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	1. Al-Manial Specialized Hospital, Cairo University 2. My lab laboratory (25 Al Kasr Al Eini, El-Sayeda Zainab, Cairo)
Address of inspected CT site	1. Cairo University Hospitals (Al-Manial Specialized University Hospital), Cairo, Egypt 2. My lab laboratory (25 Al Kasr Al Eini, El-Sayeda Zainab, Cairo)
Inspection details	
Dates of inspection	(Al-Manial Hospital: 24/08/2022; My lab: 25/08/2022).
Type of inspection	Follow-up (Triggered by findings from previous inspections dated 20/02/2022 and 10/04/2022)
Introduction	
General information about the sponsor and CT site	The inspected site is Cairo University Hospitals (Al-Manial Specialized University Hospital), Cairo, Egypt and the designated analysis laboratory My lab (25 Al Kasr Al Eini, El-Sayeda Zainab, Cairo), conducting clinical analysis for the sponsors EVA PHARMA, Veterinary Serum & Vaccine Research Institute (VSVRI), the Supreme Council of University Hospitals, and Ministry of Higher Education and Scientific Research The Principal Investigator was Dr. Amal Sayed Hassan (Professor of Clinical and Chemical Pathology – Clinical Microbiology, Cairo University). The CRO: Activities included participant vaccination (EgyVax COVID-19 vaccine candidate), clinical conduct, blood sample collection, safety monitoring, immunogenicity and safety laboratory assessments, and data documentation.
Brief report on inspection activities undertaken	
Scope and limitations	
Areas inspected	· At the clinical trial site (Al-Manial Specialized University Hospital, 24/08/2022) and the designated analysis laboratory (25/08/2022) were inspected. · Investigational Medicinal Product (IMP) management · Bioanalytical / laboratory facilities · Source documents · Quality management system This was a focused follow-up inspection with two objectives: 1)to check for implementation of submitted protocol changes and end of recruitment, and

	2) to verify the laboratory results (Raw Data).
Out of scope	Other activities not in the scope of the inspection visit.
Inspected Clinical medical research	The follow-up inspection focused on the following study: Safety and Immunogenicity Study of EgyVax Vaccine Candidate for Prophylaxis of SARS-CoV-2 Infection (COVID-19) **Trial ID**: SPHINEX22122020 **Phase:** I **EDA approval** 3 Feb. 2022
Type of IMP	Vaccine Candidate &Placebo
Part 2	
1. Facilities and equipment system	
1.1.Facilities and Trial Conduct	The clinical trial site (Al-Manial Specialized University Hospital) and the designated analysis laboratory were assessed during the follow-up inspection on 24–25 August 2022. At designated lab, all devices used for analysis were accredited and accreditation certificates were valid. All laboratory tests for all participants were performed according to the visit schedule in the approved protocol. Equipment maintenance and calibration were in place. All CAPAs from the previous inspections (20/02/2022 and 10/04/2022) that had been verified as implemented were maintained.
1.2.Computerized system	Randomization systems were in use.
2. Pharmaceutical Quality System	
2.1.Quality Management System	The site had an established Quality Management System. CAPAs from the previous inspections were reviewed for implementation status. The following previously submitted CAPAs were verified as implemented : - spillage procedures implemented and staff trained; - equipment work instructions archived in the site file; delegation log reconfirmed with the PI that all SCs and delegated site staff had proper access to source documents. - The sponsor (EVA PHARMA) submitted a study memo to EDA describing the invasive procedures of ABGs and the rationale for replacing them with VBGs. Protocol amendments were submitted to the Supreme Council of University Hospitals and EDA respectively.
2.2.SOPs and Documentation	The site-maintained SOPs governing clinical trial activities. During the follow-up inspection, the following new documentation findings were identified and required corrective action: - Missing laboratory results from some participant files for certain visits and

	Some laboratory results were not reported in participant notes. As per CAPA implementation, all missing results were filed in the relevant participant files to ensure completeness and traceability and all notes were updated with the required immunogenicity and safety results. - unsigned overwriting corrections were observed across participant notes ; all were subsequently signed and dated in compliance with GDP as per CAPA implementation.
2.3. Deviation Management	Deviation management procedures were available. Deviations were handled per available SOPs.
2.4. CAPA System	A CAPA system was established at the site. CAPAs from the previous inspections (20/02/2022 and 10/04/2022) were assessed during this follow-up inspection and implementation was verified. The majority of previously submitted CAPA activities were confirmed implemented.
3. Ethics and Participant Protection	
3.1.Informed Consent Process	The informed consent process was reviewed during the follow-up inspection. Approved ICFs were available and used. - The ICF of one of the participants was not signed by the investigator at the time of inspection. This was identified, acknowledged, and corrected as the investigator signed the ICF and the correction was documented. All other participants' ICFs were reviewed. It was recommended that all participants' notes be revised for adverse events and causality assessments to be recorded in adverse event forms and reported in follow-up reports to EDA. - The ICF translation error in the Arabic versions, was addressed by a Note to File added to the Study Master File, a new ICF version was issued along with the amendment as per CAPA implementation.
3.2.Ethics Committee Approval	- Ethics Committee of supreme council of universities Approval Date: 25/1/2022 - IRB Approval Date: 30/12/2021. - Protocol amendments were submitted to the Supreme Council of University Hospitals and to EDA, during acknowledgement of the SPHINX-EGYPT Study Memo. Protocol was the approved version at time of inspection. - All required documentation for regulatory submissions was being compiled and submitted as directed by EDA.
3.3. Participant Safety	- Safety monitoring procedures were in place. - A finding was identified during inspection regarding that a participant experienced side effect which was not recorded in the adverse event form and not reported in the weekly follow-up report sent to EDA. This was identified, acknowledged, and corrected as all participants' notes were revised for any adverse events and causality assessments were recorded.
4. Personnel and Training	

4.1.Training and qualifications	-Roles and responsibilities of study personnel were clearly defined. A delegation log discrepancy identified in the previous inspection was resolved: the study team reconfirmed with the PI that all SCs and delegated site staff had proper access to source documents in accordance with the delegation log. - GCP training records were available.
5. Investigational Product (IMP) Management	
5.1.IMP handling	-The implementation of CAPA was verified for the following: • IMP storage, temperature monitoring, and accountability were reviewed. The defective IMP shipment had been rejected by the pharmacist and returned to the sponsor. • Visual inspection of IMP temperature during transportation was established that identified in the previous inspection; the pharmacist was instructed to reject any shipment with a reported temperature excursion. • Shipping, receipt, and dispensing procedures were implemented and governed by the relevant SOPs retained at the site. Equipment use instructions for all utilized study equipment were provided and archived in the site file. • IMP labelling and traceability were adequate. IMP labels included batch number, expiry date, and the statement "for clinical trial use only." • The temperature excursion issue was resolved. Enhanced IMP temperature monitoring during transportation was implemented. No further IMP accountability deficiencies were identified during this follow-up inspection.
6. Clinical Trial Conduct	
6.1.Protocol Compliance	Approved Protocol was Implemented (Version No.:6 dated 21 Jan. 2021). -Based on the documents reviewed, facilities inspected and considering the findings of the inspection, study number (SPHINX22122020) was conducted in compliance with the protocol, GCP guidelines and applicable regulatory requirements.
6.2. Source Data and CRFs	- Source documents and participant notes were reviewed for multiple participants Key findings identified, addressed and ensure CAPA implementation during the follow-up inspection: • Many overwriting corrections in participant notes were not signed – all overwriting corrections were required and were signed and dated; many laboratory results were not available in participants' files, As per CAPA implementation all missing lab results were filed in respective participant files. • Physical examination outcomes were not documented in some visits at the time of inspection. Notes to file were added to the affected participant files by the PI to declare the physical examination outcomes for all relevant follow-up visits, ensuring complete and accurate documentation in compliance with GCP requirements.

	• Concomitant medications were not checked for one of the visits; identified and corrected in the participant file. • Missing data related to a vaccine that not taken with no reason specified; the reason was subsequently added to the participant notes. These ALCOA-related issues were identified and addressed confirmed to be legible, well organized, and maintained in full compliance with ALCOA principles throughout the study.
6.3. Delegation of Duties	Delegation logs were available and reviewed. The delegation log discrepancy identified in the previous inspection (regarding source document access) was resolved: the study team reconfirmed with the PI that all SCs and delegated site staff had proper access in accordance with the delegation log. No further delegation log deficiencies were identified.

7. Laboratory and Bioanalytical Activities (if applicable

-External laboratory (Mylab) was used for analysis. Laboratory was accredited.
-Additional lab identified during inspection which was not submitted in protocol package and not approved by EDA at time of inspection; that was corrected by the sponsor by submission as amendment to EDA.
-Laboratory procedures were defined at the lab. All laboratory equipment used for analysis were accredited with valid accreditation certificates. All laboratory tests for all participants were performed according to the visit schedule in the approved protocol.
-Sample handling and analysis were reviewed and comply with the procedures as per protocol

8. Safety Reporting (SAE)

- SOPs for SAE reporting were available at the site.
- A finding was identified: Adverse event for one of the participants which was not recorded in the adverse event form and not reported in the weekly follow-up report sent to EDA. This was identified, acknowledged, and corrected: all participants' participant notes were revised to ensure any adverse events and causality assessments recorded in adverse event forms and reported in follow-up reports to EDA.
- Procedure in place for assurance that completeness of source document and training of delegated site staff on GSDP

Part 3	**Inspection outcome**

Based on the reviewed documentation, inspected facilities, and observations identified during the inspection: The follow-up GCP inspection conducted at Al-Manial Specialized University Hospital (24–25 August 2022) confirmed that all previously identified deficiencies have been fully resolved. All corrective and preventive actions have been successfully implemented, and supportive documentation has been submitted to EDA within the stipulated timeframe. The Principal Investigator has demonstrated control over the conduct of the clinical trial (Protocol SPHINX22122020) in accordance with ICH-GCP guidelines.

All participant files were complete and traceable, participant notes were comprehensively updated, adverse events were appropriately recorded and reported, and all regulatory submissions were in place. Laboratory oversight, documentation practices, and site procedures met the required GCP standards. In light of the above, the inspectorate was satisfied that the clinical trial is being conducted under full investigator control, in compliance with GCP requirements, and in accordance with the approved protocol — ensuring the safety, integrity, and reliability of the study data.

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	
ALCOA	Attributable, Legible, Contemporaneous, Original, Accurate
CAPA	Corrective and Preventive Action
CRF	Case Report Form
CRC	Clinical research Center
CT	Clinical Trial
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
PI:	Principal Investigator
PIR	Public Inspection Report
SAE	Serious Adverse Event
SC	Study Coordinator
SOP	Standard Operating Procedure
WHO	World Health Organization

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