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>InphA GmbH
Institute for Pharmaceutical and Applied Analytics
Emil-Sommer-Straße 7 28329
Bremen
Germany</td></tr>
<tr><td>Laboratory units/divisions</td><td>Quality Control Laboratory</td></tr>
<tr><td colspan="2">Desk assessment details</td></tr>
<tr><td>Start and end dates of review</td><td>23 May 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>clarity and opalescence, coloration, pH, density, refractive index, optical rotation, loss on drying, water content, residual solvents, limit tests, tablet hardness, friability, disintegration, dissolution, uniformity of dosage units (mass, content), osmolality, particulate contamination (visible particles), particulate contamination (sub-visible particles)</td><td>clarity and opalescence, coloration, pH, density, refractive index, optical rotation, melting point, loss on drying, water content, residual solvents, limit tests, sulphated ash</td></tr>
<tr><td>Identification tests</td><td>HPLC and SCE (DAD; UV-Vis, RI, conductivity, fluorescence, ELS, MS,</td><td>HPLC and SCE (DAD; UV-Vis, RI, conductivity, fluorescence, ELS, MS,</td></tr>
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		chemiluminescence, pulsed amperometry detection), GC (FID,MS), capillary electrophoresis, TLC, UV-Vis spectrophotometry, FTIR, AAS, AES, ICP/OES, electrophoresis, isoelectric focusing, microscopy, basic tests	chemiluminescence, pulsed amperometry detection), GC (FID,MS), capillary electrophoresis, TLC, UV-Vis spectrophotometry, FTIR, AAS, AES, ICP/OES, electrophoresis, isoelectric focusing, microscopy, basic tests
	Assay, impurities and related substances	HPLC and SCE (DAD; UV-Vis, RI, conductivity, fluorescence, ELS, MS, chemiluminescence, pulsed amperometry detection), GC (FID, MS), capillary electrophoresis, TLC, UV-Vis spectrophotometry, FTIR, AAS, AES, ICP/OES, electrophoresis, isoelectric focusing, volumetric titration (visual, potentiometric), gravimetry, microscopy	HPLC and SCE (DAD; UV-Vis, RI, conductivity, fluorescence, ELS, MS, chemiluminescence, pulsed amperometry detection), GC (FID, MS), capillary electrophoresis, TLC, UV-Vis spectrophotometry, FTIR, AAS, AES, ICP/OES, electrophoresis, isoelectric focusing, volumetric titration (visual, potentiometric), gravimetry, microscopy
	Microbiological analysis	Sterility test, microbial count, specific microorganisms, bacterial endotoxins, microbiological assay of antibiotics	Sterility test, microbial count, specific microorganisms, bacterial endotoxins, microbiological assay of antibiotics
	Miscellaneous	N/A	N/A
List of documents submitted	• 1 Certificate_DAkkS_201703.pdf • 2_LIF_InphA_2019_05_07.pdf • 2_LIF_Annex_01_List_SOP_2019_04.pdf • 2_LIF_Annex_02_Organisational_Chart_2019_04.pdf • 2_LIF_Annex_03_Plan_Lab_2019_04 • 2_LIF_Annex_04_Pictures_komp.pdf • 2_LIF_Annex__05_List_of_Equipment.pdf • 2_LIF_Annex_06_List_of_ServiceLab_2019_04.pdf • 5a_MJA_Audit_Report_MJA_03_2017.pdf		

	• 5b_Attestation_MJA201703.pdf • 5c_DAkks_Audit_Report_09_2018.pdf • 6_OMCL-QA 17 18 DEF_Cas_MJA_201703.pdf • 7 Conformation by Quality Manager.pdf	
Any documents missing?	None	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last)**	
DAkkS (Deutsche Akkreditierungs-stelle, Berlin, Germany	Dates of inspection:	18 September 2018
	Type of inspection:	Monitoring the accreditation
	Unit/Division inspected:	Not listed in the report.
	Tests covered:	Not listed in the report.
EDQM – Department of Biological Standardization, OMCL Network and Healthcare	Dates of inspection:	22/3/2017 to 24/3/2017
	Type of inspection:	Joint inspection between EDQM and DAkkS Reassessment audit
	Unit/Division inspected:	Not listed in the report provided.
	Tests covered:	Not listed in the report.
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	An onsite inspection of this facility has not been conducted. A desk review was performed 5 February 2014 (INSP-2018-0156). The evidence submitted was reviewed and WHO found the laboratory to be operating at an acceptable level of compliance with WHO Good Practices for Pharmaceutical Quality Control Laboratories.	
Brief summary of activities	InphA GmbH primary activity is the testing of medicinal products and APIs for the competent authorities of the six-stake holding federal states, for the purpose of post approval market surveillance with the objective of protection of consumer health. Furthermore, the laboratory is involved in the testing of suspicious unknown products and counterfeits. It also participates in the development of monographs, in collaborative trials, market surveillance studies, testing of centrally authorized products and in inspections on behalf of the competent authorities and conducts trainings for different audiences regarding laboratory related topics. These services are also offered to third parties as long as the work on behalf of the stakeholder is not compromised.	
General information about the QCL	The institute was founded in 1995 by four German federal states (Bremen, Hamburg, Lower Saxony, and Schleswig-Holstein). In 2001 and 2002, respectively, the federal states of Hesse and Saarland joined the institute.	

<table>
<tr><td></td><td>The laboratory is involved and regularly participates in a number of proficiency testing schemes (EDQM and others if available).

At the time of this review there were a total of 26 laboratory employees.</td></tr>
<tr><td>Focus of the last WHO inspection</td><td>Desk review</td></tr>
<tr><td>Areas inspected</td><td>Not applicable</td></tr>
<tr><td>Out of scope and restrictions (last WHO inspection)</td><td>Not Applicable</td></tr>
<tr><td>WHO Prequalified tests covered by the last WHO inspection</td><td>
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	Assay, impurities and related substances	HPLC (DAD; UV-Vis, RI, conductivity, fluorescence, ELS, MS, charged Aerosol, chemiluminescence, pulsed amperometry detection), GC (FID, MS), capillary electrophoresis, TLC, UV-Vis spectrophotometry, FTIR, AAS, AES, ICP/OES, electrophoresis, isoelectric focusing, volumetric titration (visual, potentiometric), gravimetry	HPLC (DAD; UV-Vis, RI, conductivity, fluorescence, ELS, MS, charged Aerosol, chemiluminescence, pulsed amperometry detection), GC (FID, MS), capillary electrophoresis, TLC, UV-Vis spectrophotometry, FTIR, AAS, AES, ICP/OES, electrophoresis, isoelectric focusing, volumetric titration (visual, potentiometric), gravimetry
	Microbiological analysis	Sterility test, microbial count, specific microorganisms, bacterial endotoxins	Sterility test, microbial count, specific microorganisms, bacterial endotoxins
	Miscellaneous	None	None
Additional tests covered by this desk assessment:	Nil		

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 laboratory provided a copy of the Attestation that declares **InphA Institute for Pharmaceutical and Applied Analytics GmbH** to be in accordance with EDQM instruction IS7/02 on the OMCL Network Mutal Joint Audit Scheme.

Attestation number – EDQM/MJA – 122,
Strasbourg, 22 August 2017 - valid until February 2021.

b) Laboratory information file (LIF):

A comprehensive laboratory information file was provided and was arranged according to WHO requirements (2_LIF_InphA_2019_05_07.pdf)

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

The following regulatory inspections were provided.

- DAkkS, Berlin, Germany (18th September 2018) - found acceptable
- DAkkS (23rd – 24th March 2017) and OMCL network (23rd – 24th March 2017) – Joint inspection found acceptable.

d) Qualification, validation and calibration status of equipment:

A detailed description of equipment maintenance and preventive maintenance was provided in section 6.1 of the LIF. The qualification of equipment was provided in section 6.3. The laboratory performs design qualification and installation once during the life cycle of the instrument unless there are intended changes or subsequent medications are planned including if the instrument is relocated. All measuring equipment is calibrated with calibration intervals provided. The calibration intervals were determined according to the frequency of use and the risk.

List available in 2_LIF_05_List_of_Equipment.pdf

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:

An internal Audit plan is established by the quality manager who ensures that all aspects and areas of the laboratory are covered. Approval of the plan is granted by the head of the institute.

f) Additional documents submitted:

N/A

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 ***InphA GmbH Institute for Pharmaceutical and Applied Analytics***, located at ***Emil-Sommer-Straße 7 28329 Bremen, Germany,*** 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