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	Menoufia University Hospital, Internal Medicine Department.
Address of Inspected CT Site	Shebin El-Kom, Menoufia, next to the National Liver Institute – Menoufia University
Inspection Details	
Dates of Inspection	**Inspection Duration:** One-day inspection **Start Date:** 27 Nov 2025 **End Date:** 27 Nov 2025
Type of Inspection	Routine GCP Inspection (Following the sponsor's decision for early termination of the site on 28-May-2023).
Introduction	
General Information about the Sponsor and the CT Site	The inspected site is a clinical trial site (Menoufia University Hospital, Internal Medicine Department) participating in the conduct of the inspected clinical study sponsored by Eva Pharma, in accordance with applicable regulatory requirements and ethical standards. **PI Name:** Prof. Dr. Nabil Abdel Fatah El Kafrawy. 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, 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 Forms · Source documents and Electronic Case Report Forms (eCRFs) . Investigator Site File (ISF) and Essential Documents . Quality Management/Quality Assurance System . Archiving and Document Control System · Safety reporting . IMP Management Related Documents . Study Facilities and Study-Relevant Areas
Out of Scope	The investigational product storage room was not included in the facility tour, and the IMP accountability was not verified, since the IMP had been returned

	to the sponsor following the sponsor's decision for early termination of the site.
Inspected Clinical Medical Research	A Multicenter, Interventional, Two-Arm, Parallel-Group, Randomized, Double-Blinded, Placebo-Controlled, Phase IV Trial to Evaluate the Efficacy of Alpha-Lipoic Acid in the Treatment of Patients with Symptomatic Diabetic Polyneuropathy in Egypt **Protocol Number:** Cl_Tr_17122019 **Trial ID:** MIRACLE-ALA **Phase IV** **EDA Initial Approval Date:** 12 Oct 2022.
Type of IMP	Small Molecule IMP (Thiotacid 300mg tablet).
Part 2	
1. Facilities and Equipment System	
1.1. Facilities and Trial Conduct	- The trial site did not maintain adequate control and traceability of study-related equipment. Although designated examination, consultation, and procedure rooms were available and operational, certain equipment used during the conduct of the clinical trial was not available for verification at the time of the inspection, as some equipment had been returned to the sponsor following site close-out, while other equipment could not be located within the institution. Consequently, the inspectors were unable to verify the availability, status, or calibration records of the equipment, and no documented evidence was available to demonstrate that all study-related equipment had been appropriately maintained and calibrated throughout the study period. This finding is not compliant with ICH E6(R3). The finding was addressed by providing copies of the calibration certificates from the Sponsor Trial Master File (TMF) to the site for filing in the Investigator Site File (ISF). As the study had already been closed and the equipment was no longer functional or available at the site, no retrospective site-level corrective actions could be implemented. As preventive measures, the Sponsor/CRO committed to ensuring that calibration certificates for critical equipment are maintained in both the TMF and ISF, incorporating verification of calibration certificates into site file checklists, and strengthening oversight of essential document filing and equipment management during future site monitoring and quality assurance activities. - Study files were stored in a secure, access-controlled, fire- and water-resistant cabinet and were secured against unauthorized access. - A dedicated Pharmacy/Investigational product storage area was established at the site; however, it was not inspected since there was no IMP at the site during the inspection time.

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 site did not have an established quality management system supported by documented Standard Operating Procedures (SOPs). Specifically, no site-specific SOPs were available to define and govern clinical trial-related activities. This finding is not compliant with ICH E6(R3). As the study had been completed and the site terminated, no site-level corrective action could be implemented. As preventive measures, the Sponsor/CRO committed to verifying the availability of site SOPs during site feasibility and study initiation, ensuring formal adoption of Sponsor/CRO SOPs where site-specific SOPs are unavailable, and providing guidance to sites on implementing essential SOPs for future clinical trials. -The study has been monitored according to the monitoring plan.
2.2. SOPs and Documentation	-No site-specific Standard Operating Procedures (SOPs) were available to define and govern the management of clinical trial-related activities. Preventive measures were taken to avoid recurrence of this non-compliance in future clinical studies as detailed in the preceding section. -Essential documents were available and reviewed, including source documents, ICFs, eCRF, approvals, contracts, insurance, CVs, GCP certificates, IB, safety reports, progress reports, and IMP records.
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 identified findings were appropriately addressed by the site through corrective, when feasible, 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. The approved informed consent forms, ICF v3.0 dated 14/08/2022, were used throughout the study and were confirmed to be the correct IRB-approved versions. - Review of the informed consent documentation confirmed that informed consent had been obtained prior to the conduct of study-related procedures for the verified participants, with the exception of one participant. For this participant, a study-related procedure was performed before the informed consent form had been signed and dated. Consequently, the informed consent process for this participant was not

	fully compliant with ICH E6(R3). The finding was addressed through documentation of the protocol deviation. As the study had been completed and the site terminated, no participant-level corrective actions could be implemented. Preventive measures included refresher GCP training with emphasis on the informed consent process, reinforcement of informed consent verification before study-related procedures, incorporation of informed consent verification into CRA monitoring checklists, and enhanced quality assurance oversight during future studies
3.2.Ethics Committee Approval	Approvals from the IRB were available. - Initial IRB Approval dated 17 Nov 2021.
3.3. Participant Safety	No Serious Adverse Events (SAEs) were reported at the site.
4. Personnel and Training	
4.1. Training and Qualifications	-Curriculum Vitae of the Principal Investigator and Co-Investigator were confirmed to be available at the site, up to date, and filed appropriately in the Investigator Site File in compliance with GCP requirements. -Protocol-specific training records and workloads for all staff who took part in the conduct of the clinical trial were verified and filed at the site. -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 detailing the quantity and the batch numbers of the IMPs received at the site were available. -Printout of the data logger of temperature during transportation of IMP from the depot to the clinical trial site was verified. -Dispensing records were verified during the inspection. -Records of IMP return to the sponsor were verified during the inspection. -Accountability of the IMP was not performed since there was no IMP at the study site during the inspection visit, and it was returned to the sponsor following the sponsor's decision for early termination of the site.
6. Clinical Trial Conduct	
6.1. Protocol Compliance	-The study was generally conducted in accordance with the approved protocol version 3.0 dated 15 Aug 2022.
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. -Discrepancies were identified within the source documentation of one of the verified participants, where information recorded in different sections of the medical records was inconsistent regarding the presence of a study-relevant medical condition. However, a review of supporting diagnostic

	documentation confirmed that the affected participants met the relevant eligibility criteria and were appropriately enrolled in the study. -In addition, discrepancies were identified in the screening log records. For several screened participants, the documented reasons for screening failure or non-enrollment were inaccurately recorded and were not fully consistent with the protocol-defined eligibility criteria or the participants' actual status. These discrepancies reflected deficiencies in documentation and record-keeping; however, they did not affect participant eligibility determinations or study enrollment decisions. -Consequently, the documentation did not fully comply with ICH E6(R3). The findings were addressed through revision of the screening log to accurately distinguish non-randomization from screening failure/exclusion. As the study had been completed and the site terminated, no retrospective site-level corrective actions could be implemented for the first part of the finding. Preventive measures included strengthening data entry and source documentation practices, enhanced CRA monitoring and QA oversight, reinforcement of guidance on screening log completion, and implementation of a second-level review of source documents and screening logs by the Principal Investigator following data entry.
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 an external local laboratory. -The laboratory was accredited. -The laboratory procedures were defined in the laboratory manual filed in the Investigator Site File, along with the reference ranges to be accessible to the study staff.	
8. Safety Reporting (SAE)	
- No Serious Adverse Events (SAEs) were reported at the site.	
Part 3	**Inspection Outcome**
- Based on the reviewed documentation, inspected facilities, and observations identified during the inspection, the conduct of the MIRACLE-ALA study demonstrated deficiencies with respect to compliance with the protocol, GCP principles, and applicable regulatory requirements. However, on 28-May-2023, the sponsor decided to terminate the site early due to participants' non-compliance and an increased rate of participant withdrawals. Consequently, data collected from participants enrolled at this site were not included in the study analysis, the Statistical Analysis Report (SAR),	

or the Clinical Study Report (CSR).
- The identified deficiencies were communicated to the applicant and were subsequently addressed through appropriate corrective, where feasible, and preventive actions, which were evaluated and accepted by the EDA.
- This EDA-GCP-PIR remained valid until the next GCP inspection of the site.

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

Abbreviations

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
ISF:	Investigator Site File
PI:	Principal Investigator
PIR	Public Inspection Report
SAE:	Serious Adverse Event
SOP:	Standard Operating Procedure
TMF:	Trial Master File
WHO	World Health Organization