World Health Organization

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

<table>
<tr><th>Part 1</th><th>General information</th></tr>
<tr><td colspan="2">Laboratory information</td></tr>
<tr><td>Name and address of QCL</td><td>Laboratories KABS Inc
Main Buiding: 4500 De Tonnancour, Saint-Hubert, Québec, Canada J3Y 9G2
Warehouse : 4601 De Tonnancour, Saint-Hubert, Québec, Canada J3Y 9G2</td></tr>
<tr><td colspan="2">Desk assessment details</td></tr>
<tr><td>Start and end dates of review</td><td>30 September 2019 – 03 October 2019</td></tr>
<tr><td>Tests covered by this desk assessment</td><td>
<table>
<tr><th>Type of Analysis</th><th>Finished Products</th><th>Active pharmaceutical ingredients</th></tr>
<tr><td>Physical/Chemical analysis</td><td>pH, density, refractive index, viscosity, loss on drying, optical rotation, melting point/range, osmolarity, water content, disintegration, dissolution, uniformity of dosage units (mass content), friability, tablet hardness, particulate matter test.</td><td>pH, density, refractive index, viscosity, loss on drying, optical rotation, melting point/range, heavy metals, acid value, iodine value, limit tests, osmolarity, water content</td></tr>
<tr><td>Identification tests</td><td>HPLC (UV-VIS, IR, conductivity, fluorescence, ELS detection), LC/MS, GC (FID, TCD), GC/MS, TLC, capillary electrophoresis, UV-VIS spectrophotometry, FTIR, Atomic Absorption Spectrometry</td><td>HPLC (UV-VIS, IR, conductivity, fluorescence, ELS detection), LC/MS, GC (FID, TCD), GC/MS, TLC, capillary electrophoresis, UV-VIS spectrophotometry, FTIR, Atomic Absorption Spectrometry</td></tr>
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	Assay, impurities and related substances	HPLC (UV-VIS, IR, conductivity, fluorescence, ELS detection), LC/MS, GC (FID, TCD), UV-VIS spectrophotometry, Atomic Absorption Spectrometry, Fluorescence Spectrometry, Volumetric or potentiometric titrations.	HPLC (UV-VIS, IR, conductivity, fluorescence, ELS detection), LC/MS, GC (FID, TCD), UV-VIS spectrophotometry, Atomic Absorption Spectrometry, Fluorescence Spectrometry, Volumetric or potentiometric titrations, coulometry
	Stability Testing	ICH conditions	ICH conditions
	Bacterial endotoxin testing (BET)	BET by turbidimetric method	BET by turbidimetric method

List of documents submitted

- KABS Desk Review - 1a (1of2) Health Canada Notice of Compliance.pdf
- KABS Desk Review - 1a (2of2) Health Canada Corrective Action Acknowledgment Letter.pdf
- KABS Desk Review - 1b FDA GMP Compliance (included in EIR).pdf
- KABS Desk Review - 2 Site Master File (SMF-0001-E04.1)
- KABS Desk Review - 4 List of Laboratory Equipment
- KABS Desk Review - 5a Health Canada Inspection Report
- KABS Desk Review - 5b (1of2) ANVISA Inspection Report-PORTUGUESE
- KABS Desk Review - 5b (2of2) ANVISA GMP Inspection report (bilingual)
- KABS Desk Review - 5c (1of2) Russia GMP Certificate-RUSSIAN
- KABS Desk Review - 5c (2of2) Russia GMP Certificate (English Translation)
- KABS Desk Review - 5d FDA GMP Inspection Report (EIR)
- KABS Desk Review - 6a CAPA Health Canada
- KABS Desk Review - 6b CAPA ANVISA (bilingual)
- KABS Desk Review - 6d CAPA FDA
- KABS Desk Review - 7 Confirmation of Self-Inspection
- KABS Desk Review for WHO Prequalification - Cover Letter

6a Proof of CAPA implementation (Health Canada files)

- 6a CAPA A (1of20) Data Review Checklist (Form)
- 6a CAPA A (2of20) SOP-03-015-E01.1 Analytical Data Review and Issuing Certificates of Analysis
- 6a CAPA B-C (3of20) Data Integrity Risk Assessment Report
- 6a CAPA D (4of20) SOP-05-005-E02.0 Management of Access to IT

	Systems • 6a CAPA D (5of20) SOP-05-013-E01.0 Data Integrity Policy • 6a CAPA E (6of20) SOP-01-006-E01.0 Change Control • 6a CAPA E (7of20) SOP-06-001-E01.0 Use of Analytical Methods and Methods Re-Validation Policy • 6a CAPA E (8of20) SOP-06-002-E01.0 Validation of Analytical Methods • 6a CAPA F (9of20) PQMS18102R-E01.0 Cleaning Nitisinone • 6a CAPA F (10of20) PQMS18103 Cleaning norlutate • 6a CAPA G (11of20) SOP-07-008-E01.0 Sampling • 6a CAPA H (12of20) 100681-A_KABS Laboratories_ V.8.FR_2018-06-14 API Foreign Building Table A • 6a CAPA J (13of20) SOP-01-007-E01.0 Deviations • 6a CAPA K (14of20) Deviations Training list 20180525 • 6a CAPA K (15of20) Deviations Training Material 20180521 • 6a CAPA L (16of20) SOP 4002-Ver-E06 • 6a CAPA M (17of20) SOP-04-303-E01.0 Stability Rooms_ Description and Maintenance • 6a CAPA N (18of20) SOP-01-008-E01.0 Complaints • 6a CAPA O (19of20) FRM-07-014-01-E01 (Replaced F-0005-0005) • 6a CAPA P (20of20) KABS - MendeliKABS Quality Agreement (Version 04) 6b Proof of CAPA Implementation (ANVISA) • 6b (1of20) CAR AUD21802 - Attachment 1 (SOP-04-004 Water System) • 6b (3of20) CAR AUD21802 - Attachment 3 (CCR18324) • 6b (4of20) CAR AUD21802 - Attachment 4 (CAPA19041) • 6b (5of20) CAR AUD21802 - Attachment 5 (Balance Logbook Template) • 6b (6of20) CAR AUD21802 - Attachment 6 (1 of 5) (List of STPs for Nitisinone Capsules) • 6b (7of20) CAR AUD21802 - Attachment 6 (2 of 5) (STP-0121 Assay for Nitisinone) • 6b (8of20) CAR AUD21802 - Attachment 6 (3 of 5) (STP-0122 Impurities Test for Nitisinone Capsules) • 6b (9of20) CAR AUD21802 - Attachment 6 (4 of 5) (STP-0123 Content Uniformity) • 6b (10of20) CAR AUD21802 - Attachment 6 (5 of 5) (STP-0120-E02.0 Dissolution) • 6b (11of20) CAR AUD21802 - Attachment 7 (SOP-07-008-E01.0 Sampling) • 6b (12of20) CAR AUD21802 - Attachment 8 (OOS Investigation SOP) • 6b (13of20) CAR AUD21802 - Attachment 9 (SOP-06-002-E01.0) • 6b (14of20) CAR AUD21802 - Attachment 10 (SOP-03-011-E01.1 APQR) • 6b (15of20) CAR AUD21802 - Attachment 11 (PMFG19087R-E01.0 Process Validation Report) • 6b (16of20) CAR AUD21802 - Attachment 12 (SOP-03-004-E01.0 Supplier Qualification SOP)

	• 6b (17of20) CAR AUD21802 - Attachment 13 (SOP-09-023-E02.0 Dialers and Alarm Systems) • 6b (18of20) CAR AUD21802 - Attachment 14 (1 of 2) (PQMS18289R mapping of 25C storage area INC-L009) • 6b (19of20) CAR AUD21802 - Attachment 14 (2of2) (PQMS18289R mapping of 25C storage area INC-L009) • 6b (20of20) CAR AUD21802 - Attachment 15 (2-8C stability chamber FRZ-L011 Qualificat... 6d Proof of CAPA Implementation (US FDA) • 6d CAPA Implementation (1of1) SOP-04-002-E03.0 Equipment Management	
Any documents missing?	None missing	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last)**	
US FDA	Dates of inspection:	21-22 March 2019
	Type of inspection:	Surveillance cGMP inspection
	Unit/Division inspected:	Pharmaceutical control testing laboratory
	Tests covered:	Not listed
ANVISA (Agéncia Nacional de Vigilancis Santaria – Brazil)	Dates of inspection:	17-21 December 2018
	Type of inspection:	Initial inspection
	Unit/Division inspected:	Not listed
	Tests covered:	Not listed
Health Canada	Dates of inspection:	16 January 2017
	Type of inspection:	GMP Domestic – regular inspection
	Unit/Division:	Not listed
	Tests covered:	Not listed
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	WHO have not previously inspected the site.	
Brief summary of activities	Not applicable	
General information about the QCL	Not applicable	

Focus of the last WHO inspection	Not applicable
Areas inspected	Not applicable
Out of scope and restrictions (last WHO inspection)	Not applicable
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:

The site does not hold ISO 17025 certification. However, the site is GMP compliant according to FDA, Health Canada and ANVISA.

It also holds ISO 13485:2016 Medical Devices certification – Quality management systems – Requirements for regulatory purposes certification.

b) Laboratory information file (LIF):

The Laboratory Information file (Site Master File (SMF-0001-E04.1.pdf) was provided. This document was set out in accordance with WHO requirements. It contained general information on the laboratory, quality management system, document control, personnel, premises, equipment, materials, type of subcontracting and contact details, validation of analytical procedures, internal and external audits, stability and Microbiological testing

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

The site has been inspected by the following authorities

- March 2019- FDA - final outcome is currently not available.
- December 2018 – ANVISA - final outcome was acceptable.
- January 2017 – Health Canada – final outcome was acceptable.

d) Qualification, validation and calibration status of equipment:
The laboratory has a documented qualification, validation, calibration and maintenance process.

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:
A statement was provided and signed but Tanguy Houndolo (19 August 2019) that the site was frequently audited by clients and subjected to self-inspection. A total of 29 external audits of the facility had been conducted since January 2018.

Part 5	Conclusion – Desk assessment outcome

Based on the previous WHO inspections and 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 ***Laboratories KABS Inc***, located at ***4500 De Tonnancour, Saint-Hubert, Québec, Canada J3Y 9G2*** is considered to be operating at an acceptable level of compliance with WHO GPPQCL guidelines.

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

24. 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