World Health Organization

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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
DESK ASSESSMENT OF CONTRACT RESEARCH ORGANIZATION (CRO)

Part 1	**General information**	
Company information		
Name of Company	Syneos Health Clinique Inc.	
Corporate address of Company	2500 Einstein Street | Quebec, Quebec, G1P OA2 Canada	
Inspected site		
Name & address of CRO if different from that given above	PharmaNet Canada, Inc. ("PharmaNet") (The name was applicable at the time of study) Québec site: 2500, rue Einstein Québec (Québec), Canada, G1P OA2 Tel : +1 418 527 4000 / +1 800 831 4001| F : +1 418 527 3456 syneoshealth.com Montréal site 5160, boul. Décarie, suite 800 Montréal (Québec), Canada, H3X 2H9 Tel : +1 418 527 4000 / +1 800 831 4001| F : +1 514 485 7501	
Desk assessment details		
Date of review	03 June 2019	
Product and study information covered by this desk assessment	Syneos clinical trial protocol number 110071 Ethinyl estradiol - desogestrel 0.03 mg - 0.15 mg tablet	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last)**	
Health Canada	**Dates of inspection:**	26-30 November 2018
	Unit:	Québec site
	Type of study covered:	BE-study, Oral solution
ANSM & AGES – Austrian Safety and Health Authority &	**Dates of inspection:**	31 July – 3 August 2018
	Unit:	Quebec site

French National Medicines Agency	**Type of study covered:**	Two BE-studies
MHRA	**Dates of inspection:**	10-14 April 2017
	Type of inspection:	Routine inspection
	Unit:	Quebec site
	Type of study covered:	An open label, balanced, randomized, two-treatment, two-sequence, tow-period, single oral dose crossover bioequivalence study of two tablets in normal healthy adult human subjects under fasting condition.
US FDA	**Dates of inspection:**	30 January – 3 Febuary 2017 (Bioanalytical part) 6-10 Febuary 2017 (Clinical part) 3-7 April 2017 (Clinical part)
	Type of inspection:	Routine BIMO Bioequivalence
	Unit:	Quebec site
	Type of study covered:	Bioequivalence
Part 3	**Summary of the CRO's activities**	
Date and conclusion of most recent WHO inspection	Not applicable since the site had not previously been inspected by WHO.	
Brief description of the site's activities	The Syneos Health Early Phase division, a member of Syneos Health since January 2018, is comprised of five sites: • Québec City, Québec, Canada; • Montréal, Québec, Canada; • Toronto, Ontario, Canada; • Princeton, New Jersey, USA; and • Miami, Florida, USA. The submitted CRO Master File applied to both the Québec City and Montréal sites. The Syneos Health Early Phase Québec (Syneos Health-EPQ), legally named Syneos Health Clinique Inc., is comprised of two sites located in Quebec and Montreal. The Quebec site consisted of Clinical, bioanalytical and clinical pharmacology departments. The Montreal site consisted of a Clinical department. The CRO offers early and late phase drug development services to the pharmaceutical, biopharmaceutical and generic drug industries. These services	

include the conduct of clinical studies, biostatistics, data management, sample analysis, project management, patient recruitment, safety, pharmacovigilance and regulatory and drug-development consultation.

The 25,000 sq. ft. e-designed clinical facility in Québec City has 248 beds in five clinical units. The Montréal site is a satellite facility mostly used for screening and return visits.

PharmaNet Canada Inc., a Contract Research Organization, was a member of the PharmaNet Development Group when the study **110071** was conducted. PharmaNet Canada Inc. services included Phase I clinical development, bioequivalence (BE), regulatory affairs, and bioanalytical laboratory analysis.

The facilities involved in the conduct of the study are listed below:

- Clinical facility PharmaNet at 5160 Décarie Boulevard, suite 800, Montréal (Québec), Canada with a 150-bed clinic. (site used for screening, study drug administration, return visits and post-study procedures)
- For some subjects, screening, return visits and post-study procedures after confinements, were performed at the clinical facility; PharmaNet at 2500 Einstein Street, Québec (Québec), Canada. (248 beds at the present time).
- The clinical laboratory facility, PharmaNet Clinical Laboratory used for laboratory tests performed during screening and post-study procedures was located at 5160 Décarie Boulevard, suite 800, Montréal (Québec), Canada.
- Scientific and regulatory affairs facility was located at 2500 Einstein Street, Québec (Québec), Canada.
- Bioanalytical facility was located at 2500 Einstein Street, Québec (Québec), Canada.
- Accordingly, subjects were enrolled, randomized and dosed on the clinical facility PharmaNet, 5160 Décarie Boulevard, suite 800, Montréal (Québec), Canada as mentioned in the final report.

In June 2011, PharmaNet Canada Inc. closed its 150-bed clinic located in Montréal to consolidate clinical operations in Québec City. Therefore, the information contained in the CROMF reflects the current use of both Québec and Montréal clinical facilities. A notice of name change was submitted dated 4 June 2019, indicating that PharmaNet Canada, Inc., changed its legal name to inVentiv Health Clinique, Inc. on 8 Mar 2013 which was merged with INC Research on 4 Jan 2018 and changed the name to Syneos Health, Inc.

	Accordingly, effective 1 Jan 2019, InVentiv Health Clinique inc. changed its legal name to Syneos Health Clinique Inc.

Abbreviations	Meaning
BE	Bioequivalence
CCs	Calibration Curve standards
CAPA	Corrective and preventive action
CROMF	CRO master file
GCP	Good clinical practices
GLP	Good laboratory practices
IMP	Investigational Medicinal Product
NC	Non-conformity
NRA	National regulatory agency
QA	Quality assurance
QC	Quality control
SOP	Standard operating procedure
SRA	Stringent regulatory authority

Part 4	Summary of the assessment of supporting documentation

a) Clinical trial license granted by the local authority:
The province of Québec, Canada did not have a licence program in place for clinical, bioanalytical and statistical facilities.

b) CRO Master File:
Early Phase Quebec Contract Research Organization Master File, version 01; dated 3 May 2019 together with following attachments were provided:

- Floor plan Quebec (Samples handling and waste)
- Floor plan screening Montreal
- EPQ Organizational chart without names
- CQ EP Organizational chart without names
- IRB membership list
- Quebec and Montreal Computer systems
- Clinical phase Study workflow
- Bioanalytical Production Phase study workflow

The Master File was arranged in accordance with the WHO guidelines for the preparation of a contract research organization master file, Annex 7, no 957, 2010.

c) List of all regulatory inspections performed in the last 3 years and their outcome:
The list of all regulatory inspections performed in the last 5 years was provided.

For details refer to the Part 2; “Summary of SRA/NRA inspection evidence considered”.

The CRO site in Quebec was also inspected by Standards Council of Canada (SCC) for full GLP inspection on 8 Nov 2018 and 7-9 Dec 2016 in the last 3 years. The full inspection reports and the outcome were respectively submitted.

Additionally, a list of Regulatory Agency inspections at the Montreal site from 2002 to 2009 was provided. The site was inspected by FDA, HPFB, INFARMED and ANVISA with positive outcome.

d) Copy of any warning letter, or equivalent regulatory action, issued by any authority for the site:
The CRO has not received a warning letter or any equivalent regulatory action at the time of this desk review.

e) Confirmation by the senior quality assurance representative that a full self-inspection or external audit dedicated to the studies conducted for WHO product(s) has been performed and all matters dealt with:
A confirmation letter for self-inspections, stipulating that the clinical and statistical portions of the study were audited between February 28, 2011 and July 15, 2011, was provided by QA Director signed on 3 May 2019.

f) IRB/IEC clinical trial approval (including the approved protocol, the amended protocol and consent form):
The applicable protocol, together with the eMC Medicines Compendium for Marvelon and ICD (French & English) were approved by Quebec Institutional Review Board of Institutional Review Board Services. At the time of study, the CRO was doing business as PharmaNet.

g) A list of any study failures in the last three years:
The CRO maintains a list of all studies conducted without information about the outcome of the studies, since the pass/fail status of BE-studies are considered as proprietary information by the concerned sponsors.

h) Additional documents submitted:
- Inspection report relating to the inspection of Class A precursor by Health Canada on February 2017, and the respective response.
- Inspection report related to controlled substances by Health Canada on April 2016, and the respective response.

Part 5	Conclusion – Desk assessment outcome

Based on the previous WHO inspections and on the GCP/GLP/BE evidence received and reviewed, it is considered that a desk assessment is acceptable in lieu of a WHO onsite inspection. The following sites are considered to have performed the studies submitted to WHO PQT under an acceptable level of compliance with WHO guidelines.

Syneos Health Clinique Inc.

Quebec site:
2500, rue Einstein
Québec (Québec), Canada, G1P OA2

Montréal site
5160, boul. Décarie, suite 800
Montréal (Québec), Canada, H3X 2H9

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. Guidance for organizations performing in vivo bioequivalence studies. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 9. ***Short name: WHO BE guidance*** http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex09.pdf

2. Good clinical laboratory practice (GCLP), WHO on behalf of the Special Programme for Research and Training in Tropical Diseases. Geneva, 2009
Short name: WHO GCLP
https://www.who.int/tdr/publications/documents/gclp-web.pdf

3. Guidelines for good clinical practice for trials on pharmaceutical products. WHO Technical Report Series, No. 850, 1995 (pp. 97–137). ***Short name: WHO GCP***
http://apps.who.int/medicinedocs/en/d/Js5516e/19.11.html

4. 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

5. Handbook – Good Laboratory Practice (GLP): quality practices for regulated non-clinical research and development – Annex I: The OECD Principles on GLP, 2nd ed., 2009. ***Short name: OECD GLP***
   http://www.who.int/tdr/publications/documents/glp-handbook.pdf

6. Standards and operational guidance for ethics review of health-related research with human participants. Guidance Document. Geneva, World Health Organization, 2011. ***Short name: WHO Ethics Committee Guidance***
   https://www.who.int/ethics/publications/9789241502948/en/

7. 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 storage and transport guidance*** or ***TRS 961 Annex 9***
   http://apps.who.int/medicinedocs/documents/s18683en/s18683en.pdf

8. Guidelines for the preparation of a contract research organization master file, WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 7.
   Short name: WHO CROMF Guidelines or ***TRS No. 957, Annex 7***
   http://www.who.int/medicines/publications/44threport/en/

9. Glove use information leaflet, Patient Safety, Save lives clean your hands. Geneva, World Health Organization, 2009 (revised). ***Short name: Glove use information leaflet***
   http://www.who.int/gpsc/5may/Glove_Use_Information_Leaflet.pdf

10. WHO 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: Annex 5 WHO GDRMP guidance
    http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf