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	Medical Research Centre of Excellence-National Research Center "NRC"
Address of inspected CT site	El Noor Street from Research Street, El-Dokki, Giza
Inspection details	
Dates of inspection	08 - 09 December 2021
Type of inspection	Trigger to verify compliance with the protocol, Good clinical practice (GCP), procedures and regulatory requirement.
Introduction	
General information about the sponsor and CT site	- The inspected site is a Clinical Trial Site (**Medical Research Centre of Excellence-National Research Center**) that conducts clinical studies for the sponsor (**National Research Center**) in accordance with applicable regulatory requirements and ethical standards. - PI name: **Dr\ Osama Azmy** - Activities include participant recruitment, clinical conduct, sample collection, safety monitoring, and data documentation.
Brief report on inspection activities undertaken	
Scope and limitations	
Areas inspected	- Investigational Medicinal Product (IMP) management - Pharmacy / IMP storage area
Out of scope	- Clinical operations (screening, dosing, follow-up) - Bioanalytical / laboratory facilities (if applicable) - Source documents and Case Report Forms (CRFs) - Informed Consent Process - Archiving and documentation system - Quality management system
Inspected Clinical medical research	The inspection focused on the following study: -Protocol Title: A Phase 1 Clinical Trial to Evaluate the Safety, Tolerability, and Immunogenicity of Inactivated SARS-CoV-2 Vaccine Against COVID-19 in Healthy Adults -Protocol Number: COVID_VACC_1 -Phase I - EDA Initial approval date: 09/11/2021

Type of IMP	Biological (Inactivated Vaccine)
Part 2	
1. Facilities and equipment system	
1.1. Facilities and Trial Conduct	- The site facilities relevant to the scope of the trigger inspection were reviewed. - Emergency medical support and the investigational medicinal product (IMP) storage area were re-inspected. A new emergency trolley was available at the clinical trial unit as a corrective action following the previous routine inspection dated 02 . -The IMP was stored in a dedicated, access-controlled storage room under the required storage conditions, and the refrigerator temperature was verified at the time of the inspection. However, deficiencies related to IMP storage monitoring were identified, including the absence of a daily temperature data logger and documented daily temperature records for the storage room, indicating inadequate documentation of environmental monitoring **in accordance with ICH E6(R2).** In response, the sponsor implemented corrective actions by installing a temperature data logger for continuous monitoring of the investigational medicinal product (IMP) storage area, implementing and maintaining documented daily temperature monitoring records, and assigning responsibility for routine monitoring and documentation of storage temperatures to the designated pharmacy personnel. The submitted corrective and preventive actions were reviewed by EDA and considered acceptable.
1.2. Computerized system	Electronic data capture, as CRF and randomization systems were in use.
2. Pharmaceutical Quality System	
2.1. Quality Management System	The trigger inspection was conducted to verify investigational medicinal product (IMP)-related observations identified during the previous routine inspection. Quality oversight activities focused on the evaluation of corrective actions related to IMP management and compliance with Good Clinical Practice (GCP) and applicable regulatory requirements.
2.2. SOPs and Documentation	- The documentation relevant to the scope of the trigger inspection was reviewed. - Records related to investigational medicinal product (IMP) management, including IMP storage, labeling, temperature monitoring, and accountability, were verified during the inspection. However, deficiencies were identified in the documentation supporting IMP management, including inconsistencies in IMP labeling and batch identification, as well as the absence of documented daily temperature

	monitoring records for the IMP storage area, indicating deficiencies in documentation practices and compliance with ICH E6(R2). All findings were acknowledged and fully addressed as the sponsor implemented corrective actions by correcting the investigational medicinal product (IMP) labeling and batch identification records to ensure consistency and traceability, installing a temperature data logger for continuous monitoring of the IMP storage area, and implementing documented daily temperature monitoring records. The submitted corrective and preventive actions were reviewed by EDA and considered acceptable.
2.3. Deviation Management	Deviation management was not comprehensively assessed during this trigger inspection.
2.4. CAPA System	The trigger inspection identified deficiencies requiring corrective and preventive actions (CAPA). The site was requested to investigate the root causes of the identified observations, implement appropriate corrective and preventive actions, and submit supporting documentation and a proposed implementation timeline to demonstrate compliance with Good Clinical Practice (GCP) and applicable regulatory requirements.
3. Ethics and participant Protection	
3.1. Informed Consent Process	The informed consent process was out of the scope of this trigger inspection. Therefore, no review of informed consent documentation or consent procedures was performed, as the inspection focused exclusively on investigational medicinal product (IMP)-related observations.
3.2. Ethics Committee Approval	Approvals from IRB/IEC were available: **-Supreme Council of University Hospitals:** 07/07/2021
3.3. Participant Safety	- Safety monitoring procedures were in place to ensure the protection of study participants. - Participant safety was reviewed only within the scope of the trigger inspection. Emergency preparedness was verified through inspection of the emergency equipment, and a new emergency trolley was available at the clinical trial unit as a corrective action following the previous routine inspection. - No additional participant safety aspects were assessed during this trigger inspection.
4. Personnel and Training	
4.1. Training and qualifications	Training and qualifications were not comprehensively assessed during this trigger inspection. The inspection focused on investigational medicinal product (IMP)-related observations, and no detailed review of personnel qualifications, curriculum vitae (CVs), or training records was performed.

5. Investigational Product (IMP) Management	
5.1. 1IMP handling	- IMP storage conditions, temperature monitoring, and accountability records were reviewed. - The investigational medicinal product (IMP) was stored in a dedicated, access-controlled storage room under the required storage conditions, and the storage refrigerator temperature was verified to be within the protocol-specified range at the time of the inspection. - However, deficiencies related to IMP quality and management were identified, including the presence of visible black and brown particles in unopened IMP vials, unreadable and inconsistent IMP labelling, inadequate differentiation between active vaccine and placebo, discrepancies in batch identification, manufacturing and expiry information, inadequate sealing of vial closures, and the use of identical batch numbers for different investigational products. These observations indicated deficiencies in IMP quality assurance, identification, traceability, and **compliance with GCP in ICH E6(R2)** and **applicable regulatory requirements.** In response, the sponsor implemented corrective actions by quarantining the affected IMP, investigating the identified quality defects, and replacing the affected IMP batches with correctly labelled investigational products. The IMP labelling was revised to ensure clear differentiation between the active vaccine and placebo and to provide consistent batch identification, manufacturing dates, and expiry dates. In addition, procedures were implemented to verify the physical condition, labelling, and identification of IMPs upon receipt and prior to dispensing to ensure the integrity, traceability, and quality of the investigational medicinal product. The submitted corrective and preventive actions were reviewed by EDA and considered acceptable. - Additional deficiencies related to investigational medicinal product (IMP) accountability and storage monitoring were identified, including the absence of documented evidence that the IMP was inspected upon receipt by designated study personnel and the lack of documented daily temperature monitoring records for the IMP storage area. These observations indicated inadequate verification of IMP receipt and insufficient documentation of storage condition monitoring, resulting in **non-compliance with Good Clinical Practice (GCP) requirements**. In response, the sponsor implemented corrective actions by updating the delegation of responsibilities to assign a registered pharmacist to receive the investigational medicinal product (IMP), verify its physical

	appearance upon receipt in accordance with the study protocol, and document the receipt inspection. In addition, a temperature data logger and documented daily temperature monitoring records were implemented for the IMP storage area to ensure continuous monitoring and documentation of storage conditions. The submitted corrective and preventive actions were reviewed by EDA and considered acceptable.
6. Clinical Trial Conduct	
6.1. Protocol Compliance	- Protocol compliance was assessed within the scope of the trigger inspection. The inspection focused on verifying compliance with protocol requirements related to the investigational medicinal product (IMP), including IMP receipt, storage, labelling, identification, accountability, and quality. - Deficiencies were identified in the implementation and documentation of protocol requirements governing IMP management, including inadequate verification of IMP quality upon receipt, deficiencies in IMP labelling and identification, and inadequate documentation of storage monitoring, indicating **non-compliance with the study protocol, GCP, and applicable regulatory requirements.** In response, the sponsor implemented corrective actions to ensure compliance with the protocol requirements governing investigational medicinal product (IMP) management by assigning a registered pharmacist to receive, inspect, and dispense the IMP in accordance with the study protocol, correcting deficiencies in IMP labelling and identification, implementing documented procedures for verification of IMP quality upon receipt, and establishing documented daily temperature monitoring of the IMP storage area. The submitted corrective and preventive actions were reviewed by EDA and considered acceptable.
6.2. Source Data and CRFs	-Source document and Case Report Forms (CRFs) were not reviewed during this trigger inspection. The inspection was limited to the assessment of investigational medicinal product (IMP)-related observations; therefore, no verification of participant source data or CRFs was performed.
6.3. Delegation of Duties	-Delegation of duties was reviewed only within the scope of investigational medicinal product (IMP) management. - A deficiency was identified in the delegation of pharmacy-related responsibilities, as the delegation log did not clearly assign a registered pharmacist to receive the IMP, verify its physical appearance upon receipt in accordance with the study protocol, and dispense the IMP, indicating deficiencies in the documentation and assignment of IMP-related

	responsibilities **in accordance with ICH E6(R2).** In response, the sponsor implemented corrective actions by updating the delegation log to assign a registered pharmacist responsibility for receiving the investigational medicinal product (IMP), verifying its physical appearance upon receipt in accordance with Section 13.a of the study protocol, and dispensing the IMP. The submitted corrective and preventive actions were reviewed by EDA and considered acceptable.

7. Laboratory and Bioanalytical Activities (if applicable)

- External and Internal Laboratories were used for analysis.
- Laboratory and bioanalytical activities were not assessed during this trigger inspection. The inspection was limited to the evaluation of investigational medicinal product (IMP)-related observations.

8. Safety Reporting (SAE)

Safety reporting was not assessed during this trigger inspection. The inspection focused exclusively on investigational medicinal product (IMP)-related observations; therefore, adverse event (AE) and serious adverse event (SAE) reporting procedures and documentation were not reviewed.

Part 3	**Inspection outcome**

-Based on the reviewed documentation, inspected facilities, and observations identified during the inspection:

- Based on the deficiencies identified during the trigger inspection, the clinical trial activities were suspended on 12 December 2021 till a satisfactory implementation of appropriate Corrective and Preventive Actions (CAPA). Following the sponsor's implementation of the required CAPA and verification by the Egyptian Drug Authority (EDA).
- All identified deficiencies were communicated to the site. Corrective and preventive actions (CAPA) were be implemented to address the observations.

-A follow up inspection was planned to be performed to verify implementation of these corrective and preventive action(s).

-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 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 E6r2.
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
CMC	Chemistry, Manufacturing and Controls
CRF	Case Report Form
CT	Clinical Trial
CV	Curriculum Vitae
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