World Health Organization

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

Part 1	**General information**	
Company information		
Name of Company	Raptim Research Pvt. Ltd.	
Corporate address of Company	A-226 / 242 / 213, TTC Industrial Area Near Mahape Depot, Mahape MIDC Navi Mumbai - 400710 India Tel.: +91 22 27781889 / 27781887 Email: contact@raptimresearch.com	
Inspected site		
Name & address of CRO	As above	
Desk assessment details		
Date of review	16 July 2020	
Product and study information covered by this desk assessment	- Study no. BE/19/100 Darunavir and Ritonavir Tablets 800 mg/100 mg - Study no. BE/17/360 Dolutegravir (Sodium)/Lamivudine/Tenofovir disoproxil fumarate tablet, film-coated 50mg/300mg/300mg - BE/17/138 Dolutegravir (Sodium)/Lamivudine/Tenofovir disoproxil fumarate tablet, film-coated 50mg/300mg/300mg - BE/18/587 Artemether/Lumefantrine Tablet 20mg/120mg - Study no BE/18/012 Pyrimethamine/Sulfadoxine Tablet, Dispersible 25mg/500mg	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last)**	
NPRA, Malaysia	Dates of inspection:	21 - 25 Oct 2019
	Type of inspection:	Full inspection
	Unit:	Clinical (A-226) & bioanalytical sites (A-242)

	Type of study covered:	Bioequivalence study
US FDA, USA	Dates of inspection:	9 – 19 September 2019
	Type of inspection:	FY2019 analytical BIMO program inspection
	Unit:	Bioanalytical site
	Type of study covered:	Bioequivalence study
US FDA, USA	Dates of inspection:	27-29 May 2019
	Type of inspection:	Preapproval data validation inspection
	Unit:	Clinical site (A-226)
	Type of study covered:	Bioequivalence study
BfArM, Germany & HPRA, Ireland	Dates of inspection:	25-28 Mar 2019
	Type of inspection:	The inspection was to be conducted following a request from Federal Institute for Drugs and Medical Devices (BfArM), Germany in connection with evaluation of Marketing Authorization application for Levothyroxine.
	Unit:	Screening, Clinical and bioanalytical facilities
	Type of study covered:	Bioequivalence study
US FDA, USA	Dates of inspection:	18-22 Mar 2019
	Type of inspection:	FY2019 analytical BIMO program inspection
	Unit:	Bioanalytical site
	Type of study covered:	Bioequivalence studies
MHRA, UK	Dates of inspection:	24 – 28 September 2018
	Type of inspection:	Bioequivalence Good Clinical Practice (GCP) Inspection
	Unit:	Screening, Clinical and bioanalytical facilities; i.e. (A-226/A-242/A213)
	Type of study covered:	Bioequivalence studies
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	The inspection of Raptim Research Ltd was last performed by WHO PQT during 23-27 October 2017. This was the first inspection of this site. It was found compliant with three critical and 8 major deficiencies, as well as four listed as Others. All observations were adequately addressed in the respective CAPA plan	
Brief description of the site's	The facility had the capacity to perform bioequivalence/bioavailability and in-vitro studies in healthy subjects/patients.	

activities	Raptim offers services supporting Pharmacokinetic studies (BA/BE), IVRT, IVAD, Pharmacodynamic Studies and Phase II & III trials and Dermatology studies to Pharmaceutical industry and/or to CROs.
Areas inspected during the last WHO inspection	Clinical and bioanalytical part of studies in the scope of inspection.
Out of scope and restrictions (last WHO inspection)	N/A
WHO product(s) and clinical trial(s) covered by the last WHO inspection	- Lamivudine tablets 300mg - Sofosbuvir tablets 400 mg
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
QCL	Quality control laboratory
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:
Permissions and Licences to import new drugs for conducting bioequivalence studies in the scope of this desk assessment were provided.

b) CRO Master File:
A Quality Manual dated 1 Feb 2020 was submitted. The QM was arranged in accordance with WHO Technical Report Series, No. 957, 2010 Annex 7 for Guidelines for the preparation of a contract research organization master file and could be sufficiently reflected as CRO Master File.

c) List of all regulatory inspections performed in the last 3 years and their outcomes:
A list of all regulatory inspection performed in the last 3 years was provided. For more details, 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 was no warning letter, or any equivalent regulatory action issued by any authority to Raptim Research Pvt. Ltd. A declaration was digitally signed by QA-Head on 4 Jul 2020.

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:

An audit certificate for all studies in the scope of this desk assessment review was issued and respectively signed and dated by the QA-Head.

f) IRB/IEC clinical trial approval (including the approved protocol, the amended protocol and consent form):

Following documents were submitted to the respective Ethics Committees for approval:

1. Study Protocol(s)
2. Subject Information Sheet and Informed Consent Form (in English and other applicable languages)
3. Undertaking of Clinical Investigator
4. Curriculum vitae of Clinical Investigator
5. Curriculum vitae of Clinical Co-Investigators
6. Subject Compensation Break-up
7. Prescribing information of Reference product
8. Insurance copy

The applicable IEC trial approval letters of following studies were provided.

g) Additional documents submitted:

- A joint inspection report issued by CDSCO in relation with an application for grant of registration of Bioavailability/ Bioequivalence Study Centre of M/s Raptim Research Ltd., together with the respective CRO response and the registration certificate as Form CT-09.
- NABL Certificate of accreditation in accordance with ISO 15189:2012 on Medical Testing; issued 9 Jul 2019 and valid until 8 Jul 2021.
- Copy of the Establishment Inspection Reports (EIRs) for the inspections conducted at the premises, Raptim Research Ltd., A-226 Near Mahape Depot, TTC Industrial Area, Navi Mumbai, Maharashtra, 400 701, India, by the United States Food and Drug Administration (FDA) from January 19 - 24, 2017 and November 6 - 10, 2017.
- Data related to concentration, timepoints and PK parameters of studies BE-18-587 & BE-17-360.

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 site ***Raptim Research Pvt. Ltd*** located at ***A-226/ 242 / 213 Near Mahape Depot, TTC Industrial Area, Navi Mumbai, Maharashtra, 400 710, India*** is considered to have performed the studies submitted to WHO PQT under an acceptable level of compliance with 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 WHO guidelines referenced in this inspection report

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 or ***TRS996 Annex 9***
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. 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

5. 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/

6. 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

7. 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/

8. 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

9. 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: TRS 996 Annex 5 or ***WHO GDRMP guidance***
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf

10. Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability. Republication of multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability. WHO Technical Report Series No. 992, Annex 7 with a new appendix 2. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-first Report Geneva, World Health Organization, 2017 (WHO Technical Report Series, No. 1003), Annex 6. ***Short name: TRS 1003 Annex 6***
http://apps.who.int/medicinedocs/documents/s23245en/s23245en.pdf

11. Good chromatography practice. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 4.
Short name: WHO TRS No. 1025, Annex 4
https://www.who.int/publications-detail/978-92-4-000182-4

12. 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