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	CRC, Faculty of Medicine, Cairo University Hospital and Abu El Resh Hospital
Address of inspected CT site	Kasr El Ainy, Cairo, Egypt
Inspection details	
Dates of inspection	13 March 2025
Type of inspection	Routine
Introduction	
General information about the sponsor and CT site	- The inspected site is a Clinical Trial Site (**CRC, Faculty of Medicine, Cairo University Hospital and Abu El Resh Hospital**) that conducts clinical studies for the sponsor (**Global Blood Therapeutics Inc. (GBT) is a wholly owned subsidiary of Pfizer Inc.).** - PI name: **Prof. Dr. Mona Hamdy** - 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 · Source documents and Case Report Forms (CRFs) · Archiving and documentation system · Quality management system
Out of scope	The following areas were out of Scope: · Pharmacy / IMP storage area: all IMP packages had been returned to the sponsor. · Site Laboratory: No blood sampling was performed at the site, and participants were referred to an external local laboratory for blood sampling.
Inspected Clinical medical research	The inspection focused on the following study: - Protocol Title: A randomized, double blind, placebo-controlled, multicenter study to assess the safety and efficacy of Inclacumab in participants with sickle anemia disease experiencing Vaso-occlusive crisis

	- Protocol Number: GBT2104-131 -Phase: III - EDA Initial approval date: 19\06\2022
Type of IMP	Biological Monoclonal antibody (Inclacumab)
Part 2	
1. Facilities and equipment system	
1.1. Facilities and Trial Conduct	-The site facilities were generally adequate for trial conduct. -Dedicated areas were available for participant reception and waiting, examination, consultation, and clinical procedures to support the conduct of the clinical trial. -Equipment maintenance, calibration, emergency preparedness were not verified during the inspection visit.
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 established a Quality Management System (QMS) supported by Standard Operating Procedures (SOPs) governing clinical trial conduct, documentation, participant safety, investigational medicinal product management, and quality oversight to ensure compliance with GCP, ethical principles, and applicable regulatory requirements.
2.2.SOPs and Documentation	-The site-maintained SOPs governing clinical trial activities. During the inspection, the applicable SOPs and essential trial documents reviewed included the approved protocol and protocol amendments, Investigator's Brochure, informed consent forms, regulatory and ethics approvals, investigator qualifications and training records, delegation logs, investigational medicinal product management records, laboratory documentation, pharmacy manual, monitoring reports, participant records, eCRFs, source documents, contracts and agreements, safety reporting documentation, and other study-specific essential documents. -Study related Documents were appropriately controlled, maintained, periodically reviewed, and available. -One observation was identified regarding document archiving, as previous versions of the ICFs, IB, and Protocol were not archived in the Site Master File (SMF) as superseded documents according to **EMA Guideline**. In response for CAPA implementation, the previous versions of the ICFs, IB, and Protocol available in the Investigator Site Folder were marked as superseded by the Principal Investigator. The submitted CAPA was

	reviewed by the Egyptian Drug Authority (EDA) and considered acceptable.
2.3. Deviation Management	Deviations were not handled according to SOPs as one observation was identified regarding protocol deviation management, as documentation supporting the identified protocol deviations was not available in the Trial Master File (TMF) **as per ICHE6R3 guideline** or in the participants' study files, although a list of protocol deviations had been submitted to the Egyptian Drug Authority (EDA) which indicated deficiencies in the documentation and filing of protocol deviations within the essential trial records. In response for CAPA implementation, the full list of protocol deviations was received from the sponsor and filed in the Investigator Site File (ISF). As a preventive action, the study team was trained on GCP requirements, including ALCOA principles related to good documentation practice. The submitted CAPA was reviewed by the Egyptian Drug Authority (EDA) and considered acceptable.
2.4. CAPA System	-A CAPA system was established at the site. -CAPA responses for findings identified during this inspection were submitted by the site and evaluated by EDA inspectors. -The identified findings were appropriately addressed by the site through corrective and preventive actions.
3. Ethics and participant Protection	
3.1.Informed Consent Process	-The informed consent process was verified during the inspection through the review of the approved ICFs, participant source records, and other relevant essential trial documents. -The inspection confirmed that informed consent was obtained from all participants before the performance of any study-related procedures using the approved Ethics Committee-approved versions of the informed consent forms, including the following: • Main Adul Paret ICF, Version V 2.0, dated 10 May 2022, and V 3.0, dated 07 Dec 2023 • Main Adult Parent Short ICF, V 2.0, dated 10 May 2022, and V 3.0, dated 07 Dec 2023 • Adolescent assent (12-17 years old) ICF, Version 0.1, dated 1 March 2021 • Partner pregnancy ICF, V 1.0, dated 1 March 2021
3.2. Ethics Committee Approval	Approvals from IRB/IEC were available: **-MOH approval:** 07/07/2021 **-IRB approval:** 27/05/2021

3.3. Participant Safety	-Participant safety was verified during the inspection through the review of participant source records, informed consent documentation, adverse event (AE) and serious adverse event (SAE) documentation, Case Report Forms (eCRFs), medical records, and other study-related essential documents. -The inspection report confirmed that the SAE was reported to the sponsor within the protocol-specified timeline and to EDA within the specified timeframe.
4. Personnel and Training	
4.1. Training and qualifications	-Roles and responsibilities of study personnel were clearly defined. -Current curriculum vitae (CVs), professional qualifications, and training records of the Principal Investigator and delegated study personnel were available and appropriately maintained. -GCP training records for the study team were reviewed and found to be available at the site. -Protocol-specific training records had been completed and were retained in the Investigator Site File.
5. Investigational Product (IMP) Management	
5.1. IMP handling	-IMP storage conditions, temperature monitoring, shipment, receipt, dispensing, accountability, return, and destruction procedures, as applicable, were reviewed during the inspection.
6. Clinical Trial Conduct	
6.1. Protocol Compliance	- The study was generally conducted according to the approved protocol (Protocol Amendment 4 (Version 5), dated: 13 July 2023). -Protocol compliance was verified during the inspection through the review of the approved protocol, participant source records, eCRFs, informed consent documentation, IMP records, laboratory documentation, safety reporting records, monitoring documentation, and other essential trial documents.
6.2. Source Data and CRFs	- Source documents and eCRFs were reviewed during the inspection. - The inspection included comparison of participant source records with the corresponding eCRFs and other relevant study documentation which were found to be complete, legible, contemporaneous, and appropriately maintained. - Several observations were identified regarding source documentation, including overwriting in the source documents of one of the participant files, deficiencies in the documentation of laboratory results in participant files, discrepancies in participant files regarding dates of Adverse event reporting and data in questionnaire form used, and incomplete source data documentation **in accordance with ICHE6R3.** Corrective actions

	included correction and completion of the affected study documentation and filing of the full protocol deviation list in the Investigator Site File (ISF). Preventive actions included training of the study team on GCP and ALCOA principles related to appropriate documentation and record maintenance. The submitted CAPA was reviewed and accepted by the EDA.
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. - Roles and responsibilities of study personnel were documented through the delegation log.
7. Laboratory and Bioanalytical Activities (if applicable)	
- An external local Laboratory was used for analysis. - Laboratory procedures for Sample handling and analysis were generally defined. - External laboratory accreditation and qualifications were confirmed to be appropriate for the study requirements. - Laboratory procedures for sample collection, processing, storage, and transportation were implemented in accordance with the study protocol and laboratory manuals.	
8. Safety Reporting (SAE)	
- Safety reporting procedures were verified during the inspection through the review of adverse event (AE) and serious adverse event (SAE) documentation, safety-related records, applicable SOPs, and other relevant study documentation. - Reporting timelines and documentation procedures were reviewed and confirmed to be in place in preparation for study commencement.	
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 Corrective and preventive actions (CAPA) were be implemented to address the observations. -This EDA-GCP-PIR remained 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 202
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
8. EMA Guideline on the content, management and archiving of the clinical trial master file (paper and/or electronic), final version dated 06 December 2018

Abbreviation	
AE	Adverse Event
ALCOA	Attributable, Legible, Contemporaneous, Original, Accurate
CAPA	Corrective and Preventive Action
CRC	Clinical Research Center
CRF	Case Report Form
CT	Clinical Trial
CV	Curriculum Vitae
ECG	Electrocardiogram
EDA	Egyptian Drug Authority
EMA	European Medicines Agency
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
ISF	Investigator Site File
MOH	Ministry of Health
PI	Principal Investigator
PIR	Public Inspection Report
QMS	Quality Management System
SAE	Serious Adverse Event
SMF	Site Master File
SOP	Standard Operating Procedure
TMF	Trial Master File

WHO	World Health Organization

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