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	Pharma Medica Research Inc. (PMRI)	
Corporate address of Company	6100 Belgrave Road Mississauga, Ontario L5R 0B7 Canada	
Inspected site		
Name & address of CRO if different from that given above	**Bioanalytical site:** As mentioned above **Clinical site:** 4770 Sheppard Ave East Toronto, Ontario M1S 3V6, Canada	
Desk assessment details		
Date of review	26 March 2020	
Product and study information covered by this desk assessment	Study no. 2015-3826 Ethinylestradiol / Levonorgestrel Tablet, Film-coated 0.03mg/0.15mg Study no. 2015-3826 Ethinylestradiol / Levonorgestrel + Placebo Tablet, Film-coated + Tablet, Film-coated 0.03mg/0.15mg + 0mg	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last)**	
US FDA	Dates of inspection:	January 2020
	Type of inspection:	Clinical and Analytical Bioresearch Monitoring (BIMO) Inspection
	Unit:	Bioanalytical laboratory and clinical site
MHRA - UK	Dates of inspection:	30 Apr – 4 May 2018
	Type of inspection:	Bioequivalence Good Clinical Practice (GCP) Inspection
	Unit:	Bioanalytical laboratory and clinical site
	Type of study covered:	Bioavailability study
Health Canada	Dates of inspection:	19 – 23 March 2018
	Type of inspection:	Bioequivalence inspection

	Unit:	Bioanalytical laboratory and clinical site
	Type of study covered:	Bioequivalence
	Study/investigational product details:	Amoxicillin 500 mg capsules
US FDA	Dates of inspection:	11 -15 Sep 2017
	Type of inspection:	FY2017 analytical inspection
	Unit:	Bioanalytical laboratory
	Type of study covered:	Bioequivalence studies
	Study/investigational product details:	Canagliflozin tab 300 mg Dimethyl fumarate DR capsules 240 mg Methylergonovine maleate USP tab 0.2 mg Canagliflozin and Metformin tab 150 mg / 1000 mg Abiraterone acetate tab 250 mg
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	Not applicable	
Brief description of the site's activities	PMRI was founded in Toronto, Canada in 1997 and is a privately held CRO. The organization is focused on conducting early phase clinical trials and offers full services in-house. PMRI have routinely been audited by various regulatory agencies around the world. The facilities are narcotic & controlled substance / cannabis licensed, allowing the CRO to conduct studies with these compounds which require special handling. In addition, the bioanalytical laboratory is Biosafety Level (BSL) 2 and GLP licensed allowing for analysis of pre-clinical samples.	
Additional product(s) and clinical trial(s) to be covered by this desk assessment:	Not applicable	

Abbreviations	Meaning
CCs	Calibration Curve standards
CAPA	Corrective and preventive action
CROMF	CRO master file
GCP	Good clinical practices
GLP	Good laboratory practices
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:
Formal GCP Certificates / Licences are not required to be issued by government regulatory agencies.

b) CRO Master File:
The CRO Master File was provided in accordance with WHO Technical Report Series, No. 957, 2010, i.e. Annex 7 Guidelines for the preparation of a contract research organization master file.

c) List of all regulatory inspections performed in the last 3 years and their outcome:
A list of all regulatory inspections was provided in the CRO Master File. For details on the inspection performed in the last 3 years, refer to part 2 of this report.

d) Copy of any warning letter, or equivalent regulatory action, issued by any authority for the site:
There had been no warning letters or equivalent regulatory actions issued by any authority for the two sites (Clinic and Bioanalytical Lab).

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 statement was issued on 19 Jun 2015, confirming that a full QA self-inspection / internal audit was completed by QA.

f) IRB/IEC clinical trial approval (including the approved protocol, the amended protocol and consent form):
The applicable IRB approvals for the study in the scope of inspection were provided and reviewed.

g) A list of any study failures in the last three years:
A list of study failure, including 19 studies in the last three years was provided. There were no study failures for the molecules in the scope of this desk review, alone or in combination, in the last three years.

h) Additional documents submitted:

The following certificates were provided:

- Standards Council of Canada – this was for GLP compliance for Bioanalytical Laboratory
- ANVISA – Clinic and Bioanalytical Services – this was for issuance of certification
- Health Canada – Controlled Drugs and Substances License – for Bioanalytical Laboratory
- Health Canada – Controlled Drugs and Substances License – for Clinic
- Health Canada – Precursor License – for Bioanalytical Laboratory
- Health Canada – Cannabis Drug License –for Bioanalytical Laboratory
- Health Canada – Cannabis Analytical Testing - for Bioanalytical Laboratory
- Health Canada – Cannabis Drug License –for Clinic
- Bioequivalence Centre Approved by GCC

Part 5	**Conclusion – Desk assessment outcome**

Based 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 site ***Pharma Medica Research Inc.*** located at ***6100 Belgrave Road Mississauga, Ontario L5R 0B7 Canada*** is considered to have performed the studies submitted to WHO PQT under an acceptable level of compliance with applicable WHO 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. 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