GCP Inspections Metrics Report

Metrics Period: From 1/1/2024 to 31/12/2024

Report Date:

This report presents information on GCP inspections of clinical trial sites and related entities conducted between 1st January 2024 and 31 December 2024. It outlines the deficiencies identified during these inspections, with a focus on areas of non-compliance. The aim is to support clinical trial sites and applicants in enhancing their compliance with GCP guidelines and local regulations, and in preparing effectively for inspections by the Egyptian Drug Authority. The observed deficiencies are categorized into eight main areas and graded as critical, major, or minor, in alignment with the inspection frameworks of the European Medicines Agency (EMA) and other international standards.

I- Inspections Metrics:

During the period covered by this report, EDA conducted a total of 37 GCP inspections classified by Type of Inspection, Type of IMP, Study Phase, Inspection Timing, Type of Inspected Facility, Type of Clinical Trial Site, Study Sponsorship, and Geographical Region as described in Table 1 and Figures 1-7.

Table 1: Number of Conducted GCP Inspections Classified by Different Indicators.

Type of Inspection	Routine (%)	Triggered (%)	Follow up (%)			**Total number**
	37 (97%)	1(3%)	0			38
Type of IMP	**Biological**	**Pharmaceutical**	**Innovative**	**Medical Device**		
	6 (16%)	30 (79%)	1 (2.5%)	1(2.5%)		38
Study Phase	**Pre-clinical**	**Phase I**	**Phase II**	**Phase III**	**Phase IV**	
	0	20 (53%) BE	2 (5%)	10 (26%)	6 (16%)	38
Inspection Timing	**Pre-initiation**	**During the conduction**	**Post-trial**			
	0	38 (100%)	0			38
Inspected Facility	**Clinical Trial Site**	**Laboratory**	**CRO**	**Other Vendor**	**Sponsor**	
	38 (100%)	0	0	0	0	38
Type of Clinical Trial Site	**Academic Institution**	**MoH public Hospital**	**Research Center**	**NGO**	**Private Hospital**	
	7 (18%)	3 (8%)	26 (68%)	2 (5%)	0	38
Study Sponsorship	**Pharmaceutical Company**	**Investigator-Initiated Trial**				

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	36 (95%)	2 (5%)			38
Geographical Region	**Inside Cairo**	**Outside Cairo**	**Inside Egypt**	**Outside Egypt**	
	30 (79%)	8 (21%)	38 (100%)	0	38

Figure 1: Number of Conducted Inspections Classified by Inspection Type.

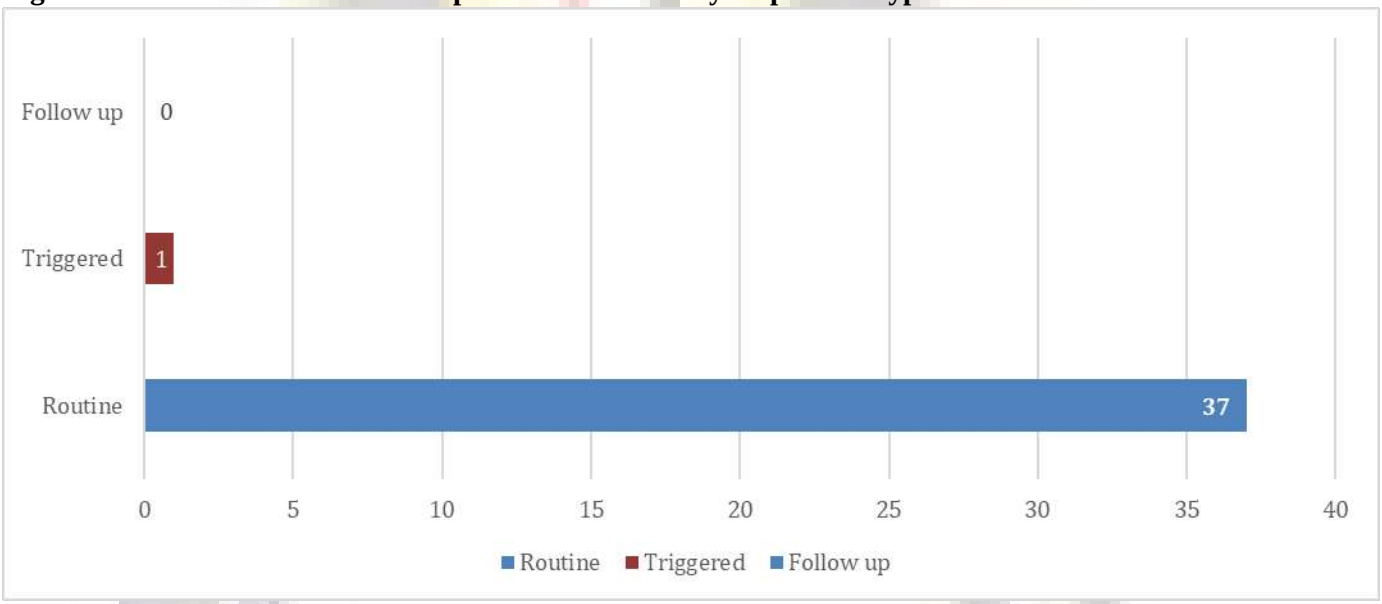

Figure 2: Number of Conducted Inspections Classified by Type of Product.

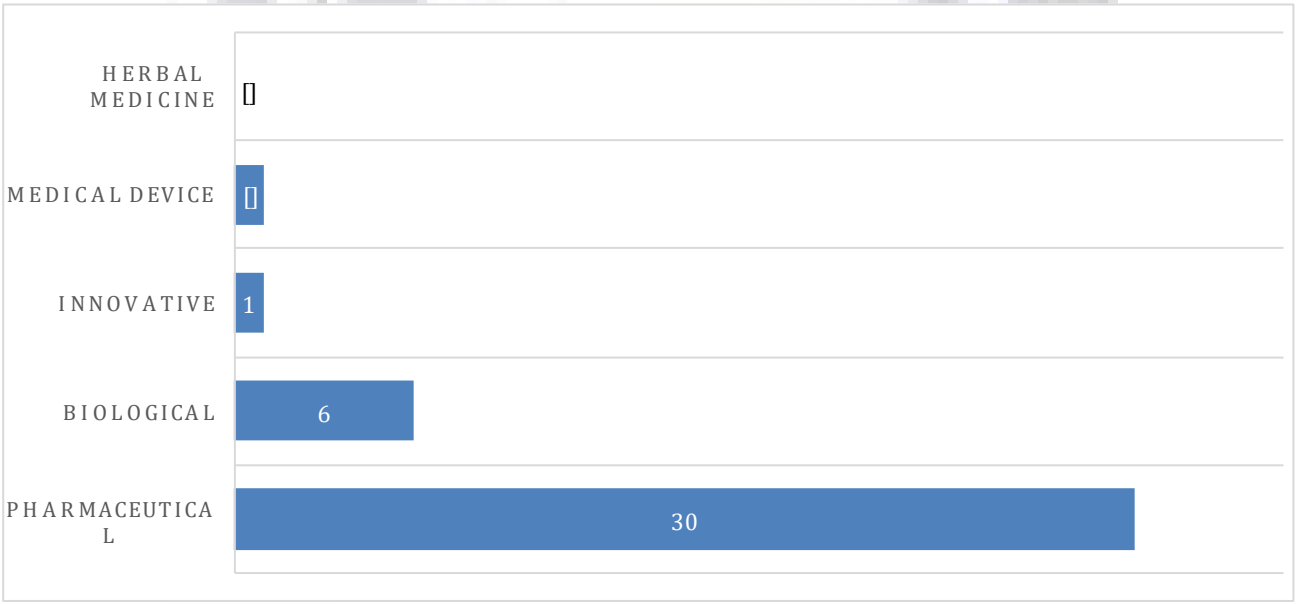

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Figure 3: Number of Conducted Inspections Classified by Study Phase.

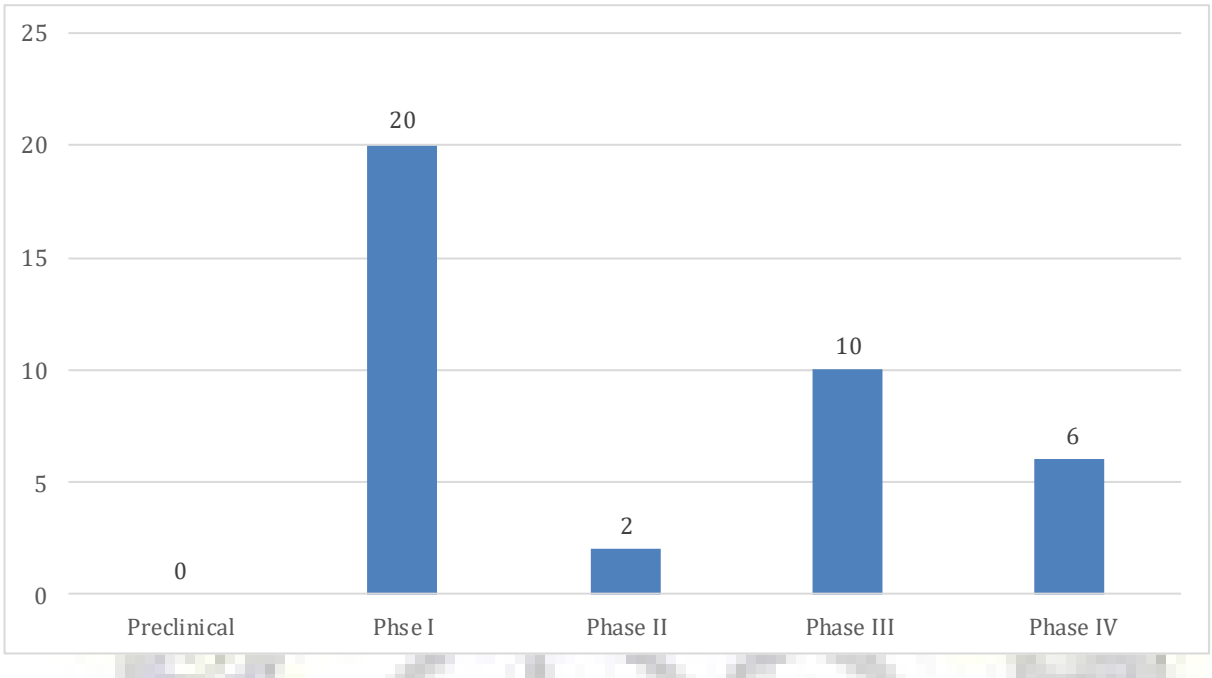

Figure 4: Number of Inspections Classified by Timing related to Study Conduction.

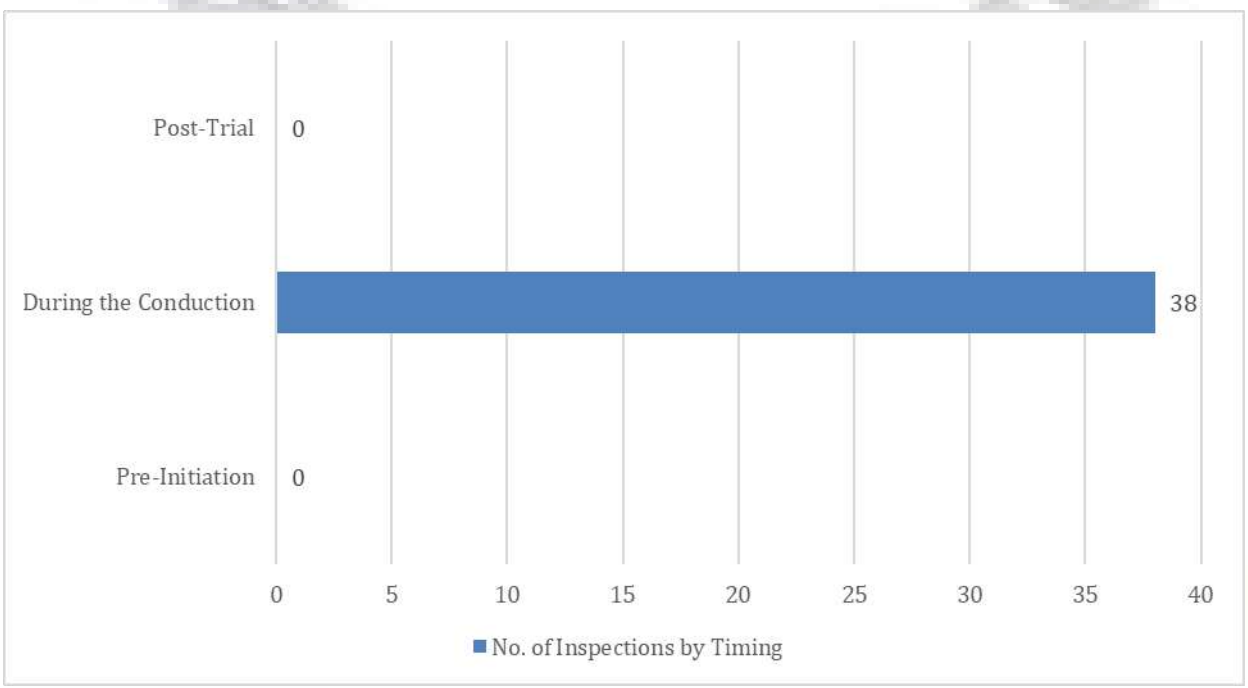

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Figure 5: Number of Inspections Classified by Inspected Facility

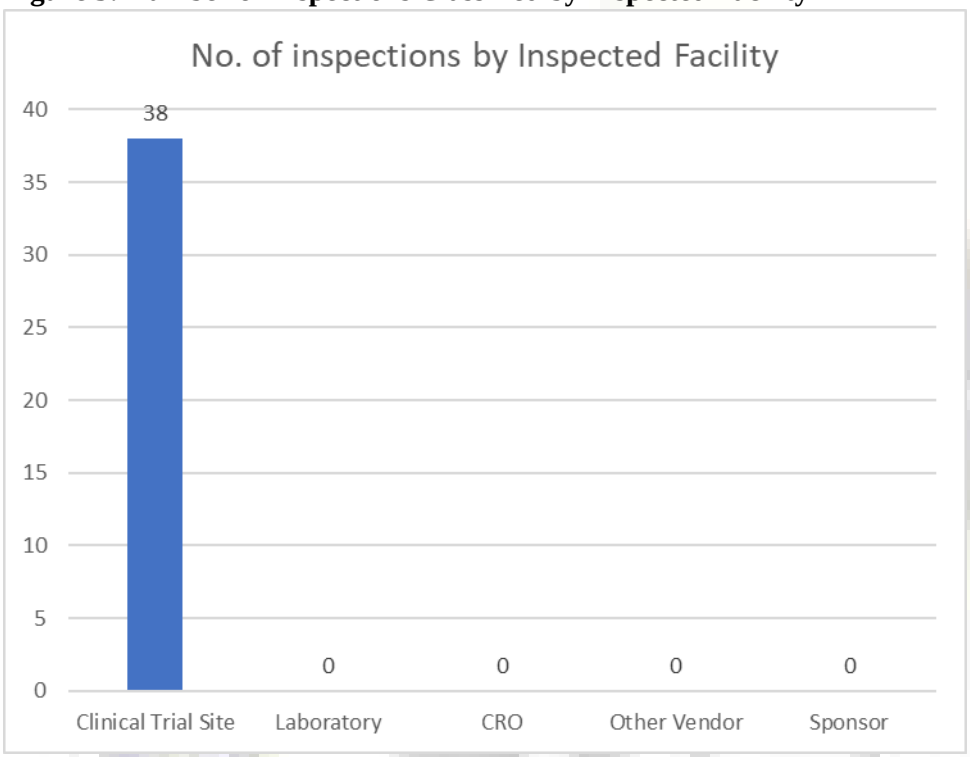

Figure 6: Number of Inspections Classified by Type of Clinical Trial Site.

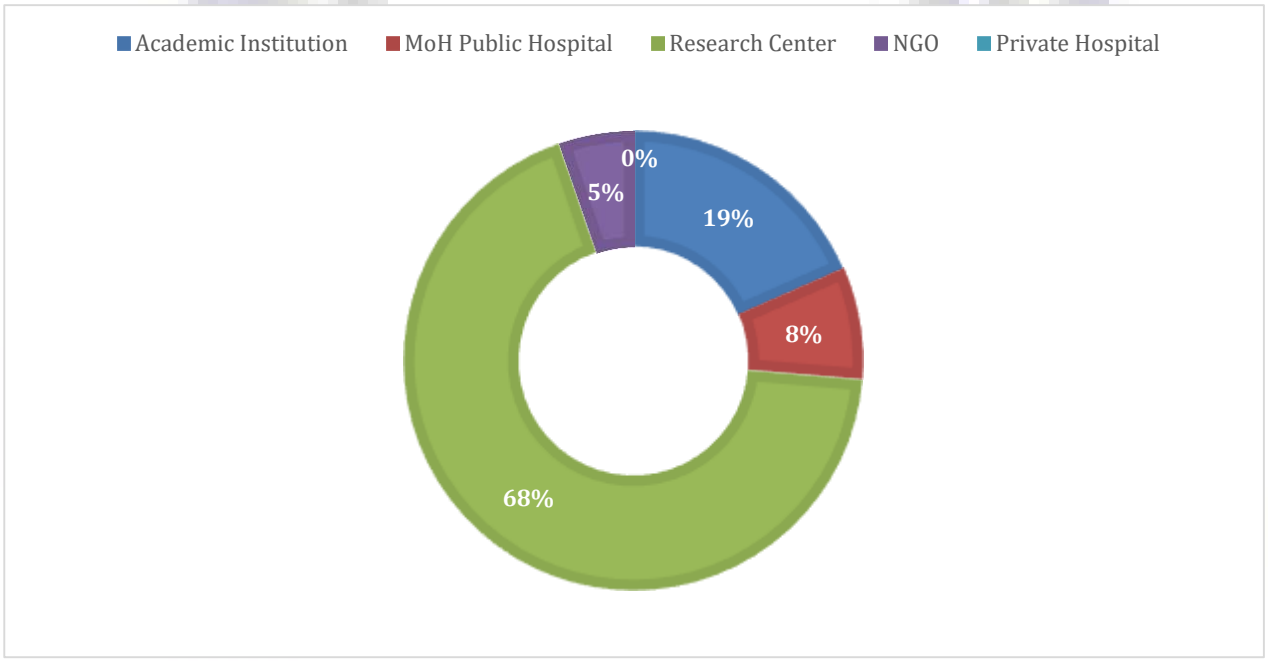

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Figure 7: Number of Inspections Classified by Study Sponsorship.

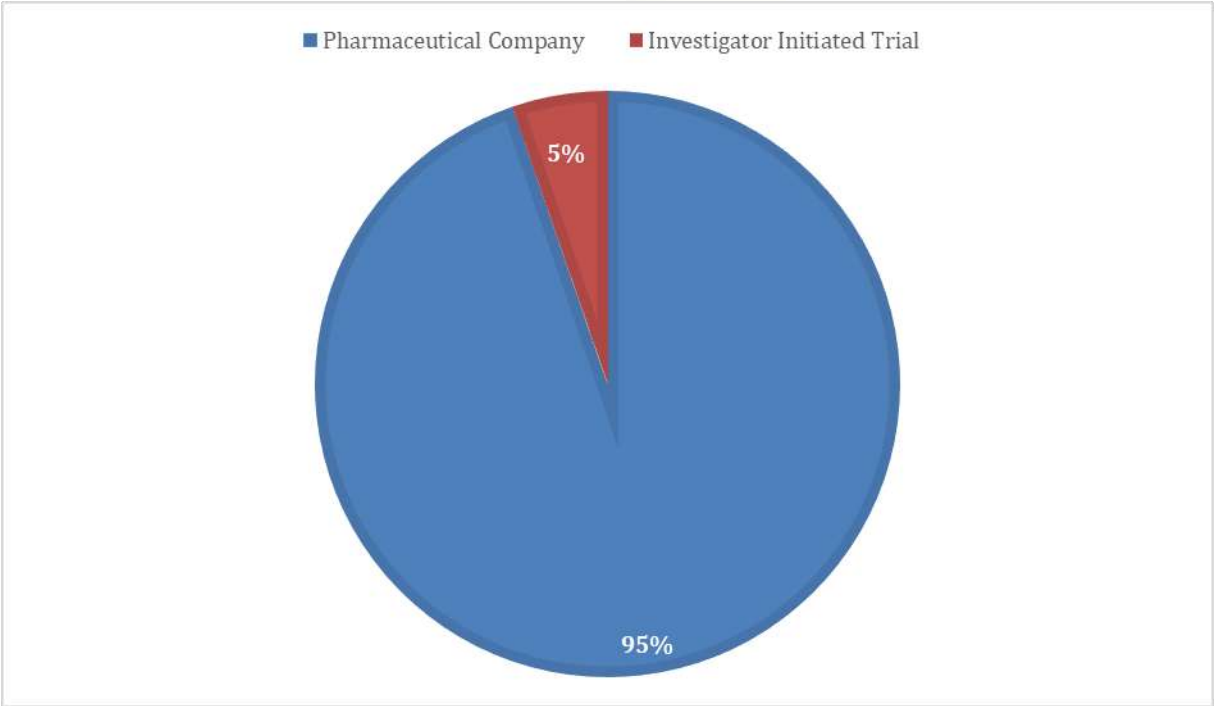
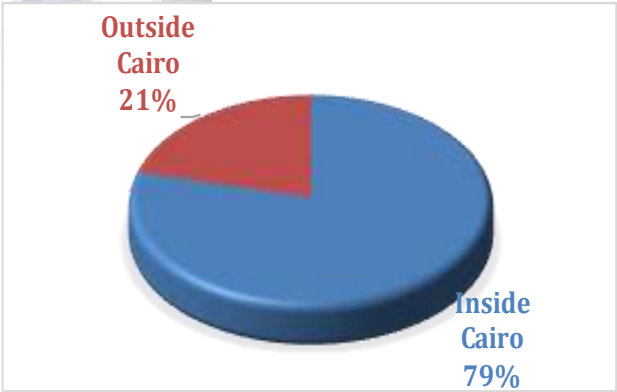


Figure 8: Number of Inspections Classified by Geographical Region.



Deficiencies addressed during the conducted inspections were identified in the 8 main categories and were graded as critical, major, or minor according to their effect on the rights, safety or well-being of the subjects and/or the quality and integrity of data. For one of the critical findings, an immediate regulatory action of suspending the enrollment of new patients was taken, while for the other one, such immediate action wasn't applicable since the study wasn't recruiting and there were no active participants at the time of the inspection. All other

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identified deficiencies were appropriately addressed by the clinical trial sites through the development of Corrective and Preventive Action Plans submitted by applicants to EDA, and all deficiencies within this reporting period have been rectified.

The number and percentage of different grades in each finding category are identified in Table 2 and presented in Figure 8.

Critical findings accounted for only 1% of the total findings, major findings accounted for 25%, and the majority (74%) were graded as minor.

The most frequently observed finding category from all conducted inspections was Trial Quality Management, representing 26% of all findings.

The modes of the finding categories for each grade (Critical, Major, Minor);

- The critical grade was observed only in two categories, namely, Protocol Compliance, as well as Trial Quality Management, representing 50% each.
- The most frequently observed finding category for major grade was Participants' Protection and Rights, representing 49% of all major findings.
- The most frequently observed finding category for minor grade was Trial Quality Management, representing 32% of all minor findings.

Table 2: Number and Grading of Identified Deficiencies by Main Category

Main Category	Critical (%)	Major (%)	Minor (%)	Total by Main Category (%)
Regulatory issues/Ethics Committee (IRB)	0 (0%)	2 (5%)	6 (5%)	8 (5%)
Investigational Medicinal Product (IMP)	0 (0%)	3 (8%)	4 (4%)	7 (5%)
Participants' Protection and Rights	0	18 (47%)	4 (4%)	22 (15.5%)
Protocol Compliance	1 (50%)	4 (11%)	11 (10%)	16 (10%)
Quality of Data/Records and Reports (Documentation)	0	1 (3%)	29 (26%)	30 (19%)
Trial Quality Management	1 (50%)	4 (11%)	35 (31%)	40 (26%)
Facility and Equipment /Laboratories/Technical Facilities	0	6 (16 %)	17 (15%)	23 (15.5%)
General and Others not listed above	0	0	6 (5%)	6 (4%)
Total	2 (1%)	38 (25%)	112 (74%)	152

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Figure 9: Summary of identified deficiencies by main categories and grades

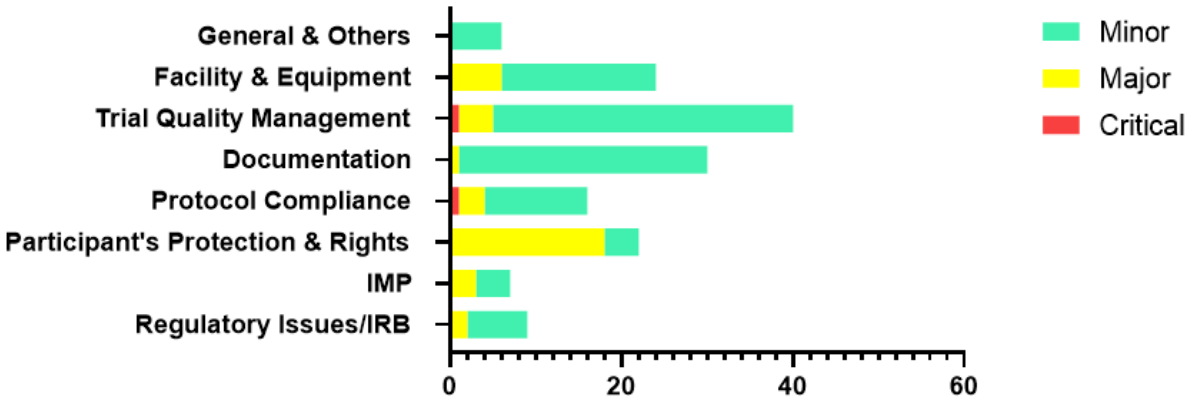
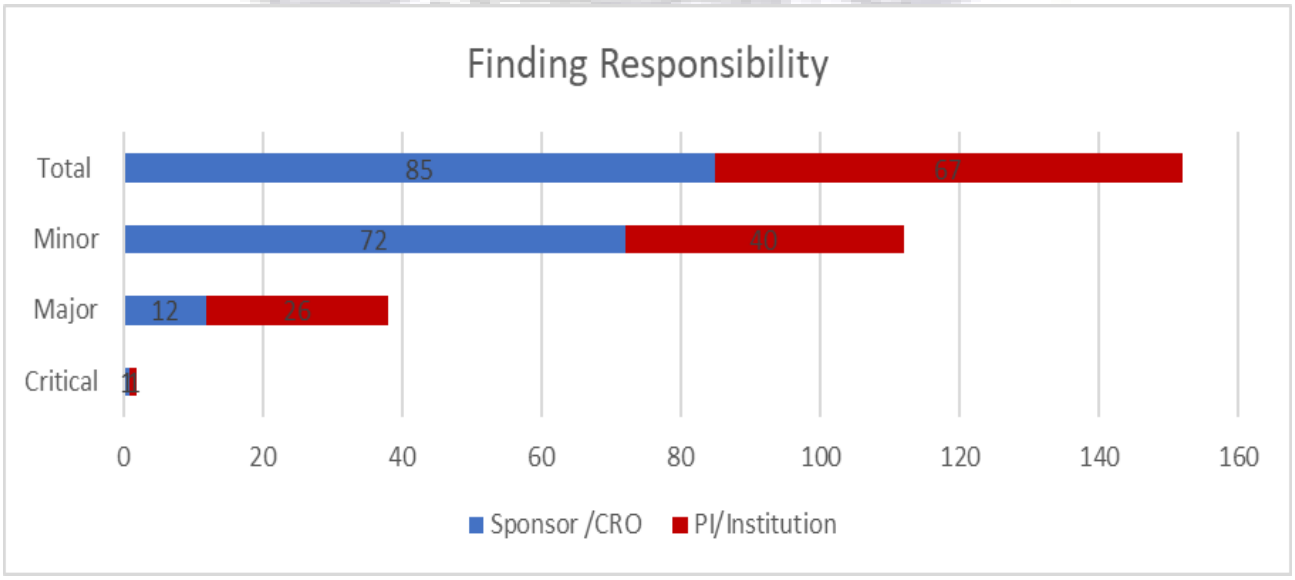


Table 3: Number of Identified Deficiencies in Each Grade by Responsibility Type.

Finding Responsibility	Critical	Major	Minor	Total
Sponsor /CRO	1	12	72	85
PI/Institution	1	26	40	67

Figure 10: Number of Identified Deficiencies in Each Grade by Responsibility Type



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The mode of responsibility type for all reported findings; most of the raised findings were under the responsibility of the CRO

The mode of responsibility type for critical grade; the raised critical findings were under the responsibility of the PI and the CRO, 1 finding each.

The mode of responsibility type for major grade; most of the major findings were under the responsibility of the Principal Investigator.

Conducted inspections covered several sites inside Cairo and various governorates outside Cairo. This part of the metrics report identifies the most frequently observed deficiency category in relation to the geographical region. The number of identified deficiencies categorized by main category and classified by geographical regions is identified in Table 4 and presented in Figure 9.

- For inspections conducted inside Cairo, the most frequently observed finding category was Trial Quality Management, representing 27% of all findings inside Cairo, followed by the finding category (Participants' Protection and Rights) and Quality of Data/Records and Reports (Documentation), representing 17% each.

- For inspections conducted outside Cairo, the most frequently observed finding category was Quality of Data/Records and Reports (Documentation), representing 31% of all findings outside Cairo, followed by Protocol Compliance and Trial Quality Management, representing 19% each.

Table 4: Number of Identified Deficiencies by Main Categories in Different Geographical Regions

Main Category	Inside Cairo	Outside Cairo
Regulatory issues/Ethics Committee (IRB)	5 (4%)	3 (12%)
Investigational Medicinal Product (IMP)	7 (6%)	0
Participants' Protection and Rights	22 (17%)	1 (4%)
Protocol Compliance	11 (9%)	5 (19%)
Quality of Data/Records and Reports (Documentation)	22 (17%)	8 (31%)
Trial Quality Management	34 (27%)	5 (19%)
Facility and Equipment /Laboratories/Technical Facilities	19 (15%)	4 (15%)
General and Others not listed above	6 (5%)	0
Total	**126 (83%)**	**26 (17%)**

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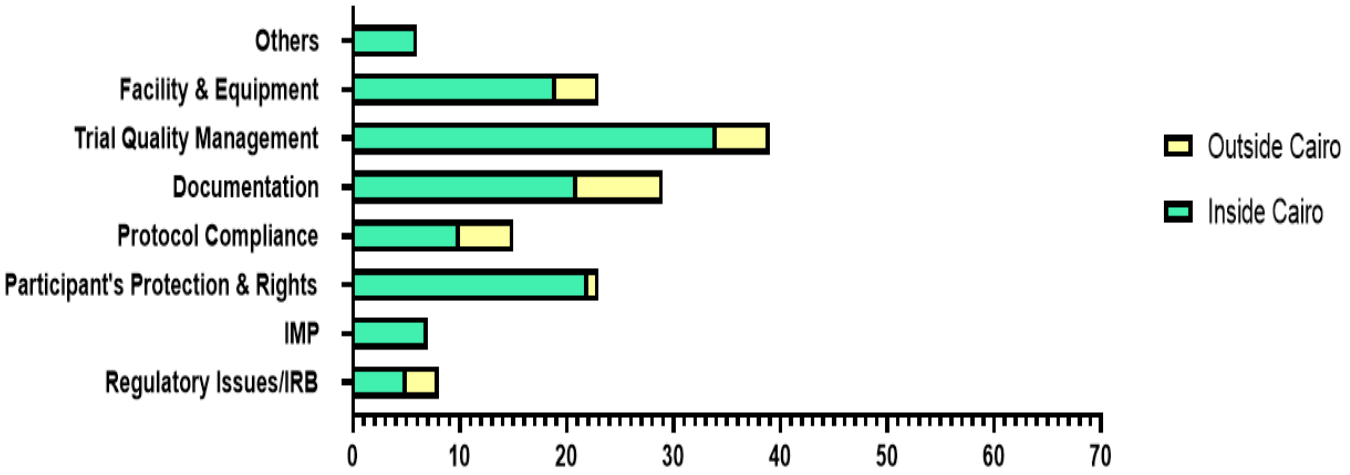
Figure 11: Identified Deficiencies by Main Category in Different Geographical Regions



For inspections conducted inside Cairo, the critical findings represented only 2% of the total findings in this geographical region, while for inspections conducted outside Cairo, no critical findings were identified. The number and percentage of findings' grades in each geographical region are identified in Table 5 and presented in Figure 10.

Table 5: Grading of Identified Deficiencies in each Geographical Region

Geographical Region	Critical	Major	Minor	Total
Inside Cairo	2 (2%)	36 (28%)	88 (70%)	126
Outside Cairo	0	2 (8%)	24 (92%)	26
Total	2	38	111	152

Figure 12: Grading of Identified Deficiencies in each Geographical Region

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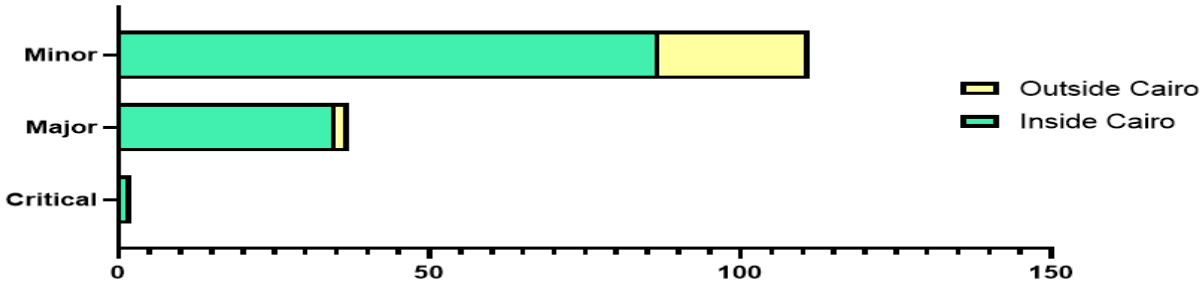

Conclusions Drawn from Identified Metrics:

- The number of conducted inspections has increased significantly compared to the last year as a result of including Bioequivalence Studies in the scope of the GCP inspection. This included 20 inspections on Bioequivalence Centers along with 17 inspections on Clinical Research Sites.
- All of the conducted inspections were routine and were carried out during the conduction of the clinical trial. No inspections were conducted at the pre-initiation stage or after the end of the clinical trial during this year. However, the SOP for GCP inspections planning is updated to include the involvement of pre-initiation inspection as well as post-trial inspections according to risk-based criteria
- All of the inspections were conducted on clinical research sites in the year 2024; however, the GCP inspection scope involves other related entities, according to the Law of regulating Clinical Trials 214/2020 and its Executive Regulation 927/2022, based on risk criteria.
- Most of the inspected sites were research centers as a result of including the Bioequivalence Centers in the scope of the GCP inspection conducted by the Administration of Protocols and Studies Follow-up. Regarding inspections conducted on clinical trials, most of the sites were affiliated to academic institutions indicating that the majority of sites involved in clinical trials in Egypt belong to this type of institution.
- Most of the inspections were carried out on clinical trials sponsored by pharmaceutical companies, since most of the clinical trial applications submitted to the Egyptian Drug Authority are sponsored by pharmaceutical companies rather than being investigator-initiated.
- Most of the inspections were inside Cairo, and this is also driven by the BE Centers that the majority of which are located inside Cairo. No inspections were conducted outside Egypt in 2024.
- Critical findings accounted for only 1% of the total findings, while most of the identified deficiencies (75%) were graded as minor, indicating a high level of compliance with GCP as well as local regulations and providing confidence in the quality of clinical trials conducted in the Arab Republic of Egypt.
- Critical findings were identified in the Protocol Compliance and Trial Quality Management categories. The critical grading in the category protocol compliance was a

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result of 6 major findings in the same category, raised to critical. In that inspection, no immediate action was taken regarding the conduct of the trial since at the time of the inspection there were no active sites in the trial (one site was closed, one site was in closing, and in the third site the enrollment was halted and there were no active participants). However, the inspection report was presented to the Scientific Committee, which decided that the results collected during the study couldn't be relied on. Concerning the critical finding in the Trial Quality Management category, this was raised due to the lack of documented evidence of the randomization process to be verified during the inspection to ensure that the treatment allocation was free from selection bias, as a result, a regulatory action was immediately taken to suspend screening and enrollment of any new patients including those in the screening phase while continuing the study drug administration and conducting follow-up visits to the already enrolled patients and the enrollment in the study is still suspended till the date of this report until the complete resolution of the issue.

- In one of the follow-up inspections performed in 2023, a finding was raised that after preliminary investigations was found to likely affect the subject's right and safety. Accordingly, a decision of trial suspension was taken in 2024, immediately followed by trigger inspection to further investigate the finding of concern. Later on, after insuring applying good clinical practice principles and complying with the Egyptian clinical trials law concerning the rights of the subjects, a decision was made of study resumption.
- Participants' Protection and Rights was the most commonly observed finding category for the major grade, primarily because Bioequivalence Centers were not aware of the GCP principles pertaining to the consenting procedure. As a result, during the inspections, knowledge about these principles were disseminated. In addition, a workshop will be held to make sure that all centers understand local laws and GCP principles.
- While most of its findings were graded as minor, the finding category, Trial Quality Management, represented a key area of non-compliance that requires improvement. This was mainly identified in inspections conducted on Bioequivalence Centers.
- Trial Quality Management was the most frequently observed category inside Cairo, and Quality of Data/Records and Reports (Documentation) was the most observed outside Cairo.

II- Inspection Findings:

This section of the report provides details on the inspection findings within each main category with highlighting the most relevant sections from ICH E6 (R2), other international guidelines, and applicable local regulations. Critical findings were identified in 2 main categories: Protocol Compliance and Trial Quality Management. The Trial Quality Management category was a key area of non-compliance that represented approximately 26% of total findings.

Regulatory Issues/ Ethics Committee (IRB)

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The applicant should adhere to the local regulations pertinent to clinical trials conduction in Egypt as stipulated in the Clinical Trials Law 214/2020, Executive Regulations 927/2022, and the Guideline for Good Regulatory Oversight of Clinical Trials by the Egyptian Drug Authority. All these regulations are published on the EDA website to be available for applicants.

Examples of findings by the sub-category include:

1- **Amendment Approvals:**

- The implemented protocol version and the used laboratory weren't granted full approval from all related entities.
- The delegated study Co-I is different from that approved by EDA, and this change wasn't notified as a non-substantial amendment to EDA before being implemented.
- The version of the pharmacy manual filed in the Investigator's Site File (ISF) was different from that submitted to and approved by EDA, and this updated version wasn't notified to EDA.
- The IRB approval for the study wasn't dated to ensure that all study documents were used and all study activities were initiated after approval of the IRB.

Guideline for Good Regulatory Oversight of Clinical Trials by Egyptian Drug Authority 7.3.4
The applicant should notify EDA of any changes to the approved protocol or its related documents.

ICH-GCP E6 (R2), Section 4.4.1:
Before initiating a trial, the investigator/institution should have written and dated approval/favourable opinion from the IRB/IEC for the trial protocol, written informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), and any other written information to be provided to subjects.

2- **Importation Authorization:**

- The importation license of the Test Product was not found in the SMF.

Investigational Medicinal Product

Clinical trials often involve the use of unapproved therapeutic goods, which have not been registered for use in Egypt or other countries and for which there is limited information. IMP-related actions from IMP receipt to return/destruction are expected to be documented in relevant records, including shipping records, IMP accountability logs, IMP return records, or destruction certificates. Management of the IMP at the site must follow strict procedures to mitigate the risks and ensure compliance with ICH GCP E6 (R2) and local regulations.

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ICH GCP E6 (R2) section 4.6 outlines the site's responsibilities relating to the management of IMP from receipt, through prescription, dispensing, accountability, treatment compliance, to return to sponsor and destruction.

Examples of findings by the sub-category include:

1- Manufacturing/Packaging/Labeling

- The IMP label was missing the information required according to the local regulation.

Egyptian guideline for conducting bioequivalence studies for marketing authorization of generic products, Year 2023 Version No: 3 (Issue Date: 17/07/2023):
"Each label should include the following information:
- Name of the sponsor,
- Study number,
- Batch number,
- Subject identification number (to which the product is destined to be given to),
- Period,
- Active ingredient and dosage,
- The storage conditions,
- Expiry date (month/year) or retest date, Identification of the product (test or reference).

2- Supply/Storage/Retrieval/Destruction

- There was no evidence of maintaining the appropriate conditions during the transport of the IMP

ICH-GCP E6 (R2) Section 4.6.4
The investigational product(s) should be stored as specified by the sponsor and in accordance with applicable regulatory requirement(s).

ICH-GCP E6 (R2) Section 5.13.2
The sponsor should determine acceptable storage temperatures, storage conditions (e.g., protection from light) and shelf life for the investigational product(s), appropriate reconstitution fluids and procedures, and devices for product administration, if any. The sponsor should inform all involved parties (e.g., monitors, investigators, pharmacists, storage managers) of these determinations.

Participants' Protection and Rights

Clinical trials are often conducted using unapproved therapeutic goods with an unknown safety profile. All parties are responsible for the protection of trial participants when conducting and overseeing a clinical trial. Informed consent is a main element of participant

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protection. Informed consent is obtained following a discussion between the participant and the medically qualified site staff and is documented by the signing of the consent form by both parties.

According to ICH GCP E6(R2) section 1.28, Informed Consent is a process by which a subject voluntarily confirms their willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form.

Examples of findings by the sub-category include:

1- **Personal Data Protection**

- The participant's names were recorded on the IMP boxes/Bottles, and according to the protocol, the used IMP Boxes/Bottles may be returned to the sponsor for destruction, which implies disclosure of the participant's personal data to the sponsor

ICH-GCP E6 (R2) Section 2.11.
The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).

2- **Informed Consent Process:**

- There were two ICFs in the participant's file, one of which wasn't personally signed and dated by the participant, instead, the participant's name and signature were filled in by the Co-I.
- There was no impartial witness during the consenting process, although the study volunteer was illiterate.
- The study volunteers didn't receive a copy of the signed and dated ICF
- The ICFs weren't personally dated by the study volunteers, instead, they were electronically dated.
- Screening procedures and laboratory tests were performed before consenting of the study volunteers.
- The ICF wasn't signed by the legal representative, although the volunteer is less than 21 years old (The age of Majority according to the local regulations).

ICH-GCP E6 (R2) Section 4.8.8.
Prior to a subject's participation in the trial, the written informed consent form should be signed and personally dated by the subject or by the subject's legally acceptable representative, and by the person who conducted the informed consent discussion.

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ICH-GCP E6 (R2) Section 4.8.1.
In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirement(s), and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. Prior to the beginning of the trial, the investigator should have the IRB/IEC's written approval/favourable opinion of the written informed consent form and any other written information to be provided to subjects.

Clinical Trials Law 214/2020 Chapter 1 Article 1, Definition of Informed Consent Executive Regulation 927/2022 Article 3 Point 4
An informed consent shall be obtained from each one of the research subjects; if the clinical research is conducted on one of the vulnerable groups that deserve an additional protection, an informed consent shall be obtained from their parents; in the event of the death of one or both parents, an informed consent shall be obtained from the person who had the right of tutelage or guardianship or from the legal representative.

Protocol Compliance:

Protocol compliance is expected from all parties involved in the trial conduct, and it is verified at multiple levels via clinical trial monitoring, quality management, quality assurance (e.g. audits) and regulatory inspections. Trials with multiple deviations from the approved protocol and procedures pose risks to the participants and may jeopardize the quality of the data generated in a trial.

ICH GCP E6 (R2) section 1.44 defines protocol as a document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial.
ICH GCP E6 (R2) section 2.6 states that a trial should be conducted in compliance with the protocol that has received prior ethics committee approval.
ICH GCP E6 (R2) section 4.5 outlines the requirements of trial conduct in compliance with the protocol.

Examples of findings by the sub-category include:

1- Eligibility Criteria

- One participant was enrolled in the study despite meeting one of the protocol exclusion criteria
- The Nerve Conduction Study (NCS) report date was after the date of randomization, although it is one of the screening tests that should be conducted before randomization according to the study protocol.
- The age of the participant was older than 64 at the time of the consent, although the inclusion age is 18 to ≤64 according to the study protocol

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- None of the protocol-specified screening data or procedures, except some laboratory tests, were collected or performed in the screening visit.
- The blood pressure measurement during the screening was not performed according to the protocol-specified method, as evidenced by the source documents.
- The laboratory tests of another study were used for screening in the current study, although they were performed more than 14 days before enrollment, which is non-compliant with the protocol requirements.
- None of the protocol-specified screening data or procedures, except laboratory tests or only the HbA1C test, were collected or performed in the screening visit as stated by the Co-I.
- In The participant's "medical history" section in the CRF, it is recorded that the Participant had **lung cancer tumor** for six months and **still ongoing**, there aren't any details mentioned regarding the stage & the grade of the cancer tumor; these are critical information to determine whether this subject meets the exclusion criterion of (terminal malignancy) as per the protocol.

2- **Recording in CRF/eCRF/Diaries/Questionnaires**

- Some of the study questionnaires were not completed due to internet connectivity issues.

3- **IMP Prescription/Administration/Compliance**

- According to the treatment administration times recorded in the patients' diaries, the participants didn't take their study treatment in the clinic on visit days as required by the study protocol
- The participant wasn't advised to take the study IMP with food as required by the study protocol.

ICH-GCP E6 (R2) Section 4.5.1.
The investigator/institution should conduct the trial in compliance with the protocol agreed to by the sponsor and, if required, by the regulatory authority (ies) and which was given approval/favorable opinion by the IRB/IEC

Quality of Data/Records and Reports (Documentation)

Clinical trial conduct is documented in multiple records defined by the trial sponsor and the site. The records may include source documentation such as participants' medical records, signed forms, laboratory and imaging results, logs, study files and other records. The trial documentation describes the details of the trial conduct at the site. It is maintained throughout the trial and archived for at least 5 years following the completion of a clinical trial according to local regulations.
The documentation allows for reconstruction of the trial conduct while it is ongoing and after its completion when the site personnel may no longer be available to answer any questions.

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The quality, integrity and reliability of clinical trial data is critical to the acceptability of the clinical trial outcome by regulatory authorities.

Examples of findings by the sub-category include:

1- **Consistency of CRF data with source documents:**

- The eCRF for some participants wasn't filled with the results of some laboratory tests

ICH-GCP E6 (R2) Section 4.9.2
Data reported on the CRF, that are derived from source documents, should be consistent with the source documents or the discrepancies should be explained.

2- **Source documents:**

- There was no description of the consenting process in the participants' source documents.
- The Communication attempts made by the site to follow up with lost participants were not sufficiently documented (the source documents did not provide the number of communication attempts or the dates).
- The Subject screening/failure log, subject enrolment and status log, and subject identification log were not signed by the PI.
- There was no documentation of the concomitant medications taken in some patients' files.
- There was no description of the consenting process or any other patient's notes in the source documents
- There was a discrepancy in the reason for the screening failure between the screening log and the participant's source documents.
- For one participant, the medical history, demographics, and concomitant medication information were not documented by the PI in the source documents.
- The original entry of a typing error in the date of one of the source documents was obscured
- The lab report of the screening stool analysis wasn't filed in the participant's file and was verified electronically by the inspectors
- There were several overwriting in the source documents.
- Source documents and some documents in the site master file, such as the Participant Screening Log and Participant Identification Log, included overwriting. In addition, the source data were hardly legible.
- The date of appendectomy surgery undergone by the volunteer was not specified in the source documents to ensure compliance with the protocol exclusion criteria.

ICH-GCP E6 (R2) Section 4.9.0

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The investigator/institution should maintain adequate and accurate source documents and trial records that include all pertinent observations on each of the site's trial subjects. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (e.g., via an audit trail).

3- Essential Documents according to ICH E6 (GCP):

- EDA renewal approval was not filed in the SMF
- The CV, GCP certificate, training records, confidentiality agreement, and conflict of interest disclosure statement for the Co-I were not filed in the ISF.
- There was no protocol deviation log established for the study.
- The last updated DSUR wasn't filed in the ISF
- Neither the originals nor certified copies of some site's IRB approvals were filed in the ISF
- The delegation log was not updated (The delegation end date, of some study personnel who are not involved in the study anymore was not included in the delegation log).
- The CVs of all nurses involved in the study, except for one, were not available for verification

ICH-GCP E6 (R2) Section 8.1

Essential Documents are those documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor, and monitor with the standards of Good Clinical Practice and with all applicable regulatory requirements. Essential Documents also serve a number of other important purposes. Filing essential documents at the investigator/institution and sponsor sites in a timely manner can greatly assist in the successful management of a trial by the investigator, sponsor and monitor. These documents are also the ones which are usually audited by the sponsor's independent audit function and inspected by the regulatory authority(ies) as part of the process to confirm the validity of the trial conduct and the integrity of data collected.

Trial master files should be established at the beginning of the trial, both at the investigator/institution's site and at the sponsor's office. A final close-out of a trial can only be done when the monitor has reviewed both investigator/institution and sponsor files and confirmed that all necessary documents are in the appropriate files. Any or all of the documents addressed in this guideline may be subject to, and should be available for, audit by the sponsor's auditor and inspection by the regulatory authority(ies).

Trial Quality Management

Clinical trial management is an important aspect of clinical trial conduct. Trial management includes careful planning of clinical trial sites' participation in a clinical trial to ensure compliance with the requirements, including proactive identification, assessment, and monitoring of the risks associated with trial conduct.

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Examples of findings by the sub-category include:

1- **SOPs:**

- The site didn't have an SOP for safety reporting.
- Site's SOPs for the clinical part were not available as signed and stamped (authenticated) hard copies for verification at the inspection time
- The ICF and CRF templates & protocols didn't have a version number or date.
- The IRB approval didn't include the version number and date of the ICF and the CRF.

ICH-GCP E6 (R2) Section 5.1.1.
The sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs to ensure that trials are conducted and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirement(s)

2- **Data Management:**

There was no documented evidence of the randomization process to be verified during the inspection to ensure that the treatment allocation was free from selection bias.

3- **Organization and Personnel:**

- The PI and Co-Is' GCP certificates were not obtained from a certified entity in GCP training.
- Neither the PI nor the Co-I (although delegated to maintain essential documents according to the Authorization Form) had access to the archiving cupboard, and it was limited to the study's Coordinator only. The PI didn't have access to the IMP storage room, and it was limited to the site's pharmacist only. This limited access may hinder the proper and timely conduct of study-related activities in case of unexpected unavailability of the primary person due to any reason, while having backups will mitigate risks of disruptions to the trial's main activities
- There were no protocol-specific training records for the study staff
- As evidenced by the signature in the study source documents, one of the study staff was performing vital signs monitoring although he has no medical background, and although, according to the delegation log, he is only authorized to perform clinical sit administrative arrangements and to complete relevant parts in SMF
- The start and end dates of the delegation were not specified for each study person.
- According to the delegation log, the screening of volunteers and ECG performing were assigned, among others, to persons with non-medical background.

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- No GCP certificates were available for study personnel

ICH-GCP E6 (R2) Section 4.2.3:
The investigator should have available an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.

ICH-GCP E6 (R2) Section 4.2.4:
The investigator should ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product(s), and their trial-related duties and functions.

ICH-GCP E6 (R2) Section 4.1.5. The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.

ICH-GCP E6 (R2) Section 5.18.4
Verifying that the investigator and the investigator's trial staff are performing the specified trial functions, in accordance with the protocol and any other written agreement between the sponsor and the investigator/institution, and have not delegated these functions to unauthorized individuals.

4- **Trial Monitoring:**

- There was no documented evidence for study monitoring during the transition phase of changing the responsible CRO**.**

ICH-GCP E6 (R2) Section 5.18.3
The sponsor should ensure that the trials are adequately monitored. The sponsor should determine the appropriate extent and nature of monitoring. The sponsor should develop a systematic, prioritized, risk-based approach to monitoring clinical trials.

Facility and Equipment/Laboratories/Technical Facilities

Examples of findings by the sub-category include:

1- **Calibration:**

- There was no evidence for calibration of the used equipment (ECG, sphygmomanometer, and weight balance used for determining body weight-based dose of IMP). The equipment had neither a label including its Serial Number and calibration dates nor a calibration certificate in the SMF.

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- The labels on the used equipment (vital monitor, data logger) didn't include a calibration date or due date.

ICH-GCP E6 (R2) Section 5.18.4.
Monitor's responsibilities
The monitor(s) in accordance with the sponsor's requirements should ensure that the trial is conducted and documented properly by carrying out the following activities when relevant and necessary to the trial and the trial site:
b) Verifying that the investigator has adequate qualifications and resources and remain adequate throughout the trial period, **that facilities, including** laboratories, **equipment, and** staff, **are adequate to safely and properly conduct the trial and remain adequate throughout the trial period.**

2- **Accreditation:**

- The laboratory used in the study for the analysis of lab result was not accredited.

ICH-GCP E6 (R2) Section 8.2.12
MEDICAL/LABORATORY/TECHNICAL PROCEDURES /TESTS - certification or - accreditation or - established quality control and/or external quality assessment or - other validation (where required) to document competence of facility to perform required test(s), and support reliability of results.

3- **Waste Disposal**

- There were no disposal containers colored according to the international color-coding system in the IMP administration room.

Safe management of wastes from health care activities WHO/FWC/WSH/17.05 World Health Organization 2017

Others:

- The Emergency trolley didn't include emergency medications such as: Epinephrine and Atropine Amp

Conclusion
The 2024 GCP Inspections Metrics Report demonstrates a significant advancement in the oversight and quality assurance of clinical trials conducted in Egypt. The inclusion of Bioequivalence Centers in the inspection scope and the increased number of inspections reflect the Egyptian Drug Authority's (EDA) commitment to upholding international standards and local regulations.
The majority of identified deficiencies were minor, with critical findings constituting only 1% of all observations—an indicator of a generally high level of compliance with GCP and national

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requirements. Most critical and major findings were related to protocol compliance, trial quality management, and participants' protection and rights, highlighting areas that require ongoing attention and targeted training, particularly in informed consent processes and documentation standards.

The implementation of corrective and preventive action plans by clinical trial sites has effectively addressed all deficiencies identified during this period. The planned expansion of inspection timing to include pre-initiation and post-trial phases, as well as continued emphasis on risk-based inspection strategies, will further strengthen the regulatory framework and enhance participant safety and data integrity.

In conclusion, the findings of this report underscore the progress made in clinical trial governance in Egypt, while also identifying key areas for continuous improvement. Ongoing education, robust quality management systems, and adherence to evolving international guidelines will be essential to maintaining and advancing the quality and credibility of clinical research in Egypt.

Abbreviations:

BE: Bioequivalence
CRO: Contract Research Organization
EDA: Egyptian Drug Authority
EMA: European Medicine Agency
GCP: Good Clinical Practice
ICF: Informed Consent Form
ICH: International Council of Harmonization
IMP: Investigational Medicinal Product
IRB: Institutional Review Board
ISF: Investigator Site File
MoH: Ministry of Health
NCS: Nerve Conduction Study
NGO: Non-Governmental Organization
PI: Principal Investigator
SOP: Standard Operating Procedure

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