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

Part 1	**General information**
Company information	
Name of Company	RA Chem Pharma Limited, Clinical Research & Biosciences Division
Corporate address of Company	Plot No. 26 & 27, Technocrat Industrial Estate (TIE) Balanagar Hyderabad, 500037 India
Inspected sites	
Name & address of sites where the studies in the scope of this desk review assessment took place	As above
Desk assessment details	
Date of review	17 September 2020
Product and study information covered by this desk assessment	Study no: 052-17 - (Only clinical part) Dolutegravir Tablets 50 mg Study no: 016-19 - (Only clinical part) Dolutegravir, Lamivudine & Tenofovir Disoproxil Fumarate Tablets 50/300/300 mg Study no: 195-18 Efavirenz, Lamivudine and Tenofovir disoproxil Fumarate Tablets 400mg/300mg/300mg Study no: 034-19 - (Only clinical part) Abacavir and Lamivudine Dispersible Tablets 120/60 mg Study no: 051-17 Ethambutol Hydrochloride Dispersible Tablets 100 mg

Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent)**	
US FDA, USA	Dates of inspection:	11-15 Nov 2019
	Type of inspection:	FY2020 analytical BIMO program inspection from the Office of Study integrity and Surveillance under Compliance Program 7348.004
	Unit:	Bioanalytical facility
	Type of study covered:	Bioequivalence
BPFK, Malaysia	Dates of inspection:	9-13 Sep 2019
	Type of inspection:	GCP & GLP inspection – Surveillance
	Unit:	Clinical & Bioanalytical units
	Type of study covered:	Bioequivalence
US FDA, USA	Dates of inspection:	22-26 April 2019
	Type of inspection:	CDER's Premarket Original BIMO Inspection
	Unit:	Clinical Unit
	Type of study covered:	Bioequivalence
GCC, Gulf Health Council	Dates of inspection:	18-19 April 2018
	Type of inspection:	GCP and GLP inspection
	Unit:	Clinical and Bioanalytical Units
	Type of study covered:	Bioequivalence
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	RA Chem was previously inspected on 12-16 Feb 2018. Four (4) major findings were identified in the inspection report which were addressed in the respective CAPA plan. The CRO was considered GCP-compliant.	
Brief description of the site's activities	The CRO consists of both clinical, bioanalytical and statistical units, with a registration and screening area, archiving facility and total 114 beds spread across five independent clinics. The facility is accredited by national regulatory authorities for conduct of BA/BE studies (all phases) on healthy population as well as patients, in accordance with GCP and applicable GLP principles. The type of service that CRO provides to its sponsors are (but not limited to): - Medical writing (Protocol, lCD, CRFs, Ethics committee approval, Integrated/clinical report preparation according to ICH GCP E6)	

	- Clinical phase execution (both on Healthy and Patient Based Population) - Bioanalytical analysis - Pharmacokinetic and Statistical Services - eCTD submissions - Quality Assurance - Clinical Trials co-ordination - Regulatory Submission
Areas inspected during the last WHO inspection	Both clinical and bioanalytical facilities were inspected.
WHO product(s) and clinical trial(s) covered by the last WHO inspection	**Study no. 053-16-WHO** Artesunate, Amodiaquine Bilayer 100 mg / 270 mg (Artesunate 200 mg +Amodiaquine 540 mg) **Study no. 096-16-WHO** Moxifloxacin Dispersible tablets 100 mg **Study no. 039-15-WHO** Sofosbuvir 400 mg Tablets

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:

An application for conducting of each bioequivalence study and import license of the respective products was submitted to CDSCO. The applicable approval letters / import licenses were accordingly issued and provided.

b) CRO Master File:

A Site Master File with version no 11 was provided. The Site Master File 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.

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

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:

As per the attachment-2 of the Site Master File dated 27 Aug 2020, the CRO was inspected 19 times since January 2013, by various regulatory bodies and all the inspections were successfully closed.

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 Quality Assurance Authentication was issued for each study to verify that audits had been conducted by the Quality assurance unit of the various stages of the study. It was certified that QA-Head and the respective team had cross checked the reports, as well as the conduct of the project, against the raw data generated. The QA-Head had declared that this study was audited at various phases for compliance to protocol and applicable Standard Operating Procedures and the results reported in study report accurately reflect the raw data of the study.

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

The studies were approved by MAARG Independent Ethic Committee. The approval letters were provided.

Following documentation were submitted & approved by the IEC:

1. CV of Principal Investigator
2. Principal Investigator's undertaking
3. Investigator's Agreement with the Sponsor (In Protocol Investigator declaration and Sponsor approval).
4. Protocol, as well as applicable amendments
5. ICD, in English and other applicable languages
6. Drug Literature:
7. Proposed Method of Volunteers Recruitment
8. A copy of Medical Insurance for the Subjects

The name and qualification of the members of the Ethics Committee presented and voted in the meeting were recorded in the approval letters.

g) A list of any study failures in the last three years:

A list of any study failures in the last three years was provided. The list was signed and dated 28 Aug 2020.

h) Additional documents submitted:

Following additional documentation was submitted and reviewed:

- CRO registration letter issued by CDSCO on 9 Sep 2020
- PK parameters & plasma concentration data for study no. 195-18 & study no. 051-17

Part 5	Conclusion – Desk assessment outcome

Based on the previous WHO inspections and 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 ***RA Chem Pharma Limited, Clinical Research & Biosciences Division*** located at ***Plot No. 26 & 27, Technocrat Industrial Estate (TIE), Balanagar, Hyderabad, 5000 37; 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 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 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