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	Zagazig University Hospital, Hematology Department
Address of Inspected CT Site	Faculty of Medicine Street, Sheeba El-Nakaria, Zagazig, Sharqia Governorate
Inspection Details	
Dates of Inspection	**Inspection Duration:** One-day inspection **Start Date:** 21 July 2025 **End Date:** 21 July 2025
Type of Inspection	Routine GCP Inspection.
Introduction	
General Information about the Sponsor and the CT Site	The inspected site is a clinical trial site (Zagazig University Hospital, Hematology Department) participating in the conduct of the inspected clinical study sponsored by Forma Therapeutics, Inc. (a Novo Nordisk company), in accordance with applicable regulatory requirements and ethical standards. **PI Name:** Prof. Dr. Mohamed Badr The inspection included verification of the study site's conduct of clinical trial activities within the defined scope, including the informed consent process, protocol compliance, participant source documentation, safety reporting, investigational medicinal product (IMP) accountability, maintenance of the Investigator Site File, and data documentation, to assess compliance with the study protocol, GCP principles, and applicable local regulations.
Brief Report on Inspection Activities Undertaken	
Scope and Limitations	
Areas Inspected	- Informed Consent Process and Informed Consent Forms (ICFs) - Source Documents and Electronic Case Report Forms (eCRFs) - Investigator Site File (ISF) and Essential Documents - Investigational Medicinal Product (IMP) Management - IMP Storage Area - Safety Reporting - Study Facilities and Study-Relevant Areas - Quality Management/Quality Assurance System - Archiving and Document Control System
Out of Scope	Not defined

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Inspected Clinical Medical Research	An Adaptive, Randomized, Placebo-Controlled, Double-Blind, Multi-Center Study of Oral Etavopivat, a Pyruvate Kinase Activator in Patients with Sickle Cell Disease **Protocol Number:** 4202-HEM-301 **Trial ID:** HIBISCUS **Phase:** Seamless II/III **EDA Initial Approval Date:** 11 Dec 2022.
Type of IMP	Small Molecule IMP (Etavopivat 200mg Tablet).
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; however, the certificates did not include details of the calibration process (e.g., calibration results and reference standards used). In addition, the weight balance and centrifuge did not bear calibration labels. This is not compliant with ICH E6(R3). The finding was resolved through recalibration of the study equipment by an external calibration service provider, issuance of detailed calibration certificates, affixing of calibration labels to the equipment, and implementation of preventive measures including staff training, and establishment of procedures to ensure timely calibration and compliance with calibration requirements. - 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, such as eCRF and randomization systems, were in use.
2. Pharmaceutical Quality System	
2.1. Quality Management System	- The study site had an established quality assurance system supported by documented Standard Operating Procedures (SOPs) to ensure compliance with GCP principles, ethical standards, and regulatory requirements. SOPs were available to define and govern the management of clinical trial-

	related activities, including procedures for Investigational Medicinal Product Management, Obtaining Informed Consent, and Adverse Events Reporting. - The study has been monitored according to the monitoring plan.
2.2. SOPs and Documentation	- SOPs governing all clinical trial activities were maintained, implemented, and confirmed to be in full compliance with GCP requirements - 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. - Two documentation-related findings were identified: incomplete documentation by the investigator regarding the clinical significance of out-of-range laboratory values for one of the verified participants, and the absence of the original initial IRB approval letter in the Investigator Site File (ISF). Consequently, the documentation did not fully comply with ICH E6(R3). The findings were subsequently resolved through completion of the required documentation, obtaining and filing a certified copy of the initial IRB approval, monitoring verification of the corrective actions, and retraining of site staff on Good Documentation Practice (ALCOA principles).
2.3. Deviation Management	Clinical trial-related deviations were managed and documented in accordance with the sponsor's applicable procedures.
2.4. CAPA System	The site was required to address all observations and submit CAPA and supportive documentation as proof of correction, in the proposed time schedule for corrections. The site appropriately addressed the identified findings through corrective and preventive actions that were assessed and accepted by EDA.
3. Ethics and Participant Protection	
3.1. Informed Consent Process	The informed consent process was reviewed and found to be compliant with GCP requirements. The correct IRB-approved versions of the informed consent forms were used throughout the study, and all participants signed the informed consent forms prior to the performance of any study-related procedures.
3.2. Ethics Committee Approval	Approvals from the IRB were available. -Initial IRB Approval dated 27 Feb 2022.
3.3. Participant Safety	No serious adverse events (SAEs) had been reported at the study site as of the inspection date.

4. Personnel and Training	
4.1. Training and Qualifications	- 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). - Protocol-specific training records, as well as workload documentation for study personnel, were available, reviewed, and appropriately maintained in the ISF. - It was verified that all study personnel were GCP-trained (certificates were found at the site).
5. Investigational Product (IMP) Management	
5.1. IMP Handling	- Shipping records documenting the quantities and batch numbers of the IMPs received at the site were available and verified. - Temperature monitoring records (data logger printouts) for IMP transportation from the depot to the study site were reviewed and found acceptable. - IMP storage conditions, and temperature monitoring in the IMP storage area were reviewed. - IMP accountability, including receipt, dispensing, return, reconciliation, and traceability, was verified.
6. Clinical Trial Conduct	
6.1. Protocol Compliance	- The study was generally conducted in accordance with the approved protocol version 6.0 dated 10 April 2024. - Based on the documents reviewed, facilities inspected, and the inspection findings, Study 4202-HEM-301 was conducted at an acceptable level of compliance with the study protocol, GCP guidelines, and applicable regulatory requirements. - However, one protocol compliance finding related to incomplete documentation of protocol-required participant assessments and study information at scheduled visits was identified. This finding is not compliant with the requirements specified in Protocol Versions 3.5EG and 4.0 and, consequently, with ICH E6(R3). The finding was subsequently resolved through completion of the missing documentation by the Sub-Investigator and retraining of site staff on ALCOA^{++} Good Documentation Practices and protocol compliance.
6.2. Source Data and CRFs	- Participant records were available for verification and were maintained in an organized and accessible manner throughout the inspection period. - Source data were generally confirmed to be legible, well organized, and maintained in compliance with ALCOA principles throughout the study.

	However, one documentation-related finding was identified concerning incomplete documentation by the investigator regarding the clinical significance of out-of-range laboratory values for one of the verified participants. Consequently, the documentation did not fully comply with ICH E6(R3), which requires complete source records. The finding was subsequently resolved through completion of the required documentation and documented retraining of the relevant site staff on Good Documentation Practice (ALCOA principles).
6.3. Delegation of Duties	The Delegation of Responsibility Log was confirmed to be available at the site, accurately completed, signed by the Principal Investigator, and reflective of the actual roles and responsibilities assigned to each study team member.

7. Laboratory and Bioanalytical Activities (if applicable)

- The study site utilized two external local laboratories: one for clinical laboratory testing and the other for pharmacokinetic sample analysis.
- The laboratories were accredited
- The laboratory procedures were defined in the laboratory manuals filed in the Investigator Site File, along with the reference ranges to be accessible to the study staff.

8. Safety Reporting (SAE)

- SOP for SAE reporting was available.
- No serious adverse events (SAEs) had been reported at the study site as of the inspection date.

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.
- The identified deficiencies were communicated to the applicant. They were appropriately addressed by the site through the implementation of appropriate corrective and preventive actions that were evaluated and accepted by EDA.
- 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 of 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	
ALCOA:	Attributable, Legible, Contemporaneous, Original, Accurate
CAPA:	Corrective and Preventive Action
CRF:	Case Report Form
CT	Clinical Trial
EDA	Egyptian Drug Authority
GCP:	Good Clinical Practice
IB	Investigator Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IMP:	Investigational Medicinal Product
IRB	Institutional Review Board
PI:	Principal Investigator
PIR	Public Inspection Report
SAE:	Serious Adverse Event
SOP:	Standard Operating Procedure
WHO	World Health Organization

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