World Health Organization

20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

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>Gimopharm</td></tr>
<tr><td>Laboratory units/divisions</td><td>1, chemin de Saulxier
91160 Longjumeau
France</td></tr>
<tr><td colspan="2">Desk assessment details</td></tr>
<tr><td>Start and end dates of review</td><td>24 January 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, optical rotation, osmolality, water content, residual solvents, limit tests, tablet hardness, friability, disintegration, dissolution, viscosity, uniformity of dosage units (mass, content), viscosity, particle size (laser,) DSC, DRX</td><td>Refractive index, optical rotation, water content, residual solvents, particle size, Differential scanning calorimetry, DRX, COT, viscosity, heavy metals, Ash, sulfuric ash</td></tr>
<tr><td>Identification tests</td><td>HPLC (UV-VIS, DAD, fluorescence detection), TLC, GC, UV-VIS spectrophotometry, IR, AAS, fluorimetry, MS, MS-MS</td><td>HPLC (UV-VIS, DAD, fluorescence detection), TLC, GC, UV-VIS spectrophotometry, IR, AAS, fluorimetry</td></tr>
<tr><td>Assay, impurities and related substances</td><td>GC-TCD/FID/ MS-MS
HPLC-UV/PDA/MS-MS/ MS/Fluo/ RI /</td><td>GC-TCD/FID/ MS-MS
HPLC-UV/PDA/MS-MS/ MS/Fluo/ RI /</td></tr>
</table>
</td></tr>
</table>

		ELSD UPLC-MS, Ionic (Dionex)	ELSD, UPLC-MS, Ionic (Dionex) Specific studies on medicinal plants: - Heavy metals - Pesticides - Quality of vegetable oils - Identification and assay of active substances
	Microbiological analysis	Microbial limit tests, disinfectant efficacy, biocharge, preservatives efficacy test	Biocharge, microbial identification
	Bacterial endotoxin testing (BET)	Bacterial endotoxins test (LAL)	Bacterial endotoxins test (LAL)
	Stability testing	25°C/40% H.R. 25°C/60% H.R. 30°C/35% H.R. 30°C/65% H.R. 30°C/75% H.R. 40°C/25 %H.R. 40°C/75% H.R. Plus other on demand	25°C/40% H.R. 25°C/60% H.R. 30°C/35% H.R. 30°C/65% H.R. 30°C/75% H.R. 40°C/25 %H.R. 40°C/75% H.R. Plus other on demand
List of documents submitted	• Laboratory Information file ((LIF1608-1) – Containing general information on the laboratory, quality management system, document control, personnel, premises, equipment, materials, type of subcontracting and contact details, handling of samples, validation of analytical procedures, OOS process, stability and Microbiological testing. • Scope of manufacture and import authorisation issued by Agence nationale de sécurité du médicament et des produits de santé (ANSM) against Directives 2001/83/EC and 2001/20/EC (15 November 2016). • GMP certification issued by Agence nationale de sécurité du médicament et des produits de santé (ANSM) (certificate number HPF/FR/237/2015, valid until 6 March 2017) • Certificate of Registration issued by U.S. Food and Drug Administration (expiry 31 December 2017) • Appendice 1 Interlaboratory comparison protocole (2016-12-09) and Appendice 2 Interlaboratory comparison protocol 2 (2016-12-22) • 171PP089_GIMOPHARM_Longjumeau_C3 and 171PP089_GIMOPHARM_Longjumeau_Ic3 – Final inspection report ANSM 23-24 May 2017 (provided in French)		

	• Appendice 7 updated ANSM authorization certificate 2016 (Authroizations number M16/371) • Appendice 8 Agence nationale du medicament vétérinaire (ANSES) authorization certificate 2016	
Any documents missing?	All documents requested were provided	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last)**	
ANSM	Dates of inspection:	*23-24 May 2017*
	Type of inspection:	Routine
	Unit/Division inspected:	Manufacturing, importation and other
	Tests covered:	The inspection that had been conducted was detailed. The report provided did not individually identify the tests that were reviewed. All areas inspected were found satisfactory.
USFDA	Dates of inspection:	*5-6 June 2014*
	Type of inspection:	Initial
	Unit/Division inspected:	Not listed in the report.
	Tests covered:	The establishment inspection report was provided. There have been no subsequent FDA inspections of the facility.
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	The site has not been previously inspected by WHO.	
Brief summary of activities	Not Applicable	
General information about the QCL	GIMOPHRM was established in 1999 as a spin off company to Novartis (physicochemical analysis laboratory). GIMOPHARM is integrated in the group NOVOVITAE SAS. GIMOPHARM employees 11 laboratory staff, including detailed job descriptions and staff qualifications Subcontracted activities include • Particles counts are subcontracted at Eurofins 16, rue Clément Ader, 68127 Sainte-Croix-en-Plaine, France). Eurofins is an inspected pharmaceutical company (GMP) by French Authority.	

	• Pesticides analysis are performed chez Phytocontrole (180, rue Philippe Maupas, 30035 Nîmes, France).
Focus of the 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:
GIMOPHARM is a company providing analytical chemistry and quality control services as a GMP pharmaceutical facility certified by French national authority ANSM: Annexes 1 and 2: Authorization to perform pharmaceutical activities n° M15/120 May 15, 2015; certified GMP HPR/FR/237/ 2015, 28 October 2015.

Certificat De Conformité aux BPF d`un Fabricant issued by ANSM, certificate number HPF/FR/237/2015.

b) Laboratory information file (LIF):
The Laboratory Information file ((LIF1608-1) 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, handling of samples, validation of analytical procedures, OOS process, stability and Microbiological testing.

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

Name of Inspecting agency	***Dates of last inspection***	***Type of inspection***	***Outcome***
ANSM	23 – 24 May 2017	Re-inspection	Acceptable
ANSM	28 October 2015	Not available	Acceptable
USFAD	5-6 June 2014	Not available	Acceptable

d) Qualification, validation and calibration status of equipment:
An established process was available for the qualification, validation and calibration of equipment.

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 laboratory performs three types of internal audits per year in the following areas

- Equipment –equipment lists, labelling, qualification and follow-up book.
- Premises – security, cleanliness
- Quality system – revision and update of procedures, implementation of corrective and preventive actions and complaints.

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 ***Gimopharm, 1 chemin de Saulxier, 91160, Longjumeau, France*** is considered to be operating at an acceptable level of compliance with WHO GPPQCL guidelines.

This WHOPIR will remain valid for 3 years from the date of the last ANSM inspection or when another inspection is conducted by an agency against whose report the approval was based, 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