EDA-GCP Public Inspection Report (PIR) of Clinical Trial Site

Part 1	
Clinical medical research site details	
CT site information	
Name of CT site	Al-Manial Specialized Hospital, Cairo University
Address of inspected CT site	Abdelaziz Al Soad – El Manial, Cairo, Egypt
Inspection details	
Dates of inspection	20 February 2022
Type of inspection	Routine Inspection
Introduction	
General information about the sponsor and CT site	The inspected site is Cairo University Hospitals (Al-Manial Specialized University Hospital) conducting clinical study 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) – Principal Investigator: Dr. Amal Sayed. Site Activities include subject recruitment, clinical conduct, sample collection, safety monitoring, and data documentation for the Safety and Immunogenicity Study of EgyVax Vaccine Candidate for Prophylaxis of SARS-CoV-2 Infection (COVID-19).
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	None defined.
Inspected Clinical medical research	The 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 trial site at (Al Manial Specialized University Hospital) was verified to have adequately established facilities and equipment to support the conduct of the trial. A designated reception and waiting area, examination room, consultation room, counseling room, and procedure room were all made available and rendered operational. -Pharmacy/IMP storage room was Not available as a permanent facility. As justified by the site the Vaccine was being delivered to site and received by PI on day of administration (when participant presented on vaccination days). -An emergency trolley was not available at the procedure area at the time of inspection. This finding was acknowledged and fully addressed. As per the CAPA implementation, A dedicated emergency trolley equipped with emergency medications was placed and made readily available at the clinical trial procedure area. A letter of commitment confirming emergency access to any university hospital for any participant was obtained and filed in the Trial Master File. The availability and readiness of the emergency trolley were documented and verified by the delegated team during monitoring. -All site equipment was found to be uncalibrated with no calibration labels or certificates available at the time of inspection. This finding was acknowledged and addressed. As per the CAPA implementation, All equipment was calibrated by a certified calibration company, valid calibration labels were affixed to each device, and calibrated infra-red thermometers replaced mercury thermometers. All calibration certificates were filed in the Trial Master File and due dates were established and tracked for periodic recalibration. Valid calibration labels and certificates for all equipment involved in the clinical trial were obtained, completed, and made available at Al Manial Specialized University Hospital, with all certificates filed in the site master file, in compliance with GCP requirements. -Operation and procedure rooms were found to be unlabeled and no controlled access to participant files was in place at the time of inspection. All findings were acknowledged and addressed. As per the CAPA implementation, All operation and procedure rooms were clearly labelled in accordance with the site workflow. A secure archiving area with locked cabinets was established, access was restricted to delegated staff only, and all site staff were trained on access control procedures to ensure ongoing compliance with participant confidentiality and data protection requirements.The disposal container checking frequency and waste disposal procedure documentation were found

	to be inadequate at the time of inspection. This finding was acknowledged and addressed. As per the CAPA implementation, A designated disposal container was confirmed to be available at the site with a verified checking frequency of 24 hours. The waste disposal procedure was reviewed, documented, and confirmed to be consistently followed by all site staff. -No infection control system was in place at the time of inspection; As per the CAPA implementation, an infection control system was established at the site, and all site personnel were trained on infection control principles. ensuring that all participants and study personnel wore masks throughout all study-related activities. No electricity shutdown procedure was in place at the time of inspection. This finding was acknowledged and fully addressed. As per the CAPA implementation, The availability of an electricity generator covering the entire hospital, including the ICU, was confirmed and documented.
1.2.Computerized system	-Randomization systems were in use.
2. Pharmaceutical Quality System	
2.1.Quality Management System	-The site had a quality assurance system described in SOPs in place. For: Obtaining Informed Consent, Management of Clinical Trial Drug Supplies, Compensation in Clinical Trials, Adverse Events, Serious Adverse Events, and Safety Reporting, Handling Protocols Deviations, Maintenance -The study has been conducted according to the monitoring plan. -It was observed that all study personnel were GCP trained (certificates were found at the site). -Follow up Report/Week was sent to EDA on regular basis
2.2.SOPs and Documentation	- SOPs governing all clinical trial activities were maintained, implemented, and confirmed to be in full compliance with GCP requirements. -SOPs for IMP handling, transportation, and destruction, as well as for laboratory sample handling, transportation, and waste disposal, were not available at the clinical trial site at the time of inspection. As per the CAPA implementation, IP-relevant SOPs were obtained from the manufacturing site and retained at the study site. Laboratory SOPs were obtained from the Lab Quality Assurance department and retained at the site. SOPs for the handling and transportation of blood samples from the clinical trial site to the designated laboratory were retrieved, reviewed, filed at the site, and confirmed to be accessible to all relevant site staff. SOPs for the handling and transportation of the IMP from -EVA Pharma, including cold chain maintenance, were retrieved from the manufacturing site, reviewed, filed in the site master file, and confirmed to be accessible to all relevant site staff involved in IMP handling and transportation.

2.3. Deviation Management	-Deviation management procedures were available. -Deviations were reported and handled as per available SOPs.
2.4. CAPA System	-A CAPA system was in place. 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 and preventive actions. EDA had planned for triggered/follow-up inspection.
3. Ethics and Subject Protection	
3.1. Informed Consent Process	- The PI confirmed and documented the recruitment process for all participants enrolled from Al Manial Specialized University Hospital, ensuring full compliance with the approved protocol and GCP requirements. - The approved informed consent forms were used throughout the study and were verified to be IRB-approved versions. - All informed consents were signed by participants prior to the performance of any study-related procedures, in full compliance with GCP guidelines. - in accordance with GCP requirements to ensure the record was accurate, complete, and traceable. - Overwriting in the ICFs of multiple participants, missing dates were identified, All findings were acknowledged and fully addressed, as per CAPA implementation, and Good Documentation Practice training was provided to all investigators to prevent recurrence. - An invalid protocol date in the Supreme Council approval form was identified at the time of inspection. Which was corrected as per CAPA implementation. - The procedure for obtaining informed consent from participants was verified to be fully in line with the requirements of GCP guidelines, and no further deviations in the informed consent process were identified upon re-review.
3.2. Ethics Committee Approval	Ethics Committee of supreme council of universities Approval Date: 25/1/2022 IRB Approval Date: 30/12/2021.
3.3. Subject Safety	-SOP for Serious Adverse Event (SAE) reporting was confirmed to be available at the site, reviewed by all relevant staff, and implemented in full compliance with GCP requirements and applicable regulatory standards. -No SAEs were reported at the time of inspection
4. Personnel and Training	
4.1.Training and qualifications	- Curriculum Vitae of the Principal Investigator(s), Sub-Investigator(s), Nurse(s), and Site Coordinator(s) were confirmed to be available at the site, up to date, and filed appropriately in the site master file in compliance with GCP requirements. GCP training records and workloads for all staff who took part in the conduct of

	the clinical trial was verified, confirmed, complete, and archived at the site. Training Sheets and Agendas for all training sessions were reviewed, found to be adequate, and retained in the site master file as supporting documentation.
5. Investigational Product (IMP) Management	
5.1.IMP handling	- Shipping records detailing the quantity and the batch numbers were available. - Dispensing Form (clarifying No. of the used IMP samples) and Accountability Form Were Found. - Data Logger of Cold Chain Was Found. GMP Certificate for Both Placebo & Drug. - Print out of data logger of temperature during transportation of IMP from manufacture site to clinical site indicates compliance with storage condition as per protocol - A spillage procedure for IMP was not available at the clinical trial site at the time of inspection; the PI stated that IMP destruction takes place at the manufacturing site. This finding was acknowledged and addressed. as per CAPA implementation, A formal spillage procedure was developed, approved, and implemented at the clinical trial site, covering all steps to be followed in the event of an IMP spillage incident. The study team was trained on the procedure and training records were documented and archived accordingly. IMP destruction procedures were reviewed and clarified, with relevant documentation made available at the site.
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 at an acceptable level of compliance with the protocol, GCP guidelines and applicable regulatory requirements.
6.2. Source Data and CRFs	- Participant records were confirmed to be available for verification and were maintained in an organized and accessible manner throughout the inspection period. - Source data were confirmed to be legible, well organized, and maintained in full compliance with ALCOA principles throughout the study. - The security of participant records was reviewed and corrected as per CAPA implementation. The fireproof metal cupboard used for storing participant records was secured against unauthorized access through the implementation of a controlled access system - Confidentiality of all participant records was restored and maintained in

	compliance with GCP requirements and applicable data protection regulations. - All screening and randomization records were reviewed, verified, and confirmed to be accurate and complete.
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. - The absence of a registered pharmacist delegated for all IMP-related tasks was identified as a finding and was fully addressed. As per CAPA implementation a registered and qualified pharmacist was assigned to the clinical trial site and was made responsible for all dispensing activities related to the investigational products, in compliance with GCP requirements and applicable regulatory standards. - The delegation of IMP-related tasks to Nurse without qualified personnel in place was identified, escalated, and corrected. During site CAPA implementation All relevant delegation documents were updated, signed, and archived accordingly.
7. Laboratory and Bioanalytical Activities (if applicable	
- An external laboratory used for analysis of blood samples. The laboratory was accredited. - SOPs for the handling and transportation of blood samples from the clinical trial site to designated lab were obtained, reviewed, and made available at the clinical trial site. The relevant SOPs were retrieved from the designated laboratory, archived at the site, and confirmed to be accessible to all relevant site staff.	
8. Safety Reporting (SAE)	
- There is SOP for Serious Adverse Event (SAE) reporting at the site. - Reporting timelines and documentation were reviewed. - No critical SAE reporting deficiencies were identified up to the date of inspection.	
Part 3	**Inspection outcome**
Based on the inspection conducted at the clinical trial site (Al Manial Specialized University Hospital) on 20/02/2022 all deficiencies identified by the inspection team were acknowledged by the sponsor and the Principal Investigator. Comprehensive corrective and preventive actions (CAPAs) were developed, implemented, and documented for each observation raised during the inspection. Supporting documentation was implemented and submitted as proof of correction for each identified observation, in compliance with GCP requirements as prescribed in the ICH Guide to GCP and applicable regulatory standards. All submitted corrective actions were successfully implemented at the clinical trial site, and the site was brought into full compliance with the protocol, GCP guidelines, and applicable regulatory requirements. The sponsor confirmed that all observations were resolved and that the necessary	

measures were in place to ensure ongoing compliance and to prevent recurrence of the identified deficiencies. A follow-up triggered inspection was planned on 10 April 2022 to verify the effective implementation of all corrective and preventive actions.	
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
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
PI:	Principal Investigator
PIR	Public Inspection Report
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
WHO	World Health Organization