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	National Hepatology Tropical and Medicine Research Institute "NHTMRI"_Site (EG10002)
Address of inspected CT site	Kasr Al Ainy Street, Cairo, Egypt
Inspection details	
Dates of inspection	17 February 2025
Type of inspection	Routine
Introduction	
General information about the sponsor and CT site	- The inspected site is a Clinical Trial Site (**National Hepatology Tropical and Medicine Research Institute "NHTMRI")** that conducts clinical studies for the sponsor (**Janssen Scientific and Medical Affairs**) - PI name: **Prof. Dr. Kamal El Atrebi** - 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 · Pharmacy / IMP storage area · Source documents and Case Report Forms (CRFs) · Archiving and documentation system · Quality management system
Out of scope	Not defined
Inspected Clinical medical research	The inspection focused on the following study(ies): - Study Title: A Phase 3, randomized, placebo-controlled, parallel group, multicenter study to evaluate the efficacy and safety of Guselkumab in participants with fistulizing, peri-anal Crohn's disease "Fuzion CD" - **Protocol Number:** CNTO1959CRD3005 - **Phase:** III - **EDA Initial approval date:** 13\08\2023
Type of IMP	Biological Monoclonal antibody (Guselkumab)

Part 2	
1. Facilities and equipment system	
1.1. Facilities and Trial Conduct	- The trial site had the facilities, equipment, and infrastructure required to support the conduct of the clinical trial. The inspection verified the availability and suitability of the study facilities and equipment, with the observations noted below. - Dedicated examination, consultation, and procedure rooms were available and operational for study-related activities. - Calibration certificates for the weight balance, sphygmomanometer, and centrifuge used for sample processing were available; - Study files were stored in a secure, access-controlled, fire- and water-resistant cabinet. - A dedicated investigational medicinal product (IMP) storage room was available, and the IMP storage conditions were maintained in accordance with the Pharmacy Manual
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) governing clinical trial activities were available and implemented. - Essential documents were available and reviewed, including source documents, ICFs, eCRF, approvals, contracts, insurance, CVs, GCP certificates, IB, safety reports, progress reports, IMP records, and calibration records.
2.3. Deviation Management	-Deviation management procedures were handled according to the site Standard Operating Procedures (SOPs). - Protocol deviations and Good Clinical Practice (GCP) non-compliances identified during the inspection were documented as inspection observations and communicated to the sponsor for corrective and preventive action (CAPA).
2.4. CAPA System	-A corrective and preventive action (CAPA) system was established at the site. - CAPA responses for the findings identified during this inspection were submitted by the site, reviewed and evaluated by the Egyptian Drug

	Authority (EDA) inspectors, and updated following EDA requests for clarification and submission of additional deliverables. The identified findings were appropriately addressed through corrective and preventive actions, and the final CAPA was reviewed by EDA and considered acceptable.
3. Ethics and participant Protection	
3.1. Informed Consent Process	-The informed consent process was reviewed and found to be compliant with Good Clinical Practice (GCP) and applicable regulatory requirements, and no deficiencies were identified. - Approved Informed Consent Forms (ICFs) were available and used and that informed consent was obtained from each participant prior to the performance of any study-related procedures.
3.2. Ethics Committee Approval	Approvals from IRB/IEC were available, date of approval: • **IRB approval** on: 06\09\2022 • **MOH approval(s)** on: 31/05\2023
3.3. Participant Safety	-Safety monitoring procedures were in place. Participant safety measures were reviewed during the inspection, including participant follow-up, adverse event documentation, emergency procedures, and investigational medicinal product (IMP) management as they relate to participant protection. Participant safety was generally compliant. -No SAE reporting during the study conduction till this inspection date. with minor deficiencies observed.
4. Personnel and Training	
4.1. Training and qualifications	-Roles and responsibilities of study personnel were clearly defined. Delegation records, personnel qualifications, and curriculum vitae were available and reviewed during the inspection. -GCP training records and protocol-specific training were available and reviewed. -Current curriculum vitae (CVs) for the Principal Investigator, Co-Investigator(s), Pharmacist, Site Coordinator, Pediatric Cardiologist, and Laboratory Nurse was available and appropriately filed in the Investigator Site File (ISF). - The training system was generally adequate which demonstrated that investigators and delegated study personnel had received the training necessary to perform their assigned trial-related activities that support the conduct of the clinical trial as well as workload documentation for study personnel, were available, reviewed, and appropriately maintained in the ISF.

	-Following the inspection observations related to the delegated study personnel was not adequately qualified/trained to perform the delegated ECG-related study activity, resulting in incorrect documentation of participant data in the ECG report and requiring subsequent correction, a refresher training was conducted on Good Documentation Practice (GDP), ALCOA-C principles, correct ECG data entry, investigational medicinal product (IMP) temperature monitoring, thermometer usage, temperature excursion (TOR) reporting, and accurate temperature monitoring to reinforce compliance with Good Clinical Practice (GCP) requirements as part of CAPA.
5. Investigational Product (IMP) Management	
5.1. 1IMP handling	- IMP storage conditions, temperature monitoring, and accountability records were reviewed during the inspection. The IMP was stored in a dedicated, access-controlled storage area under the required storage conditions. - However, a deficiency was identified, as frequent IMP temperature excursions occurred without prompt and appropriate action. In addition, no timely sponsor communication was documented, no backup data logger was available at the site, and deficiencies were identified in temperature monitoring and oversight of IMP management. These observations indicated **non-compliance with ICH E6(R3)** requirements for investigational medicinal product management and storage. In response, the sponsor investigated the root causes and implemented corrective actions by assigning a new delegated pharmacist while retaining the initial pharmacist as backup, escalating the quality issue and pharmacy oversight to the Principal Investigator and Sponsor, establishing and documenting a revised IMP temperature monitoring process through a Note to File, providing a calibrated backup Min/Max data logger thermometer, and conducting training on IMP temperature monitoring, thermometer use, temperature excursion (TOR) reporting, and accurate temperature monitoring. The sponsor also assessed each impacted temperature excursion, communicated the outcomes through TOR reports, and implemented the appropriate measures for the affected IMP based on sponsor stability assessments. Preventive measures included daily review of temperature charts by the CRA for an initial monitoring period, implementation of a second signature on the daily temperature log, continued pharmacist training, and routine sharing of temperature monitoring records. The submitted

	corrective and preventive actions were reviewed by EDA and considered acceptable. - Shipping, receipt, and dispensing procedures were implemented. - Labeling and traceability were generally adequate.
6. Clinical Trial Conduct	
6.1. Protocol Compliance	- The study was generally conducted according to the approved protocol. - Protocol-required study procedures, participant eligibility, investigational medicinal product (IMP) management, safety reporting, and study documentation were reviewed during the inspection. - However, a deficiency was identified in the implementation of protocol requirements related to investigational medicinal product (IMP) management, including repeated temperature excursions without prompt and appropriate action, inadequate temperature monitoring and oversight, and the absence of a backup data logger. These observations indicated **non-compliance with the study protocol, GCP, and applicable regulatory requirements.**
6.2. Source Data and CRFs	- Source documents and eCRFs were reviewed to verify the accuracy, completeness, and consistency of trial data. Participant records, source documentation, and electronic study records were available for review. - Participant records were available for verification and were maintained in an organized and accessible manner throughout the inspection period. - Data were generally consistent between the reviewed source documents and CRFs. - Source data were confirmed to be legible, well organized, and maintained in full compliance with ALCOA principles throughout the study.However, deficiencies in documentation practices were identified, including overwriting on the Principal Investigator's GCP Declaration and inappropriate corrections in an ECG report for one participant, indicating **non-compliance with Good Documentation Practice (GDP), ALCOA-C principles, and ICH E6(R3) requirements** for maintaining accurate, traceable, and complete trial records. In response, the sponsor corrected the Principal Investigator's GCP Declaration by issuing a newly signed version in accordance with GCP requirements, as the previously retained printout could not be amended. The ECG documentation was corrected with appropriate signature and date, and refresher training on Good Documentation Practice (GDP), ALCOA-C principles, and correct ECG data entry was conducted for the Principal Investigator and Co-investigators. Updated training records were

	submitted. The submitted corrective and preventive actions were reviewed by EDA and considered acceptable.
6.3. Delegation of Duties	- Delegation logs were available. - Roles and responsibilities of study personnel were clearly defined and documented in the delegation log. Delegated trial-related activities were assigned to appropriately qualified study personnel in accordance with their responsibilities. - Following the inspection, the delegation log was updated to assign an additional pharmacist to support investigational medicinal product (IMP) management activities and provide backup coverage as part of the implemented corrective and preventive actions.
7. Laboratory and Bioanalytical Activities (if applicable)	
- An External central Laboratory used for analysis of bio samples and protocol required assessments and National radiology center for nuclear medicine services. - The laboratories involved in the study were appropriately accredited, and laboratory facilities were available to support protocol-required testing. - Laboratory procedures were generally defined in the laboratory manuals maintained in the Investigator Site File (ISF), together with the applicable laboratory reference ranges to ensure accessibility by the study personnel during trial conduct. - Sample handling and analysis were reviewed. - Laboratory activities were generally conducted in accordance with the study protocol, Good Clinical Practice (GCP), and applicable regulatory requirements, and no deficiencies related to laboratory or bioanalytical activities were identified.	
8. Safety Reporting (SAE)	
- SOPs for SAE reporting were available governing adverse event (AE) and serious adverse event (SAE) reporting were available and implemented at the site. - Adverse event (AE) and serious adverse event (SAE) documentation, safety reporting procedures, and related records were reviewed during the inspection to verify compliance with the study protocol, Good Clinical Practice (GCP), and applicable regulatory requirements. - No SAE were reported during the study conduction till the date of this inspectio. - Reporting timelines and documentation were generally followed.	
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. Corrective and preventive actions (CAPA) should be 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 E6r3.
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
CT	Clinical Trial
CV	Curriculum Vitae
EDA	Egyptian Drug Authority
GDP	Good Documentation Practice
GCP	Good Clinical Practice
ICF	Informed Consent Form
IB	Investigator Brochure
ICH	International Conference of Harmonization
IMP	Investigational Medicinal Product
IRB/IEC	Institutional Review Board / Ethics Committee
ISF	Investigator Site File
MOH	Ministry of Health
PI	Principal Investigator

PIR	Public Inspection Report
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
TOR	Temperature excursion Report
WHO	World Health Organization

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