GCP Inspections Metrics Report

Metrics Period: From 01/01/2025 to 31/12/2025
Report Date:

This report provides an overview of GCP inspections conducted at clinical trial sites, including bioequivalence entitys, between 1 January and 31 December 2025. It highlights the deficiencies identified during these inspections, with a focus on areas of non-compliance. The report aims to support clinical trial sites and applicants in improving compliance with GCP guidelines and applicable local regulations, as well as in preparing effectively for inspections by the Egyptian Drug Authority. Identified deficiencies are categorized into eight main areas and classified 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 62 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
	59 (95%)	2 (3%)	1 (2%)			62
Type of IMP	**Biological**	**Pharmaceutical**	**Innovative**	**Medical Device**	**Herbal medicine**	
	13 (21%)	47 (76%)	1 (2%)	1 (2%)	0	62
Study Phase	**Pre-clinical**	**Phase I**	**Phase II**	**Phase III**	**Phase IV**	
	0	30 (48%) BE	3 (5%)	23 (37%)	6 (10%)	62
Inspection Timing	**Pre-initiation**	**During the conduction**	**Post-trial**			
	1 (2%)	49 (79%)	12 (19%)			62
Inspected	**Clinical Trial**	**Laboratory**	**CRO**	**Sponsor**	**Other**	

Facility	**Site**				**Vendor**	
	62 (100%)	0	0	0	0	62
Type of Clinical Trial Site	**Academic Institution**	**MoH Public Hospital**	**Research Entity**	**NGO**	**Private Hospital**	
	20 (32%)	4 (6%)	37 (60%)	1 (2%)	0	62
Study Sponsorship	**Pharmaceutical Company**	**Investigator-Initiated Trial**				
	60 (97%)	2 (3%)				62
Geographical Region	**Inside Cairo**	**Outside Cairo**	**Inside Egypt**	**Outside Egypt**		
	39 (63%)	23 (37%)	62 (100%)	0		62

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

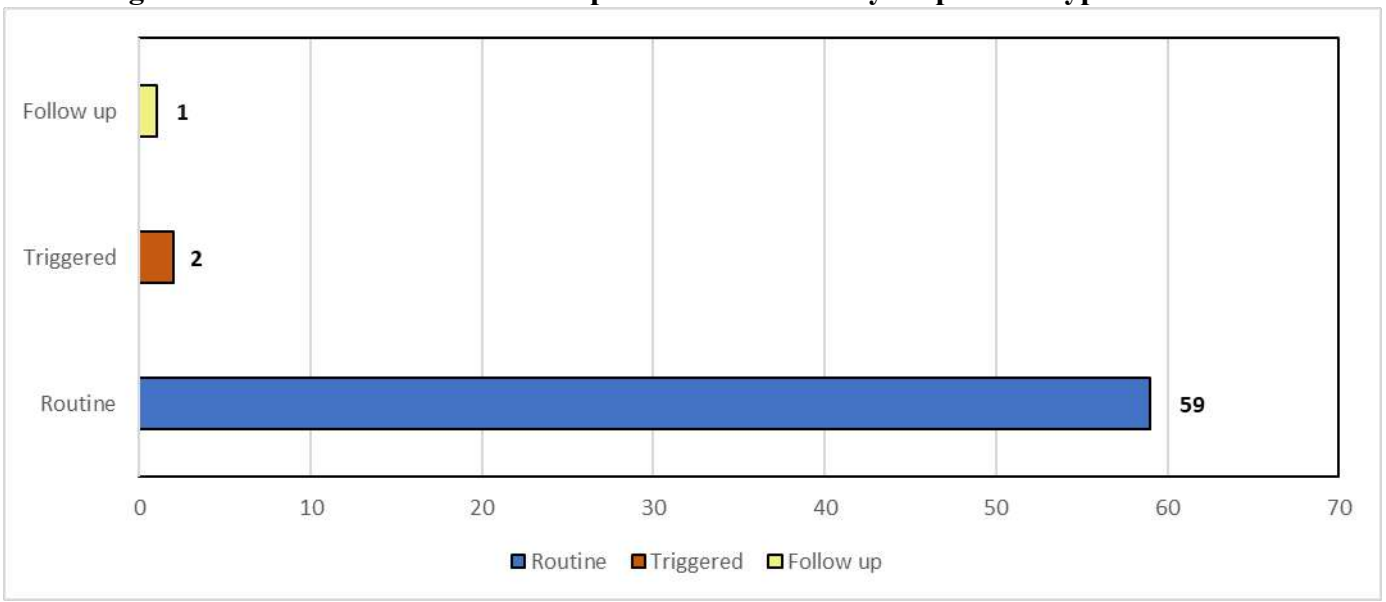


Figure 2: Number of Conducted Inspections Classified by Type of IMP.

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

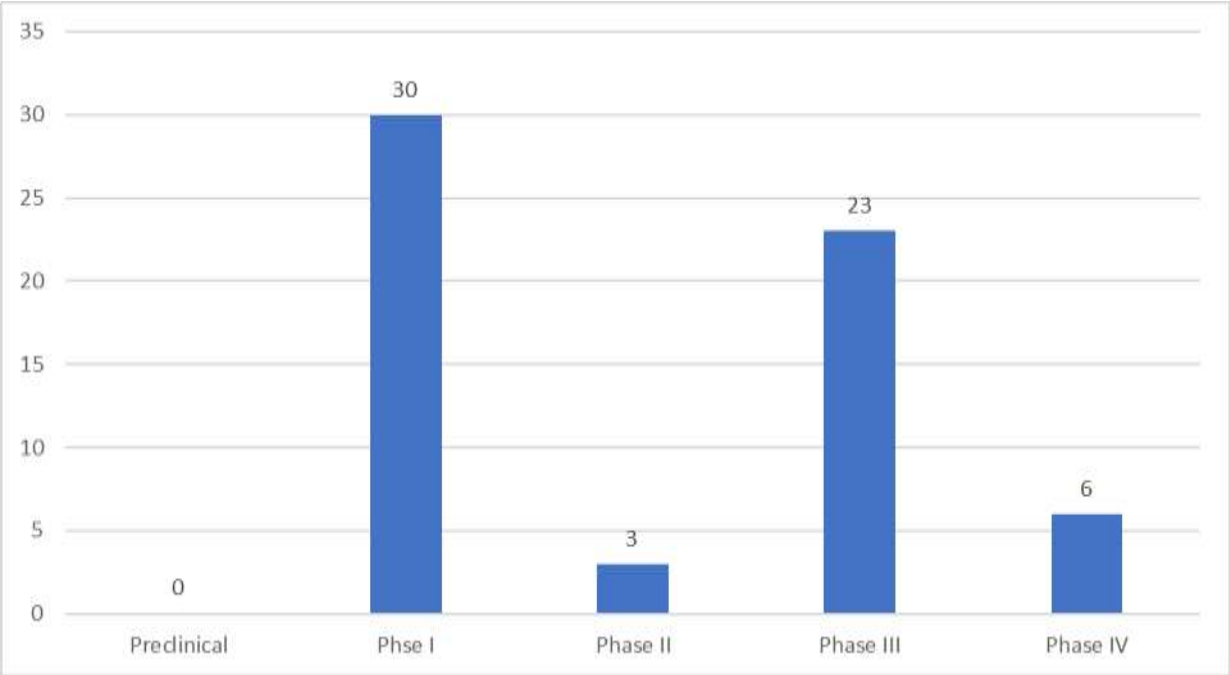


Figure 4: Number of Inspections Classified by Timing Related to Study Conduction.

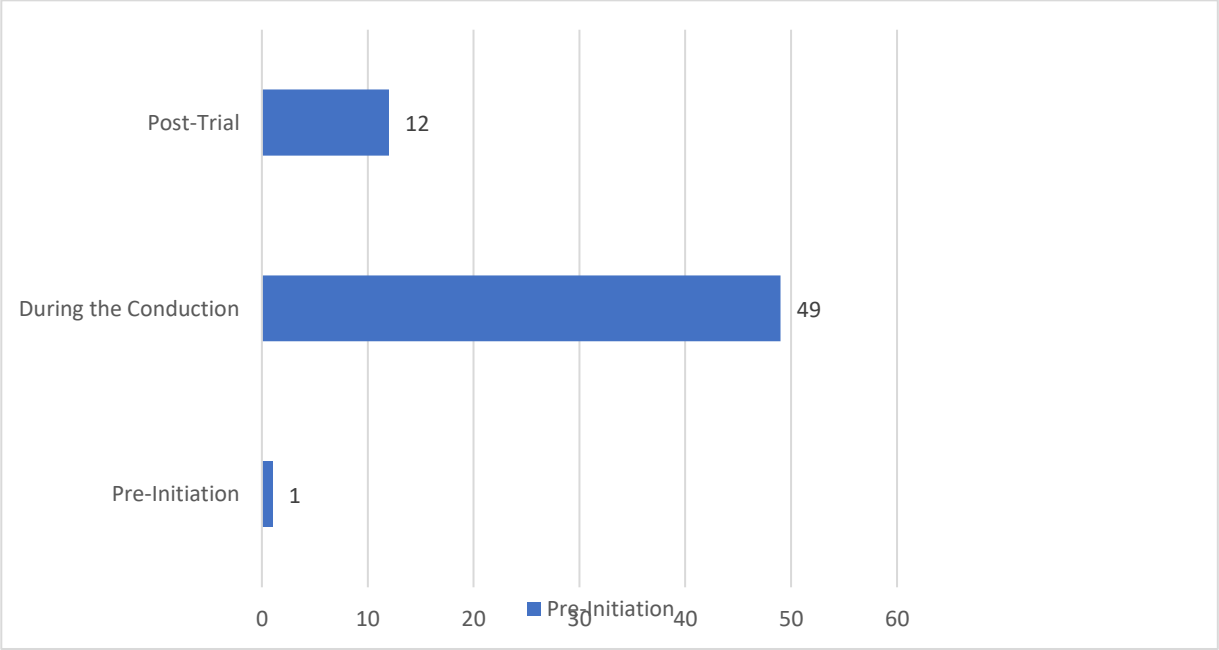


Figure 5: Number of Inspections Classified by Type of Clinical Trial Site.

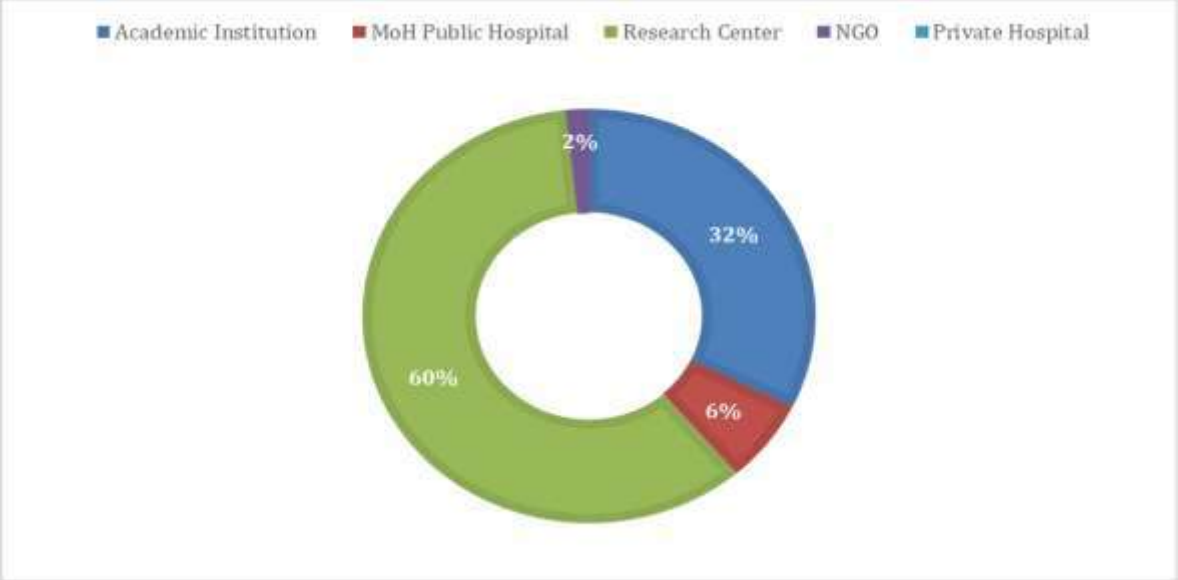


Figure 6: Number of Inspections Classified by Study Sponsorship.

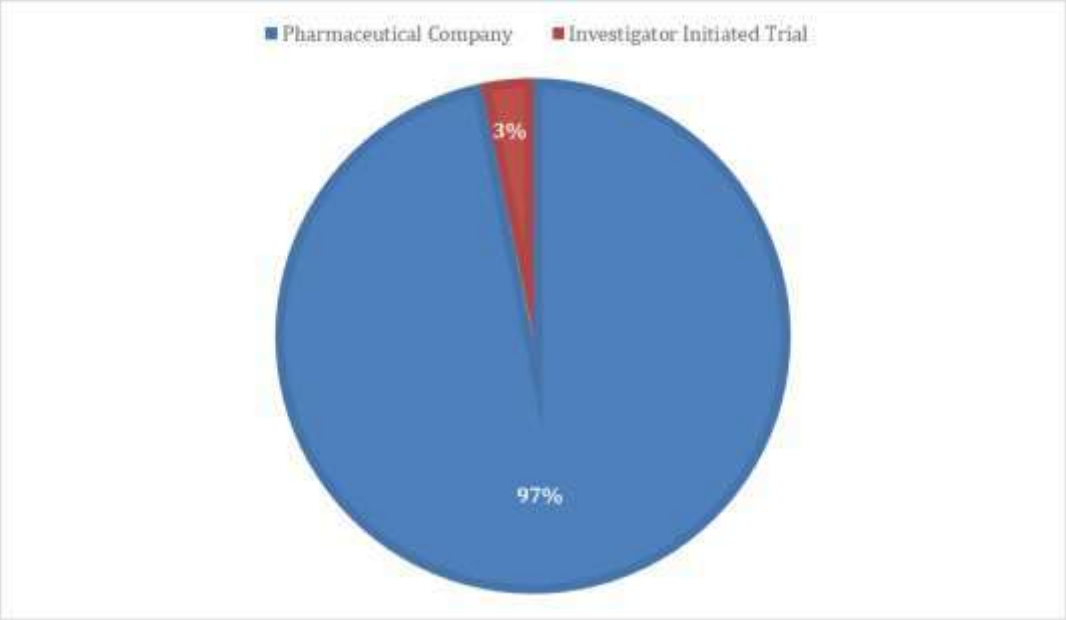
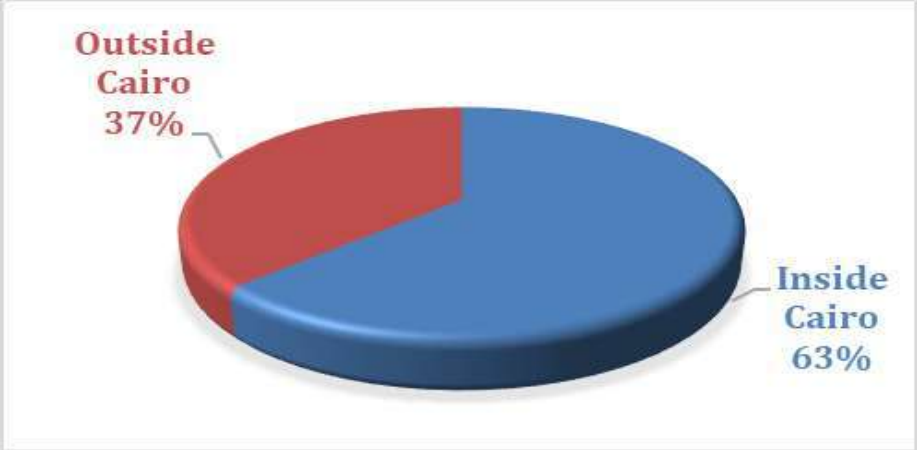


Figure 7: Percentage of Inspections Classified by Geographical Region.



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 participants and/or the quality and integrity of data. All the 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 28%, and the majority (71%) were graded as minor.

The most frequently observed finding category from all conducted inspections was Quality of Data/Records and Reports (Documentation), representing 25% of all findings.

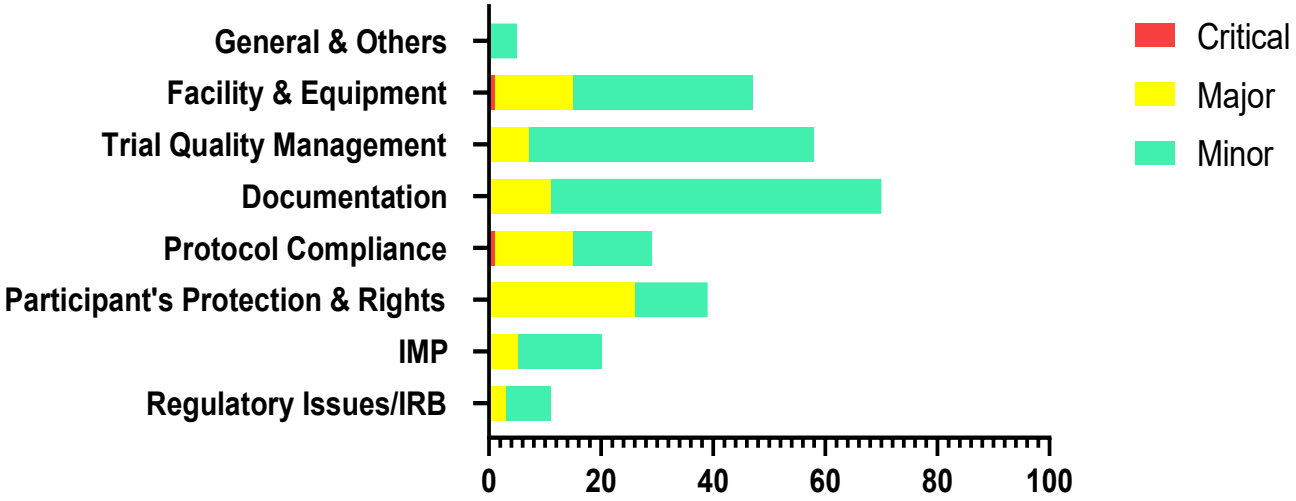
The modes of the finding categories for each grade (Critical, Major, Minor);

- The critical grade was observed only in two categories, namely, Protocol Compliance as well as Facility and Equipment, representing 50% each.
- The most frequently observed finding category for major grade was Participants' Protection and Rights, representing 32% of all major findings.
- The most frequently observed finding category for minor grade was Quality of Data/Records and Reports (Documentation), 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	3 (4%)	8 (4%)	11 (4%)
Investigational Medicinal Product (IMP) management	0	5 (6%)	15 (8%)	20 (7%)
Participants' Protection and Rights	0	26 (32%)	13 (6%)	39 (14%)
Protocol Compliance	1 (50%)	14 (17.5%)	14 (7%)	29 (10%)
Quality of Data/Records and Reports (Documentation)	0	11 (14%)	59 (30%)	70 (25%)
Trial Quality Management	0	7 (9%)	51 (26%)	58 (21%)
Facility and Equipment /Laboratories/Technical Facilities	1 (50%)	14 (17.5 %)	32 (16%)	47 (17%)
General and Others not listed above	0	0	5 (3%)	5 (2%)
Total	2 (1%)	80 (28%)	197 (71%)	279

Figure 8: Summary of Identified Deficiencies by Main Categories and Grades

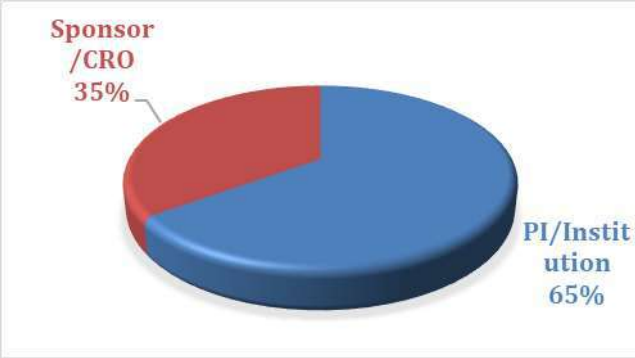


The mode of responsibility type for all reported findings; most of the raised findings were under the responsibility of the PI/Institution.
The mode of responsibility type for critical grade; the raised critical findings were under the responsibility of the PI/Institution.
The mode of responsibility type for major grade; most of the major findings were under the responsibility of the PI/Institution.
The number and percentage of different grades under each responsibility type are identified in **Table 3** and presented in **Figure 9**.

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

Finding Responsibility	Critical	Major	Minor	Total
Sponsor/CRO		22	75	97
PI/Institution	2	58	122	182

Figure 9: Percentage of Identified Deficiencies in Each Grade by Responsibility Type.



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 region is shown in **Table 4** and presented in **Figure 10**.

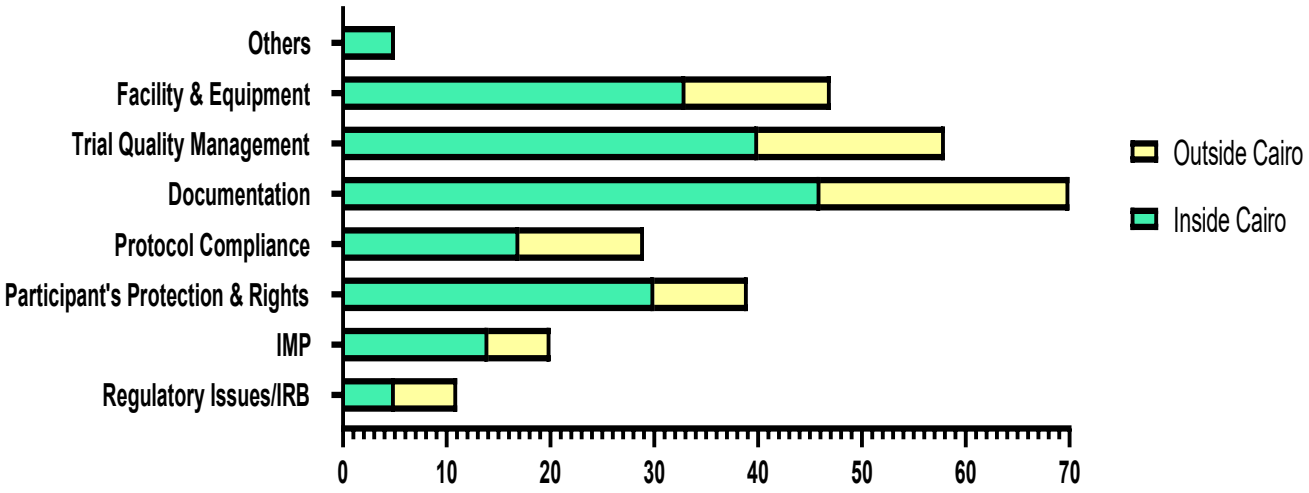
- For inspections conducted inside Cairo, the most frequently observed finding category was Quality of Data/Records and Reports (Documentation), representing 24% of all findings, followed by Trial Quality Management (21%) and Facility and Equipment (17%).
- Similarly, for inspections conducted outside Cairo, Quality of Data/Records and Reports (Documentation) remained the most frequently observed finding category, representing 27% of all findings, followed by Trial Quality Management (20%) and Facility and Equipment (16%), reflecting the same pattern observed in inspections inside Cairo.

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 (2.6%)	6 (7%)
Investigational Medicinal Product (IMP) management	14 (7%)	6 (7%)
Participants' Protection and Rights	30 (16%)	9 (10%)

Protocol Compliance	17 (9%)	12 (13%)
Quality of Data/Records and Reports (Documentation)	46 (24%)	24 (27%)
Trial Quality Management	40 (21%)	18 (20%)
Facility and Equipment /Laboratories/Technical Facilities	33 (17%)	14 (16%)
General and Others not listed above	5 (3%)	0
Total	**190 (68%)**	**89 (32%)**

Figure 10: Identified Deficiencies by Main Category in Different Geographical Regions

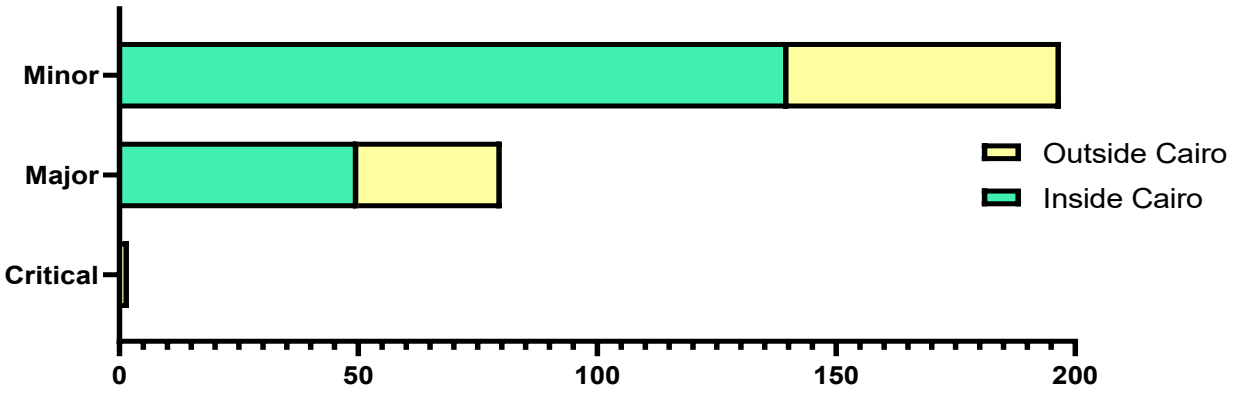


For inspections conducted inside Cairo, no critical findings were identified, while for inspections conducted outside Cairo, the critical findings represented only 2% of the total findings in this geographical region. The number and percentage of findings' grades in each geographical region are identified in **Table 5** and presented in **Figure 11.**

Table 5: Grading of Identified Deficiencies in each Geographical Region

Geographical Region	Critical	Major	Minor	Total
Inside Cairo	0	50 (26%)	140 (74%)	190
Outside Cairo	2 (2%)	30 (34%)	57 (64%)	89
Total	2	80	197	279

Figure 11: Grading of Identified Deficiencies in each Geographical Region



Conclusions Drawn from Identified Metrics:

- The increased number of inspections reflects the Egyptian Drug Authority's (EDA) commitment to upholding international standards and applicable local regulations.
- Inspections conducted during 2025 encompassed all types, including routine, triggered, and follow-up inspections.
- Inspections conducted during 2025 were carried out across all stages of the clinical trial lifecycle, including pre-initiation, during study conduct, and post-trial completion.
- All inspections were conducted at clinical research sites during 2025. However, the scope of GCP inspections may extend to other related entities, in accordance with the Clinical Trials Law No. 214/2020 and its Executive Regulation No. 927/2022, based on risk-based criteria.

- The majority of inspected sites were research entities, largely driven by the inclusion of bioequivalence (BE) studies within the scope of GCP inspections.
- For clinical trials, most inspected sites were affiliated with academic institutions, indicating that such institutions represent a significant proportion of clinical trial sites in Egypt.
- Most inspections were conducted on clinical trials sponsored by pharmaceutical companies, reflecting the predominance of industry-sponsored studies among clinical trial applications submitted to the EDA, as opposed to investigator-initiated studies.
- The majority of inspections were conducted within Cairo, which is primarily attributed to the concentration of BE centers in this region. No inspections were conducted outside Egypt during 2025.
- Critical findings represented a very small proportion of the total findings, and were identified in the areas of protocol compliance and facility and equipment, while the majority of deficiencies were graded as minor, indicating a high level of compliance with GCP principles and local regulations, and reinforcing confidence in the quality of clinical trials conducted in Egypt.
- Findings related to participants' protection and rights constituted the most frequently observed category among major findings, largely due to gaps in awareness of GCP principles related to the informed consent process at certain bioequivalence centers. In response, a dedicated workshop was conducted to enhance awareness and ensure alignment with applicable regulations and GCP standards.
- Although most findings were graded as minor, deficiencies related to the quality of data, records, and reports (documentation) represented a key area of non-compliance and require continued improvement.
- The distribution of findings by responsibility shows that most overall findings were attributed to the Sponsor/CRO, while critical and major findings were primarily attributed to the PI/Institution.
- The same pattern of finding categories was observed in inspections conducted both inside and outside Cairo, with Quality of Data/Records and Reports (Documentation) being the most frequently reported, followed by Trial Quality Management and Facility and Equipment.

II-Inspection Findings:

This section of the report provides details on the inspection findings within each main category, highlighting the most relevant sections from ICH E6 (R3), other international guidelines, and

applicable local regulations. Critical findings were identified in 2 main categories: Protocol Compliance, as well as Facility and Equipment. The finding category Quality of Data/Records and Reports (Documentation) was a key area of non-compliance that represented approximately 25% of total findings.

Regulatory Issues/ Ethics Committee (IRB)

The applicant should adhere to the local regulations pertinent to the conduct of clinical trials 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- IRB Composition, Functions, Operations

- The IRB Approval didn't include the reviewed documents and their version numbers and dates
- The IRB Approval Date preceded the Protocol's Issue Date
- The IRB approval was obtained on the same date as the study protocol.
- The IRB did not provide a final decision for the initial protocol version, leaving both approval and rejection boxes unmarked in the IRB decision form

References:

- **ICH-GCP E6 (R3), Section 2.4.2:**
  Before initiating a trial, the investigator/institution should have a documented and dated approval/favourable opinion from the IRB/IEC for the trial protocol, informed consent materials, participant recruitment procedures (e.g., advertisements), and any other trial-related information to be provided to participants.

- **ICH-GCP E6 (R3), Section 1.2.3:**
  The IRB/IEC should review a proposed clinical trial within a reasonable time and document its reviews, clearly identifying the trial, the documents reviewed, and the dates for the following:
  (a) Approval/favourable opinion;
  (b) Modifications required prior to its approval/favourable opinion;
  (c) Disapproval/negative opinion;

2- **Amendment approvals**

- A Local laboratory was used to perform part of the protocol-specified laboratory tests without obtaining EDA's approval before its use.
- As evidenced by the delegation log, two new Co-Investigators were involved in trial-related activities prior to obtaining EDA approval for their involvement.
- The number of human samples exported for analysis has exceeded the limit specified in the MoH approval.

References:

- **Guideline for Good Regulatory Oversight of Clinical Trials by the Egyptian Drug Authority**
  It is mandatory to obtain EDA approval before implementing any amendment to the approved clinical trial application package, except when it is necessary to eliminate an immediate hazard to human participants

- **ICH-GCP E6 (R3), Section 1.4.7:**
  No deviations from or changes to the protocol should be initiated without prior documented IRB/IEC approval/favourable opinion of an appropriate protocol amendment, except when necessary to eliminate immediate hazards to the participants or, in accordance with applicable regulatory requirements, when the change(s) involves only logistical or administrative aspects of the trial;

3- **Safety and Periodic Reporting to REC/IRB**

- There was a missing coverage period in the progress reports submitted to the IRB, in reviewed SMF, with no evidence of documentation for this period.

References:

- **ICH-GCP E6(R3) Section 3.2:**
  Periodic review of the trial by the IRB/IEC should also be conducted in accordance with applicable regulatory requirements.

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, site receiving form, IMP accountability logs, and

IMP return to sponsor records/ destruction certificates. Management of the IMP at the site must follow strict procedures to mitigate the risks and ensure compliance with ICH GCP E6 (R3) and local regulations.

ICH GCP E6 (R3) section 2.10 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- IMP Accountability

- Discrepancies were identified between the IMP accountability records and the actual quantities available at the site.

Reference:

- **ICH-GCP E6 (R3) Section 2.10.1:**
  Responsibility for investigational product(s) management, including accountability, handling, dispensing, administration, and return, rests with the investigator/institution."

- **ICH-GCP E6 (R3) Section 2.10.4:**
  The investigator/institution and/or a pharmacist or other appropriate individual should maintain records of the product's delivery, the inventory, the use by each participant (including documenting that the participants were provided the doses specified by the protocol), and the return to the sponsor and destruction or alternative disposition of unused product(s). These records should include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational product(s) and trial participants.

2- Manufacturing/Packaging/Labeling

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

Reference:

- **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,
  - The storage conditions,
  - Expiry date (month/year) or retest date, Identification of the product (test or reference).

3- Supply/Storage/Retrieval/Destruction

- There was no evidence of maintaining the appropriate conditions during the transport of the IMP
- The IMP was reconstituted in an external cup of unknown origin, rather than in the IMP's original bottle, which increases the risk of contamination and mix-up.
- The protocol does not mention the storage conditions for the test and reference products
- Frequent IMP temperature excursions were identified without evidence of prompt and appropriate corrective actions or communication with the sponsor

References:

- **ICH E6 R3 section C.3.3 Essential Records Table:**
  Documentation of investigational product storage conditions, including during shipment.

- **ICH-GCP E6 (R3) Section 11.2:**
  Measures should be in place to ensure that the investigational product provided to trial participants retains its quality.11.6 Appropriate processes should be implemented for the handling, shipping, storage, dispensing, returning, and destroying or alternatively disposing of the investigational product.

- **ICH-GCP E6 (R3) Section 3.15.2:**
  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.

- **ICH-GCP E6 (R3) Section 3.15.3:**
  The sponsor should ensure that instructions are available for the investigator/institution or trial participants on the handling and storage of investigational product(s).

- **ICH-GCP E6 (R3) Section 2.10.5:**
  The investigational product(s) should be stored as specified by the sponsor and in accordance with applicable regulatory requirement(s).

Participants' Protection and Rights

Informed consent is a key element of participant protection, as clinical trials are often conducted with unapproved therapeutic goods with an unknown safety profile, all parties are

responsible for protecting trial participants during and after a clinical trial. 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 (R3) section 2, Informed consent is an integral feature of the ethical conduct of a trial. Clinical trial participation should be voluntary and based on a consent process that ensures participants (or their legally acceptable representatives, where applicable) are well-informed.

Examples of Findings by the Sub-Category Include:

1- Personal Data Protection

- The X-Ray films, including the participant's confidential data (participant's name) were with one of the sponsor's representatives.

Reference:

- **ICH-GCP E6 (R3) Section 1.6:**
  The confidentiality of information that could identify participants should be protected in accordance with applicable privacy and data protection requirements.

- **ICH-GCP E6 (R3) Section 3.16.1:**
  The sponsor should implement appropriate measures to protect the privacy and confidentiality of personal information of trial participants, in accordance with applicable regulatory requirements on personal data protection.

2- Informed Consent Process:

- The verified ICFs were neither dated by the participant nor by the person who conducted the consenting process.
- For all verified participants, the laboratory tests were performed before obtaining informed consent, as informed by the site personnel.
- The study participants didn't receive a copy of the signed ICF, as informed by the study personnel.
- The ICF wasn't signed by the legal representative, although the participant is less than 21 years old (The age of Majority according to the local regulations).
- One of the participants was illiterate, and the impartial witness during the informed consent process was the participant's recruiter, which compromises the impartiality of the process.
- The informed consent process was not attended by an impartial witness, as the informed consent forms lacked impartial witness signatures, although participants' interviews confirmed that they are illiterate.

- The informed consent process was conducted by one of the study personnel who didn't have a medical background and didn't have protocol-specific training
- No fingerprint was present on the signed ICFs for all the study participants.

References:

- **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 participants; 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.

- **Clinical Trials Law 214/2020 Chapter 1 Article 1, Point 21, Definition of Informed Consent**
  Informed Consent: A written statement based on a completely free and voluntary will and issued by a legally competent person to indicate express consent as substantiated by the **signature and the fingerprint o**f that person to take part in the clinical medical research after having been informed and enlightened of all aspects of that research, and particularly, the potential effects or risks that may affect that person's decision to take part in the research. Informed consent is issued by the legal representative of the person in cases stipulated under the provisions of this law.

- **ICH-GCP E6 (R3) Section 2.8.7:**
  Prior to trial participation, the informed consent form should be signed and dated by the participant or by the participant's legally acceptable representative and, where appropriate, by an impartial witness and by the investigator or delegated investigator site staff who conducted the informed consent discussion.

- **ICH-GCP E6 (R3) Section 2.1:**
  Freely given informed consent should be obtained and documented from every participant prior to clinical trial participation. For potential participants unable to provide informed consent, their legally acceptable representatives, acting in the participants' best interest, should provide consent prior to clinical trial participation.

- **ICH-GCP E6 (R3) Section 2.8.11:**
  Prior to participation, the participant or the participant's legally acceptable representative should receive a copy of the signed and dated informed consent form and any other

informed consent materials provided, in accordance with applicable regulatory requirements.

- **ICH-GCP E6 (R3) Section 2.8.9**:
  If a participant or the legally acceptable representative is unable to read, an impartial witness should be present (remotely or in-person) during the entire informed consent discussion. After the informed consent form and any other information is read and explained to the participant or the participant's legally acceptable representative and they have orally consented to the participant's trial participation and, if capable of doing so, have signed and dated the informed consent form, the witness should sign and date the consent form. By signing the consent form, the witness attests that the consent information was accurately explained to and apparently understood by the participant or the participant's legally acceptable representative and that informed consent was freely given by the participant or the participant's legally acceptable representative.

3- Compensation and Payment to Participants

- The ICF did not specify the compensation amount for participants
- In the Informed Consent Form (ICF) template: Compensation was stated as contingent upon the full completion of the study, with no provision for timely payments

Reference:

- **ICH-GCP E6 (R3) Section 1.2.8:**
  If the trial participants are compensated for their participation in the trial, the IRB/IEC should review both the amount and method of payment to participants to assure that neither presents problems of coercion or undue influence on the trial participants. Payments to a participant should be timely, prorated, and not wholly contingent on completion of the trial by the participant. Reasonable reimbursement of expenses incurred by participants, such as for travel and lodging, is not coercive.

- **ICH-GCP E6 (R3) Section 1.2.9:**
  The IRB/IEC should ensure that information regarding payment to participants, including the methods, amounts, and schedule of payment to trial participants, is set forth in the informed consent materials and any other information to be provided to participants.

4- Safeguarding the safety and well-being of participants

- There was no documented evidence of follow-up on an AE or its treatment.
- The participant's blood pressure on the IMP administration day was recorded as 183/110; however, the participant was not administered medication for this emergency case and was not withdrawn as required by the protocol

- The housing room with 8 beds was used for the housing of 9 participants.

References:

- **ICH-GCP E6 (R3) Section 2.7.1:**
  Medical Care of Trial Participants(c) During and following participation in a trial, the investigator/institution should ensure that adequate medical care is provided to a participant for any adverse events, including clinically significant laboratory values, related to the trial. The investigator/institution should inform a participant when medical care is needed for intercurrent illness(es) of which the investigator becomes aware.

- **ICH-GCP E6 (R3) Section 2.5.2:**
  The investigator should comply with the protocol, GCP, and applicable regulatory requirements.

- **WHO Annes 9 Section 9.6:**
  Proper care of participants who require emergency or other medical care, with emergency or first-aid equipment and appropriate medication for use in emergencies.

- **ICH-GCP E6 (R3) Section 1.1:**
  The rights, safety, and well-being of the participants are the most important considerations and should prevail over the interests of science and society.

5- Informed Consent Form Content:

- Adverse events outlined in the IMP package insert were not documented in the informed consent form

Reference:

- **ICH-GCP E6 (R3) Section 2.8.10:**
  The informed consent discussion and the informed consent materials to be provided to participants should explain the following as applicable:
  (f) The reasonably foreseeable risks or inconveniences to the participant

6- Insurance:

- The insurance did not cover the total number of participants in all studies estimated to be conducted during the insurance period.
- The insurance certificate didn't include the number of participants covered by the insurance

- The scope of the insurance certificate is personal accidents & it does not cover clinical trial activities.

References:

- **ICH-GCP E6 (R3) Section 3.14.1:**
  If required by the applicable regulatory requirement(s), the sponsor should **provide insurance** or should indemnify (legal and financial coverage) the investigator/the institution against claims arising from the trial, except for claims that arise from malpractice and/or negligence.

- **ICH-GCP E6 (R3) Section 3.14.2:**
  The sponsor's policies and procedures should address the costs of treatment of trial participants in the event of trial-related injuries in accordance with the applicable regulatory requirement(s).

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 (R3) defines the 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 (R3) section 2.5 outlines the requirements of trial conduct in compliance with the protocol.
ICH GCP E6 (R3) section 3.1 states that a trial should be conducted in compliance with the protocol that has received prior ethics committee approval.

Examples of Findings by the Sub-Category Include:

1- Assessment of Efficacy

- The participant was not discontinued from the study despite meeting the criteria of inadequate response.

2- Safety Reporting to the Sponsor

- There was no evidence that the participant performed the required monthly home pregnancy tests, and the site did not follow up on the test results
- Information about adverse events and concomitant medications was not collected during the unscheduled visit as required
- The vital signs monitor that will be utilized by the site to measure blood pressure as part of the vital signs assessment does not meet the specifications outlined in the study protocol

3- IMP Prescription/Administration/Compliance

- The compliance of some participants with IMP administration was low, with no documentation of communication with the participants regarding the reasons for non-compliance or any re-training efforts.
- There was no documented evidence that the participant was advised to take the study IMP with food as required by the study protocol.

4- Recording in CRF/eCRF/Diaries/Questionnaires

- The inclusion and exclusion criteria listed in the CRF were different from those stated in the study protocol.
- The inclusion criterion in the CRF regarding the gender of eligible participants was inconsistent with that in the study protocol.
- The concomitant medication section of the eCRF was not completed.
- Some of the questionnaires required by the study protocol were not performed in the scheduled visits.

5- Eligibility Criteria

- There was no evidence that a complete physical examination was performed during the screening visit, as required by the study protocol.
- It was noted during CRF review that one of the participants consumed 12 cigarettes per day, which violates the protocol's inclusion criteria that allow only non-smokers or individuals who smoke fewer than 10 cigarettes per day to participate in the study.
- ECG and laboratory tests, used as part of the screening assessments, were outside the protocol-specified screening window.
- Some of the laboratory tests required by the study protocol were not conducted in the screening visit.
- One of the participants was enrolled despite having a BMI higher than the protocol-specified higher limit
- A participant was enrolled despite presenting with conditions that fall under the study protocol's exclusion criteria.

References

- **ICH-GCP E6 (R3) Section 2.5.2:**
  The investigator should comply with the protocol, GCP, and applicable regulatory requirements.

- **ICH-GCP E6 (R3) Section 2.5.4:**
  The investigator should follow the protocol and deviate only where necessary to eliminate an immediate hazard(s) to trial participants.

- **ICH-GCP E6 (R3) Section 3.1:**
  A trial should be conducted in compliance with the protocol that received prior IRB/IEC approval/favourable opinion.

- **ICH-GCP E6 (R3) Section 3.9.2**:
  The sponsor should ensure that trial processes are conducted in compliance with the trial protocol and related documents, as well as with applicable regulatory requirements and ethical standards.

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 and issuance of CSR 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. 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 participant's weight was recorded as 80 kg in the CRF, although the actual weight obtained upon weighing the participant during the inspection was 69 kg.
- The age in the ECG record was different from that in the CRF.

References:

- **ICH-GCP E6 (R3) Section 2.12.5:**
  The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the data acquisition tools completed by the investigator site (e.g., case report form (CRF).

- **ICH-GCP E6 (R3) Section 2.12.6:**
  Data reported to the sponsor should be consistent with the source records, and the discrepancies explained. Changes or corrections in the reported data should be traceable, should be explained (if necessary), and should not obscure the original entry.

2- Source Documents:

- The values of some laboratory tests were out of the normal range without documentation regarding the clinical significance of these results by the investigator
- For all verified participants' files: Some source records were signed by either the initials or the first name only, and some pages in the CRF were not signed; therefore, they were not attributable
- There was no evidence of verification of ECG records and lab reports by the investigator
- **The reason for screening failure was not documented in either the CRF or the laboratory results form for one of the participants.**
- The type of fascioliasis diagnosis, whether acute or chronic, was not recorded in the source documents.
- Overwriting was identified in certain sections of the source documents.
- Several discrepancies were identified between the source documents (CRF) and the individual data listing in the CSR

References:

- **ICH-GCP E6 (R3) Section 2.12.2:**
  The investigator/institution should maintain adequate source records that include pertinent observations on each of the trial participants under their responsibility. Source records should be attributable, legible, contemporaneous, original, accurate and complete. Changes to source records should be traceable, should not obscure the original entry and should be explained if necessary (via an audit trail).

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

- There was no delegation log listing the site staff delegated by the PI for performing study-related activities
- The Investigator Letters, related to the early study termination, weren't filed in the Site Master File
- The lab report from the baseline visit was not included in the participant's file. The PI reported the results, with a note that they were reviewed electronically
- The initial IRB approval was available in the Investigator Site File only as a copy; the original was not available
- There was no contract between the BE entity and the study sponsor
- There was no participant screening log available for verification in the Investigator Site File
- There was no contract between the BE entity and the destruction vendor

References:

- **ICH-GCP E6 (R2) Section C.1.3**:
  The essential records permit and contribute to the evaluation of the conduct of a trial in relation to the compliance of the investigator and sponsor with Good Clinical Practice (GCP) and applicable regulatory requirements and the reliability of the results produced. The essential records are used as part of the investigator oversight and sponsor oversight (including monitoring) of the trial. These records are used by the sponsor's independent audit function and during inspections by regulatory authority(ies) to assess the trial conduct and the reliability of the trial results. Certain essential records may also be reviewed by the institutional review board/independent ethics committee (IRB/IEC) in accordance with applicable regulatory requirements. The investigator/institution should have access to and the ability to maintain the essential records generated by the investigator/institution before and during the conduct of the trial and retain them in accordance with applicable regulatory requirements.

- **ICH-GCP E6 (R2) Section 2.3.3**:
  The investigator should ensure a record is maintained of the persons and parties to whom the investigator has delegated trial-related activities.

- **ICH-GCP E6 (R2) Essential Records Table:**
  - Dated, documented approval/favourable opinion of IRB/IEC of information provided to the IRB/IEC
  - Notification by sponsor to investigators of safety information, where required
  - Source records
  - Signed agreement between involved parties, for example:
    - Investigator/institution and sponsor

- Investigator/institution and service providers
- Documentation of delegation of trial-related activities by the investigator
- Completed participants' screening log

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.

Examples of Findings by the Sub-Category Include:

1- SOPs:

- SOP of safety and IMP destruction were not updated to comply with EDA regulations.
- The site didn't have a Quality Assurance System as there were no procedures (SOPs) found at the site for implementing and maintaining quality assurance e.g. SOPs for IMP handling, transportation, storage, use of study-related equipment, waste disposal, and reporting of serious adverse events
- The protocol, ICF, and the CRF didn't have a version number or date
- The Standard Operating Procedure for Good Clinical Practice has not been updated to reflect the current changes introduced in ICH E6(R3).

- **References:**
  - **Guideline for Good Regulatory Oversight of Clinical Trials by Egyptian Drug Authority Section 8.5.4.1:**
    Safety Reporting Procedure: The PI is responsible for reporting all Serious Adverse Events to Bio Inn and the Supreme Council simultaneously by adding both entities as recipients in the same email within the specified timelines.

  - **Guideline for Good Regulatory Oversight of Clinical Trials by Egyptian Drug Authority Section 8.4.5.1:**
    Destruction Inside Egypt: • The applicant shall notify Bio-Inn upon planning for IMP destruction by submitting all required documents by e-mail.

  - **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).

- **ICH E6 (R3) Section C.2 Management of Essential Records C.2.1:**
Records should be identifiable and version-controlled (when appropriate) and should include authors, reviewers, and approvers as appropriate, along with date and signature (electronic or physical), where necessary.

2- Organization and Personnel/Training and Qualifications:

- There was no GCP certificate available for verification for the PI and other site staff
- The CVs of the PI and Co-Is weren't filed in the Investigator Site File.
- The delegation log wasn't dated by the PI, didn't include all tasks of the study (e.g., consenting, screening, ECG performing, randomization, assessment of AEs/SAEs, confirmation of eligibility, and blood samples withdrawal from study participants, etc.), and didn't include the nurses involved in the study
- There was no protocol-specific training for the entity's staff involved in the study
- According to the study delegation log, the evaluation of study-related test results was assigned to the Study Coordinator, who is not specialized in the relevant disease area.
- There was no GCP certificate for some of the personnel delegated in the study.
- Despite being delegated to and performed by the Co-Investigator, the consenting and screening activities were additionally delegated to clinical specialists lacking a medical background.
- GCP certificates of the PI & other stuff were obtained from uncertified entities.
- According to the delegation log, the IMP management was delegated only to the Study Coordinator, who didn't have a relevant educational and professional background

References:

- **ICH-GCP E6 (R3) Section 2.2.2**:
The investigator should have sufficient time, an adequate number of available and qualified staff, and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.

- **ICH-GCP E6 (R3) Section 2.3.2:**

The investigator should ensure that persons or parties to whom the investigator has delegated trial-related activities are appropriately qualified and are adequately informed about relevant aspects of the protocol, the investigational product(s) and their assigned trial activities (including activities conducted by staff provided by other parties in accordance with local regulatory requirements). Trial-related training to persons assisting in the trial should correspond to what is necessary to enable them to fulfil their delegated trial activities that go beyond their usual training and experience.

- **ICH-GCP E6 (R3) Section C.3 Essentiality of Trial Records:**

Documents that the investigator and those individuals delegated significant trial-related activities by the investigator are qualified by education, training, and experience to undertake their activities, particularly where the activities are not part of their normal role;

Facility and Equipment/Laboratories/Technical Facilities

Examples of Findings by the Sub-Category Include:

1- Calibration:

- There was no evidence of calibration of the weight balance, Sphygmomanometer, and the ECG used for the physical examination and vital signs monitoring of study participants.
- The calibration of the Data Logger used for monitoring the Pharmacy Room Temperature was expired.
- The defibrillator was not calibrated.
- There were calibration certificates for the weight balance and the sphygmomanometer; however, these certificates didn't include details of the calibration process.
- The calibration of equipment is performed internally by the institution, which is not an authorized body to perform equipment calibration

References:

- **ICH-GCP E6 (R3) Essential Records Table:**

Records demonstrating fitness for purpose (e.g., maintenance and calibration) for equipment used for important trial activities

- **ICH-GCP E6 (R3) Section 2.2.2.2**:

The investigator should have sufficient time, an adequate number of available and qualified staff, and **adequate facilities** for the foreseen duration of the trial to conduct the trial properly and safely.

- **ICH-GCP E6 (R3) Section 3.11.4.5.2**:

(a) Selecting the site and confirming that the investigator and individuals or parties involved in the trial conduct have **adequate** qualifications, resources, and facilities, including laboratories, **equipment,** and investigator site staff, to conduct the trial safely and properly."

- **WHO Annex 9 Guidance for Organizations Performing In Vivo Bioequivalence Studies**
Section 9.9: Equipment used should be appropriately calibrated at predefined intervals.
Section 9.10: The adequate function and performance of emergency-use equipment (e.g. defibrillators) should be verified at appropriate intervals.
Section 24.7: There should be SOPs for the operation, use, calibration, checks and preventive maintenance of equipment.

2- Facility Premises:

- There was no nurse call beside each bed in the housing rooms
- The nurse call system in the participants' rooms was not working.
- The study files were stored in a cupboard that is neither waterproof nor fireproof.
- The Ultra Low Deep Freezer (-80°C) used for storage of plasma samples doesn't have an alarm system for cases of power failure, and it wasn't connected to the UPS at the inspection time.

References:

التوافر والتكافؤ الحيوي ومعدل الذوبان سنة 2024 تحديثات إشتراطات المراكز التي تقوم بإجراء دراسات-
فيما يخص التجهيزات الخاصة بغرف المركز **(Participants' Housing Room):**

-توفير Call **Nurse بجوار** جميع الأسرة

- **WHO Annex 9 Guidance for Organizations Performing In Vivo Bioequivalence Studies**
Section 6.1: The CRO should have sufficient and appropriately secure storage space, which should be fireproof, relative humidity-controlled, and pest-controlled, for archiving of the trial-related documentation. Archives should also be protected from flooding.

- **WHO Annex 9 Guidance for Organizations Performing In Vivo Bioequivalence Studies**
Section 24.3: Key sample storage systems or other areas requiring environmental controls should be adequately qualified, calibrated, and maintained. There should be an alarm

system or an adequate monitoring system to control the temperature of the critical stage areas and key sample storage systems, such as freezers.

3- Accreditation:

- The laboratory used in the study for the analysis of screening tests was not accredited.
- Some of the protocol-required laboratory tests were performed in the site's internal lab rather than the accredited one.

References:

-ICH-GCP E6 (R3) Essential Records Table:

Certification or accreditation or other documentation including of validation (where required) to confirm the suitability of medical/laboratory/technical procedures/tests used during the trial conduct

- **WHO Annex 9 Guidance for Organizations Performing In Vivo Bioequivalence Studies**

Section 10.4: The CRO should receive information about the analytical methods used in the laboratory, a dated list of laboratory normal ranges, and, if available, the accreditation certificate of the laboratory.

Others:

- One of the emergency medications, Hydrocortisone, was found to have an expiry date different from the one recorded in the Emergency Medications Log.
- Regarding the log used to record the dispensing of Emergency medications, a discrepancy was identified between the recorded remaining quantity of Dexamethasone vials and the actual stock available on site.

References:

- **Egyptian Guideline for Conducting Bioequivalence Studies for Marketing Authorization of Generic Products Year 2023 Section XV**:

2. First-aid emergency equipment and **appropriate rescue medication** should be available at the study site and adequate facilities for the proper care of participants who require emergency or other medical care."

Conclusion:

The 2025 GCP Inspections Metrics Report demonstrates a notable advancement in the oversight and quality assurance of clinical trials conducted in Egypt. The breadth and

diversity of inspections conducted throughout the year, covering various study types, stages, and settings, reflect a mature and evolving regulatory oversight framework aligned with both national legislation and international standards.

The observed level of compliance across inspected sites indicates a growing commitment among stakeholders to adhere to Good Clinical Practice (GCP) principles and applicable local regulations. The effective implementation of corrective and preventive actions further highlights the responsiveness of clinical trial sites to regulatory expectations and their continuous efforts toward quality improvement. In addition, the distribution of findings by responsibility indicates that while most overall deficiencies were attributable to the sponsor/CRO, higher-severity findings (critical and major) were primarily associated with the PI/Institution, highlighting the central role of site-level oversight in ensuring compliance with GCP requirements.

At the same time, the findings emphasize the importance of sustained focus on key areas such as documentation practices, trial quality management, and the protection of participants' rights. These areas remain central to ensuring the integrity, reliability, and ethical conduct of clinical research. The proactive initiatives undertaken, including targeted awareness and capacity-building activities, demonstrate the Authority's commitment to addressing identified gaps and strengthening overall compliance.

In conclusion, the outcomes of this report reflect steady progress in clinical trial governance in Egypt, while underscoring the need for ongoing education, robust quality management systems, and continuous alignment with evolving international guidelines. Such efforts will be essential to maintaining and further enhancing the quality, credibility, and global recognition of clinical research conducted in the Arab Republic of Egypt.

Abbreviations:
BE: Bioequivalence
CRO: Contract Research Organization
CSR: Clinical Study Report
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
NGO: Non-Governmental Organization
PI: Principal Investigator
SOP: Standard Operating Procedure

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