by this desk assessment:	None

Abbreviations	**Meaning**
API	Active pharmaceutical ingredient
CAPA	Corrective and preventive action
FPP	Finished pharmaceutical product
FTIR	Fourier transform infrared spectrophotometer

GC	Gas chromatograph or gas chromatography
GLP	Good laboratory practices
GPPQCL	Good practices for pharmaceutical quality control laboratories
HPLC	High performance liquid chromatograph
QA	Quality assurance
QCL	Quality control laboratory
SOP	Standard operating procedure

Part 4	**Summary of the assessment of additional supporting documentation**

a) Authorization granted by the local authority (if any) or ISO 17025 certificate:

GMP certificate issued by AFMPS - GMP certificate BE/GMP/2017/032 (27/6/2017).

b) Laboratory information file (LIF):

The Laboratory Information file (LIF) was provided (Document_2_LIF ULg Pharmacy Department 2019.pdf). The LIF was arranged in accordance with the WHO guidelines. A summary of processes was available within this document and found to adequately address WHO requirements.

c) List of all regulatory inspections performed in the last 3 years and their outcomes:

Two inspection reports were provided from AFMPS – full inspection performed 29-30 May 2017 and a shortened inspection performed 4 September 2018 to allow for the introduction of a new activity.

d) Qualification, validation and calibration status of equipment:

The facility had in place a documented procedure for the IQ/OQ/PQ of equipment. An equipment list was provided detailing the qualification period with each item of equipment assigned a unique identifier.

e) Confirmation by the quality manager that a full self-inspection dedicated to the tests submitted for prequalification has been performed and all matters dealt with:

The facility provided a copy of the internal audit planning schedule for 2018 and 2019. The plan included internal audits of the production area, technical documentation in various analytical areas, quality manual including deviations. From the inspection provided it was concluded that the facility had adequately covered the critical areas of the quality management system within the audit schedule.

f) Additional documents submitted:

Annexe_1_PTS Results_2015_2018.pdf was provided with the results of Proficiency testing performed for the period between 2015 to 2018.

Part 5	Conclusion – Desk assessment outcome

Based on the GPPQCL evidence received and reviewed, it is considered that a desk assessment is acceptable in lieu of a WHO onsite inspection. The site, ***University of Liège, Faculty of Medicine - Department of Pharmacy,*** located at ***Building B36, Tour de Pharmacie, Niveau +2 Quartier Hôpital Avenue Hippocrate 15 4000, Liège, Belgique*** is considered to be operating at an acceptable level of compliance with WHO GPPQCL guidelines. This compliance status shall be valid until ***May 2020***or when another inspection is conducted by WHO or by a WHO-recognized authority.

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

Part 6	List of guidelines referenced in this inspection report

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 GPPQCL Guidelines or ***TRS No. 957, Annex 1***
   http://www.who.int/medicines/publications/44threport/en/

2. WHO guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Second Report. Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 9. ***Short name: WHO TRS 1010, Annex 9***
   https://www.who.int/medicines/areas/quality_safety/quality_assurance/TRS1010annex9.pdf?ua=1

3. 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 GMP Guidelines*** or ***TRS No. 986, Annex 2***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

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. 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/

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 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/

9. 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/

10. 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

11. 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

12. 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

13. 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

14. 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

15. 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/

16. 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/

17. 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

18. 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

19. 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

20. 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

21. 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

22. 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 TRS No. 996, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

23. 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