EDA-GCP Public Inspection Report (PIR) of Clinical Trial Site

Part 1	**General Information**
Clinical medical research site details	
CT site information	
Name of CT site	MASRI CRC, Faculty of Medicine, Ain Shams University
Address of inspected CT site	Abbassia, Cairo, Egypt
Inspection details	
Dates of inspection	20 October 2024
Type of inspection	Routine
Introduction	
General information about the sponsor and CT site	- The inspected site is a Clinical Trial Site (**MASRI CRC, Faculty of Medicine, Ain Shams University**) that conducts clinical studies for the sponsor (**Roche Egypt LLC**) - PI name: **Prof. Dr. Magd Zakaria** - Activities include participant recruitment, clinical conduct, sample collection, safety monitoring, and data documentation.
Brief report on inspection activities undertaken	
Scope and limitations	
Areas inspected	- Clinical operations (screening, dosing, follow-up) - Informed Consent Process - Investigational Medicinal Product (IMP) management - Bioanalytical / laboratory facilities (if applicable) - Source documents and Case Report Forms (CRFs) - Archiving and documentation system - Quality management system
Out of scope	Pharmacy / IMP storage area as the IMP was returned to the sponsor
Inspected Clinical medical research	The inspection focused on the following study: - Study Title: Single-arm, Open-label, 4-year study to evaluate the effectiveness and safety of Ocrelizumab treatment in patients with progressive multiple sclerosis -Protocol Number: MN39159 -Phase: III - EDA initial approval date: 20\09\2022
Type of IMP	Biological Monoclonal antibody (Ocrelizumab)
Part 2	

1. Facilities and equipment system	
.1. Facilities and Trial Conduct	-The inspection included a tour of the site had the facilities, equipment, and infrastructure to support clinical trial conduction which were generally adequate for trial conduct. -Dedicated examination, consultation, and procedure rooms were available and operational for study-related activities. -A dedicated investigational medicinal product (IMP) storage room was available, and the IMP storage conditions were maintained in accordance with the Pharmacy Manual. -Calibration certificates for study equipment, used during the conduct of the clinical trial, including the IMP refrigerator, temperature data loggers, electrocardiograph (ECG), DC shock device, sphygmomanometer, weight scale, and volumetric pump, were reviewed to verify that the equipment was appropriately calibrated during the conduct of the clinical trial.
1.2. Computerized system	Electronic data capture, as eCRF and randomization systems were in use.
2. Pharmaceutical Quality System	
2.1. Quality Management System	-The site has established a Quality Management System supported by SOPs governing trial conduct, documentation, safety reporting, and IMP handling to ensure compliance with GCP principles, ethical standards, and regulatory requirements. The system aims to ensure participant safety, rights, and data integrity.
2.2. SOPs and Documentation	-Standard Operating Procedures (SOPs) and essential clinical trial documentation were reviewed during the inspection to verify their availability, implementation, and compliance with the approved protocol, GCP, and applicable regulatory requirements. - The documentation reviewed included the approved protocol and amendments, Investigator's Brochure (IB), regulatory and ethics committee approvals, confidentiality agreements, insurance certificate, clinical trial agreement, investigator and study personnel qualifications, Good Clinical Practice (GCP) training records, delegation log, approved informed consent forms (ICFs), participant screening and identification logs, participant source records, case report forms (eCRFs), investigational medicinal product (IMP) shipment, receipt, dispensing, accountability and destruction records, laboratory accreditation certificates, calibration certificates, monitoring reports, protocol

	deviation records, progress reports, and other study-related essential documents.
2.3. Deviation Management	-Deviation management were reported and handled according to the site Standard Operating Procedures (SOPs).
2.4. CAPA System	-The inspection findings were communicated to the sponsor and the clinical trial site for corrective and preventive action. Observations related to source documentation, monitoring documentation, and protocol compliance were identified during the inspection. In response, the sponsor submitted a CAPA plan addressing each observation, including correction of study documentation, updates to monitoring records, protocol-specific training, refresher training on source documentation in accordance with ALCOA principles, and training on the completion of participant-reported outcome (PRO) questionnaires. The submitted CAPA was reviewed by the Egyptian Drug Authority (EDA) and was considered acceptable.
3. Ethics and participant Protection	
3.1. Informed Consent Process	-The informed consent process was reviewed and assessed through the review of the approved informed consent forms and participant source records, to verify that the informed consent had been obtained using the approved Informed Consent Forms (ICFs) as follows: • Main ICF V3.1 (19\10\2021), V4 (8\11\2021), and Addendum 1 (V1. 16\01\2022). • ICF for authorization for use and disclosure of "Pregnancy outcome and infant health Information of the first year of life V2 (25\05\2021). • Dry Run MRI procedure and to allow images to be sent to central analysis center V2 (08\03\2020) • ICF for obtain optical coherence tomography (OCT) images and for the release of images for Certification purposes V1 (17\03\2020). - The approved versions of the ICFs were used and documented prior to the performance of study-related procedures, in accordance with the approved protocol, Good Clinical Practice (GCP), and applicable regulatory requirements. -One observation was identified during the inspection. A discrepancy was noted in the source documentation of the informed consent process, where an incorrect date had been recorded for the participant's informed consent. In addition, documentation of participant re-consenting was not reflected in the corresponding monitoring follow-up report. In response, the site corrected the source documentation, the monitoring records were

	updated to reflect the re-consenting activity, and refresher training was provided to the study team and clinical research associates (CRAs) on source documentation and ALCOA-C principles. The submitted CAPA was reviewed and accepted by the EDA.
3.2. Ethics Committee Approval	Approvals from IRB/IEC were available, date of approval: • **IRB approval** on: 22/01/2019 • **MOH approval** on: 31/10/2018
3.3. Participant Safety	- Participant safety was assessed during the inspection through review of participant source records, informed consent documentation, eCRFs, medical records, and other study-related essential documents - including safety-related assessments such as physical examinations, concomitant medications, and participant-reported outcome (PRO) questionnaires, as applicable to the study protocol - to verify that participant rights, safety, and well-being were protected in accordance with the approved protocol, GCP, and applicable regulatory requirements. - The inspection identified a documentation deficiency in accordance with ICH E6R2 related to delayed documentation of physical examinations, incomplete recording of concomitant medications, and missing participant questionnaires due to internet connectivity issues. These observations did not indicate deficiencies affecting participant safety. CAPA were implemented by the site, including correction of study records and protocol-specific refresher training for the study team, and the submitted CAPA was reviewed and accepted by the EDA.
4. Personnel and Training	
4.1. Training and qualifications	- Roles and responsibilities of study personnel were clearly defined. - The qualifications and training of the investigator and study personnel were reviewed during the inspection verified that delegated staff were appropriately qualified and trained to perform their assigned trial-related responsibilities. - The inspection included verification of curriculum vitae (CVs), GCP training records, protocol-specific training documentation, delegation of responsibilities log, and other relevant personnel qualification records.
5. Investigational Product (IMP) Management	
5.1. IMP handling	-IMP documentation included IMP shipment, receipt, dispensing, accountability, and destruction records, as well as certificates of analysis and other relevant essential records related to IMP management was verified to comply with the approved protocol, GCP, and applicable regulatory requirements.

	-As the investigational medicinal product had been returned to the designated vendor for destruction prior to the inspection, the pharmacy and IMP storage area were outside the scope of the inspection. Based on the documentation reviewed.
6. Clinical Trial Conduct	
6.1. Protocol Compliance	- The clinical trial was conducted in accordance with the approved protocol, GCP, and applicable regulatory requirements. - Protocol compliance was assessed through the review of the approved protocol (Version: 5.0, dated: 28/09/2021), participant source records, eCRFs, ICFs, monitoring documentation, and other study-related essential documents.
6.2. Source Data and CRFs	- Source data and eCRFs were reviewed during the inspection to verify the completeness, accuracy, consistency, and traceability of clinical trial data in accordance with the approved protocol, GCP, and applicable regulatory requirements. - Comparison of participant source records with the corresponding eCRFs and monitoring documentation was verified for the accuracy and completeness of the recorded study data. - Deficiencies were identified in source documentation and monitoring records, including delayed documentation of participant re-consenting and physical examination and the omission of these activities from the corresponding monitoring follow-up report, as well as an incorrect date recorded in the source documentation for the informed consent process. Incomplete recording of concomitant medications, missing participant questionnaires due to internet connectivity issues, and incomplete documentation of questionnaire records. - In response, the sponsor and the clinical trial site implemented corrective and preventive actions, including correction of source documentation, updating monitoring records, protocol-specific training, refresher training on source documentation in accordance with ALCOA principles, and training on protocol schedule of assessments and participant-reported outcome (PRO) completion. The submitted CAPA was reviewed and accepted by the EDA.
6.3. Delegation of Duties	- The Site Signature and Delegation of Responsibilities (Authorization) Log to verify that trial-related responsibilities were appropriately assigned to study personnel were reviewed. -The review also included curriculum vitae (CVs), GCP training records, protocol-specific training documentation, and other relevant personnel

	qualification records confirmed that delegated responsibilities were supported by appropriate qualifications and training.

7. Laboratory and Bioanalytical Activities (if applicable)

- An external central and local Laboratories were used for analysis of bio samples.
- Laboratory activities were assessed through review of the procedures relevant to the conduct of the clinical trial.
- The inspection verified the laboratory accreditation certificates, laboratory manuals, and other laboratory related essential records to assess compliance with the approved protocol, GCP, and applicable regulatory requirements.
- Sample handling and analysis were reviewed.

8. Safety Reporting (SAE)

- SOPs for SAE reporting were available and verified as part of the verification of essential clinical trials records.
- Based on the inspection activities performed, no observations related to safety reporting were identified during the inspection.

Part 3	**Inspection outcome**

- Based on the reviewed documentation, inspected facilities, and observations identified during the inspection: The clinical trial site was considered to be operating at an acceptable level of compliance with GCP guidelines and applicable regulatory requirements. As All identified deficiencies were communicated to the site and the CAPA were implemented to address the observations.
- This EDA-GCP-PIR remains valid until the next inspection, provided no critical findings, safety concerns, or regulatory actions arise.

Part 4	**List of national Laws and GCP Guidelines referenced in the inspection report**

1. Law of Regulating Clinical Medical Research no.214/2020.
2. Prime Minister's Decree No. 927 of 2022 On Promulgating the Executive Regulation of Law on Regulating Clinical Medical Research Promulgated by Law No. 214 of 2020
3. EDA Chairman Decree No.111 for 2022.
4. Guideline for Good Regulatory Oversight of Clinical Trials by Egyptian Drug Authority "EDREX.GL.Bioinn.006".
5. Guideline for Good Clinical Practice ICH E6r2.
6. Declaration of Helsinki
7. WHO Handbook for Good Clinical Research Practice (GCP) -Guidance for Implementation

Abbreviation

AE	Adverse Event
ALCOA	Attributable, Legible, Contemporaneous, Original, Accurate

CAPA	Corrective and Preventive Action
CRA	Clinical Research Associate
CRF	Case Report Form
CRC	Clinical Research Center
CT	Clinical Trial
CV	Curriculum Vitae
ECG	Electrocardiograph
EDA	Egyptian Drug Authority
GCP	Good Clinical Practice
IB	Investigator Brochure
ICF	Informed Consent Form
ICH	International Conference of Harmonization
IMP	Investigational Medicinal Product
IRB/IEC	Institutional Review Board / Ethics Committee
MOH	Ministry of Health
MRI	Magnetic Resonance Imaging
OCT	Optical Coherence Tomography
PI	Principal Investigator
PIR	Public Inspection Report
PRO	Patient reported outcome
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
WHO	World Health Organization

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