GUIDELINES FOR CONDUCT AND REPORTING OF GOOD CLINICAL PRACTICE INSPECTIONS

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Edition History

Change #	Effective date	Reason for Revision
Edition 01		-
Edition 02	18-03-2024	Addition of "RISK BASED SELECTION OF TRIAL/RESEARCH FOR GCP INSPECTION" at under heading 8 at page 11
Edition 03	16-06-2025	• Inclusion of Risk Calculation of Clinical Trials • Revision of "RISK BASED SELECTION OF TRIAL / RESEARCH FOR GCP INSPECTION" • Inclusion of GCP Inspectors competency matrix, training requirements and minimum eligibility criteria.

1. HISTORY

This is the third edition of this document.

2. APPLICATION

These guidelines are applicable to the Sponsors, Principal Investigators (PI), Site Investigators (SI), Contract Research Organizations (CROs), Clinical Trial Site, BA/BE Study Center and Bio-Analytical Laboratories involved in conduct of Clinical Research related to therapeutic goods and to the CSC nominated experts / Clinical Research Applications Evaluators/Assessors / GCP inspectorate of the DRAP to explain the procedure conduct and reporting of GCP inspections of Clinical Research related to therapeutic goods regulated by the DRAP.

3. PURPOSE

This document is intended to provide general guidance to applicants (e.g. the Sponsors, Principal Investigators, Site Investigators, Contract Research Organization (CROs), Clinical Trial Site, BA/BE Study Center and Bio-Analytical Laboratories) involved in conduct of Clinical Research related to therapeutic goods and guideline describes the Risk-Based selection of Clinical Trials for GCP inspection, GCP inspector's competency/qualification and regulatory requirements and procedure for conduct and reporting of GCP inspections to the CSC nominated experts / Clinical Research applications Evaluators/Assessors / GCP inspectors of the DRAP involved in Clinical Research Oversight activities.

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4. GLOSSARY (ABBREVIATIONS / ACRONYMS)

ADR	Adverse Drug Reaction
ALSS	Advanced Life Support Systems
BA/BE	Bioavailability / Bioequivalence
BAL	Bioanalytical Laboratory
CoA	Certificate of Analysis
CPR	Cardio-pulmonary resuscitation
CR	Clinical Research (pertains to Clinical Trial or BA/BE Study)
CRO	Contract Research Organization
CRF	Case Report Form
CSC	Clinical Studies Committee
CV	Curriculum Vitae
DRAP	Drug Regulatory Authority of Pakistan
DSMB	Data Safety Monitoring Board
ERC	Ethics Review Committee
GCP	Good Clinical Practices
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practice
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IEC	Independent Ethics Committee
IP	Investigational Product
IRB	Institutional Review Board
IRC	Institutional Review Committee
ISF	Investigator's Site File
NA	Not applicable
NBC	National Bio-Ethics Committee
PI	Principal Investigator
SI	Site Investigator
RA	Regulatory Authority
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
TMF	Trial Master File
WHO	World Health Organization

5. DEFINITIONS:

Adverse Drug Reaction	"Adverse drug reaction" or "ADR" means response to medicines which is noxious and unintended that occurs at doses normally used for the prophylaxis, diagnosis, or therapy of disease or for the restoration, correction or modification of physiological function. A response in this context means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility. An adverse reaction, in contrast to an adverse event, is characterized by the fact that a causal relationship between a medicinal product and an occurrence is suspected; *OR* In the pre-approval clinical experience with a new therapeutic goods or its new usages, particularly as the therapeutic dose(s) may not be established: all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase responses to a medicinal product means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e. the relationship cannot be ruled out. Regarding marketed medicinal products: a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function.
Adverse Event	"Adverse event" or "AE" means any untoward medical occurrence in a patient or clinical investigation subject administered a medicine and which does not necessarily have a causal relationship with this treatment; OR Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.
Applicable Regulatory Requirement(s)	DRAP Act, 2012 Bio-Study Rules, 2017 DRAP's Guidelines on Conduct of Clinical Research in Pakistan Latest

	ICH-GCP Guidelines.
Audit	A systematic and independent examination of trial related activities and documents to determine whether the evaluated trial related activities were conducted, and the data were recorded, analyzed and accurately reported according to the protocol, sponsor's Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and other applicable regulatory requirement(s).
Audit Certificate	A declaration of confirmation by the auditor that an audit has taken place.
Audit Report	A written evaluation by the Sponsor's or Regulatory Authority's auditor of the results of the audit.
Audit Trail	Documentation that allows reconstruction of the course of Audit.
Blinding/Masking	A procedure in which one or more parties to the trial are kept unaware of the treatment/intervention assignment(s). Single-blinding usually refers to the subject(s) being unaware, and double blinding usually refers to the subject(s), investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment/intervention assignment(s).
Case Report Form (CRF)	A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject.
Clinical Research	Any type of research involving Human Subjects with Clinical Intervention of therapeutic goods. e.g. Clinical Trial(s) and/or BA/BE Study.
Clinical Trial / Research Application	The Clinical Trial/Research application is the dossier that includes all documentation pertaining to the conduct of clinical trial/research in country according to the regulation. The dossier includes a cover letter, CV's of investigators, protocol and an investigator's brochure or product information etc. (Protocol and Investigator's brochure should be in accordance with ICH- GCP guidelines).
IPs/Drug Import License (DIL)	DRAP, authorizing the licensee to import any product for purposes of clinical trials, notwithstanding that the product is not a registered / enlisted product, or a license issued by DRAP authorizing the licensee to import any registered / enlisted or unregistered /un-enlisted product for purposes of clinical trials.

Clinical Trial/ Study Report	A written description of a trial/study of any investigational product conducted in human subjects, in which the clinical and statistical description, presentations, and analyses are fully integrated into a single report (see the ICH Guideline for Structure and Content of Clinical Study Reports).
Clinical Trial/Study	Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other Pharmacodynamics effects of an investigational product(s) and/or to identify any adverse reactions to an investigational product(s) and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy. The terms clinical trial and clinical study are synonymous.
Clinical Trials (Phase)	A systematic study on therapeutic goods products in human subjects (including patients and other volunteers) in order to discover or verify the effects of and/or identify any adverse reaction to investigational products, and/or to study the absorption, distribution, metabolism and excretion of the products with the object of ascertaining their efficacy and safety. Clinical trials are generally classified into Phases I to IV. It is not possible to draw distinct lines between the phases, and diverging opinions about details and methodology do exist.
Clinical Trial / Study Report	A written description of a trial/study (of any investigational product) conducted on human subjects, in which the clinical and statistical description, presentations, and analyses are fully integrated into a single report
Comparator Product	An investigational or marketed product (i.e. active control) or placebo, used as a reference in a Clinical Trial.
Compliance (in relation to trials)	Adherence to all the trial-related requirements, Good Clinical Practice (GCP) requirements, and the applicable regulatory requirements.
Confidentiality	Prevention of disclosure, to other than authorized individuals, of a Sponsor's proprietary information or of a subject's identity.
Contract	A written, dated, and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters. The protocol may serve as the basis of a contract.
Contract Research Organization (CRO)	A person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial- related duties and functions.

Co-Investigator / Sub investigator	Any individual member of the clinical trial team designated and supervised by the Principal Investigator at a trial site to perform critical trial- related procedures and/or to make important trial-related decisions, (e.g., associates, residents, research fellows).
Direct Access	Permission to examine, analyze, verify, and reproduce any records and reports that are important for evaluation of a clinical trial. Any party (e.g., domestic and foreign regulatory authorities, sponsor's monitors and auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory requirement(s) to maintain the confidentiality of subjects' identities and sponsor's proprietary information.
Documentation	All records, in any form (including, but not limited to, written, electronic, magnetic, and optical records, and scans, x-rays, and electrocardiograms etc.) that describe or record the methods, conduct, and/or results of a trial, the factors affecting a trial, and the actions taken.
Drug Regulatory Authority of Pakistan (DRAP)	National Regulatory Authority established in Pakistan for the purpose of regulating the Control of Therapeutic Goods. Regulates all activities related to import, procurement of raw and packing materials, production and import of finished therapeutic goods, export, sales, pricing, etc.
Essential Documents	Documents which individually and collectively permit evaluation of the conduct of a study and the quality of the data produced. (See Section 12 of these guidelines)
Good Clinical Practice (GCP)	A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance, that the data and reported results are credible and accurate, and the rights, integrity, and confidentiality of trial subjects are protected.
Impartial Witness	A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject.

Informed Consent	A process by which a subject voluntarily confirms his or her 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. Informed consent should be in accordance with Section 4.8 of the ICH-GCP Guidelines, and should be in English, National (Urdu) and / or Local language (if required).
Inspection	The act by a regulatory authority(ies) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority(ies) to be related to the clinical research/trial that may be located at the site of the trial, at the sponsor's and/or Contract Research Organizations (CRO's) facilities, or at other establishments deemed appropriate by the regulatory authority(ies).
Inspectee	One who undergoes an inspection. For these guidelines inspectee means PI, Sponsor, or Site representative involved in Clinical Research.
Institution (Medical)	Any public or private entity or agency or medical or dental facility (approved from relevant Health Care Commission & DRAP) where clinical trials are conducted.
Institutional Review Committee (IRC) or Institutional Review Board (IRB)	An independent body constituted of medical, scientific, and non-scientific members whose responsibility is to ensure the protection of the rights, safety and well–being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trial protocol and amendments and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects and providing continuing review of trial protocol and amendments and of the methods and material to be used.
Interim Clinical Trial/ Study Report	A report of intermediate results and their evaluation based on analyses performed during the course of a trial.
Investigational Products (IPs)	A pharmaceutical dosage form of an active ingredient or placebo or any device being tested or used as a reference in a clinical trial, including a registered / enlisted product when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication or when used to gain further information about an approved use.
Investigator	A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called

	the principal investigator. Principle Investigator will be responsible for whole Clinical Studies / Trial.
Site Investigator	A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team at the site and may be called the site investigator.
Investigator's Brochure	A compilation of the available clinical and non-clinical data on the investigational product(s) which is relevant to the study of the investigational product(s) in human subjects or animals. Investigator brochure should be in accordance with Section 7 of ICH-GCP guidelines, as per Rule 15 of the Bio-Study Rules 2017.
Manufacture	All operations that include purchase of materials and products production, quality control, release of finished products, and related controls.
Manufacturer	A company that carries out at least one step of production as well as the final release of the finished product.
Monitoring	The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), the Bio-Study Rules 2017, DRAP Act 2012 and the rules made under.
Monitoring Plan	A document that describes the strategy, methods, responsibilities, and requirements for monitoring the trial.
Monitoring Report	A written report from the monitor to the sponsor after each site visit and/or other trial-related communication according to the sponsor's SOPs.
Multi-Center Trial	A clinical trial conducted according to a single protocol but at more than one site(s) in a country, and therefore, carried out by more than one investigator.
Multi-Countries Clinical Trial	A clinical trial conducted according to a single protocol at multiple sites, situated in multiple countries.
Multi-Regional Clinical Trial	A clinical trial conducted according to a single protocol and/or with some amended protocol due to different ethnic factors of different demographic regions of the world, at multiple sites, situated in different demographic regions of the world.
Phase I	These are the first trials of a new active ingredient or new formulation in humans/animals often carried out in healthy

	volunteers. Their purpose is to establish a preliminary evaluation of the safety and the pharmacokinetic, and where possible the pharmacodynamics profile of the active ingredient(s) in humans/animals
Phase II	These trials are performed in a limited number of subjects and are often, at a later stage, of a comparative (e.g. placebo-controlled) design. Their purpose is to demonstrate therapeutic activity and to assess short-term safety of the active ingredient in patients suffering from a disease or condition for which the active ingredient is intended. This phase also aims at the determination of appropriate dose ranges or regimens and (if possible) clarification of dose-response relationships in order to provide an optimal background for the design of extensive therapeutic trials.
Phase III	Trials in larger (and possibly varied) patient groups with the purpose of determining the short-and long-term safety/efficacy balance of formulation(s) of the active ingredient, and of assessing its overall and relative therapeutic value. The pattern and profile of any frequent adverse reactions must be investigated and special features of the product must be explored (e.g. clinically-relevant drug interactions, factors leading to differences in effect such as age). These trials should preferably be of a randomized double-blind design, but other designs may be acceptable, e.g. long-term safety studies. Generally, the conditions under which these trials are carried out should be as close as possible to normal conditions of use.
Phase IV	Studies performed after marketing of the pharmaceutical product. Trials in phase IV are carried out on the basis of the product characteristics on which the marketing authorization was granted and are normally in the form of post- marketing surveillance, or assessment of therapeutic value or treatment strategies. Although methods may differ, these studies should use the same scientific and ethical standard as applied in premarketing studies. After a product has been placed on market, clinical trials designed to explore new indications, new methods of administration or new combinations, etc. are normally considered as trials for new pharmaceutical products.
Protocol	A document that describes the objective(s), design, methodology, statistical considerations, and organization of a clinical trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents. Throughout these Guideline the term protocol refers to protocol and

	protocol amendments. The protocol should be in accordance with section 6 of the ICH-GCP guidelines.
Protocol Amendment	A written description of a change(s) to or formal clarification of a clinical trial protocol.
Quality Assurance (QA)	All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported incompliance with Good Clinical Practice (GCP) and the applicable regulatory requirement(s).
Quality Control (QC)	The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled.
Randomization	The process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.
Registered / Enlisted Product	Any product approved or permitted to be marketed in the country by DRAP
Serious Adverse Event or Serious Adverse Drug Reaction	Any untoward medical occurrence that at any dose: Results in death. Is life –threatening. Requires inpatient hospitalization or prolongation of existing hospitalization Results in persistent or significant disability/in capacity, or Results in a congenital anomaly/birth defect.
Side effect	Unintended effect occurring at normal dose related to the pharmacological properties of a drug.
Source Documents / Data	Original documents, data, and records (e.g. hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial).
Sponsor	An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial.

Subject / Participants Identification Code	A unique identifier assigned by the investigator to each trial subject to protect the subject's identity and used in lieu of the subject's name when the investigator reports adverse events and/or other trial related data.
Subject / Trial Subject / Participant	In this guideline, subject means human participants in a clinical Trial/BA/BE Studies. An individual who participates in a Clinical Trial/ BA/BE Studies, either as a recipient of the investigational product(s) or as a control.
Trial Site	The location(s) where trial-related activities are actually conducted.
Unexpected Adverse Reaction	An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator's Brochure)
Unregistered / Un-enlisted Product	Any product that is not registered / enlisted or permitted to be marketed in the country by the DRAP.
Well-being (of the trial subjects)	The physical and mental integrity of the subjects in a Clinical Trial/ BA/BE Studies.

6. DESCRIPTION AND GRADING OF GCP INSPECTION FINDING/ OBSERVATIONS:

Critical (CR)	Conditions, practices or processes that adversely affect the rights, safety or wellbeing of the subjects and/or the quality and integrity of data. Critical observations are considered totally unacceptable.
Major (MA)	Conditions, practices or processes that might adversely affect the rights, safety or wellbeing of the subjects and/or the quality and integrity of data. Major observations are serious deficiencies and are direct violations of GCP principles.
Minor (MI)	Conditions, practices or processes that would not be expected to adversely affect the rights, safety or wellbeing of the subjects and/or the quality and integrity of data.

7. INTRODUCTION:

These guidelines have been drafted in conformity with the legal requirements of the Bio-Study Rules, 2017. It is required that all the Therapeutic Goods and Health Products used in Pakistan are registered / enlisted with the Drug Regulatory Authority of Pakistan (DRAP) and any Clinical Trial using any registered / enlisted or unregistered / un-enlisted products must receive written approval (i.e. license for Clinical Trial Site and Registration for Clinical Studies) from DRAP, under the Bio-Study Rules 2017 for this purpose.

Pursuant to the Bio-Study Rules 2017, the Authority shall monitor and inspect Clinical Research Sites/Centers during the course of the research/trial and at such intervals as it may determine, this guideline has been developed to facilitate the enforcement of best practices in the conduct of approved clinical research/trials in Pakistan and, to set out the procedures that should be followed by the inspectee and the inspectorate for conduct of GCP inspection of Clinical Research in Pakistan at any stage.

As defined by the ICH-GCP, an inspection is the act by a regulatory authority of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority to be related to the clinical research/trial and that may be located at the trial site/center, at the sponsors and/or Clinical Research's facilities, or at other establishments deemed appropriate by the regulatory authority.

Good Clinical Practice (GCP) inspection is necessary to ensure the protection of the rights, safety and wellbeing of study subjects and to assure the integrity of study data. It helps to determine whether the Clinical Research is conducted in accordance with approved protocol, GCP guidelines, ethical standards and other applicable regulatory requirements. The areas for the inspection, include but are not limited to, data and information relating to regulatory approvals, ethics review committee & NBC approvals, protocols, Case Report Forms, Progress Report, Clinical Trial Reports, research participants and participant's data, Sponsors, Investigators and personnel involved in the research/trial, and laboratory data.

All clinical trials including bioavailability and bioequivalence studies, be designed, conducted, recorded and reported in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with latest ICH-GCP and the applicable regulatory requirements mentioned in the Bio-Study Rules 2017 and guidelines made under.

8. RISK CALCULATION AND RISK BASED SELECTION OF TRIAL / RESEARCH FOR GCP INSPECTION PLAN:

Risk Calculation and Risk-Based GCP Inspection Planning is an essential activity under the Bio-Study Rules, 2017 and guidelines made under, the objective of Risk-Based GCP Inspections is to proactively identify, assess, and manage potential risks that could affect the quality, safety, and integrity of the trial and the well-being of participant.

Risk-Based Inspection planning helps prioritize inspections of Clinical Trials that can potentially poses risk to trial participant's safety, data integrity, and regulatory compliance. Risk calculation of Clinical Trials will be started once Clinical Trial application received by the Pharmacy Services Division and initial risk calculation report will be part of the "Summary Evaluation Report" and presented before the CSC.

8.1 Risk-Based Selection of Clinical Trials/Research:

The selection of trials/research for GCP inspection planning includes, but is not limited to the following factors;

i. Trial-Related Risks:
   a. Complexity of protocol (Multiple Arms & Complex Study Design)
   b. Number of investigational sites and countries
   c. Phase of trial (e.g., Phase I-II often carries higher safety risks)
   d. Investigational product nature, novelty or first-in-human use
   e. Blinding/randomization complexity

ii. Sponsor/CRO Oversight
   a. Quality Management System maturity
   b. Frequency and quality of audits
   c. Outsourced functions and CRO management

iii. Site Performance & History
   a. High rate of protocol deviations
   b. Data entry delays or inconsistencies
   c. Previous inspection findings or warnings

iv. Participant Safety
   a. Inclusion of vulnerable populations (e.g., pediatrics, pregnant women etc.)
   b. High-risk therapeutic areas (e.g., oncology, CNS etc.)
   c. Use of invasive procedures or novel delivery methods

v. Data Integrity Concerns
   a. Inconsistent AE/SAE reporting
   b. Remote monitoring challenges
   c. Adverse trends found through central monitoring

vi. Regulatory or Public Interest
   a. CSC or Authority directions
   b. Media reports or whistleblower complaints
   c. Trials that inform critical drug approvals or policy changes

8.2 Risk Calculation and Scoring of Clinical Trials/Research:

The following scoring system will be utilized for selection / prioritization of clinical trials/research for GCP inspection planning;

S. No.	Category	Scoring Criteria	Score Range				Result
			4	3	2	1	
i.	Phase of Trial	Phase I (4), II (3), III (2), IV (1)					
ii.	Population Risk	Vulnerable/High Risk (4), Moderate Risk (3) Low Risk (2), General (1)					
iii.	Number of Site of CT	>15 (4), 10–15 (3), 5–10 (2), ≤ 5 (1)					
iv.	Protocol Complexity	High (4), Moderate (3), Low (2) General (1)					
v.	High Risk Therapeutic Goods	Investigational product nature, novelty or first-in-human use IND (4), therapeutic goods used for life threatening condition e.g. narrow therapeutic index drugs, Class-III MD (3), therapeutic goods in vulnerable population e.g. pediatrics/ geriatrics (2), general (1)					
vi.	High Risk Therapeutic Areas	Oncology/CNS/cardiology Gene Therapy (2), Others (1)					
vii.	Use of invasive/novel drug delivery system.	Yes (2) No (1)					
viii.	Data Integrity Risks (Previous history)	Multiple major/minor observations reported in GCP inspections (2), None (1)					
ix.	Previous GCP	Major findings (3), Minor					

	Inspection History	(2), Good Compliance (1)					
x.	Sponsor Oversight	Poor (no CRO or monitor assigned) (3), Adequate (CRO assigned) (2), Strong (CRO with DSMB) (1)					
xi.	Regulatory Priority	High-profile/Approval-linked (2), Routine MRCT (1)					
Total							

* Duration of study

Total Possible Score: 44

Interpretation of Scores

- **>35** = High-risk → **Priority inspection**
- **25–35** = Medium-risk → **Monitor closely**
- **11–24** = Low-risk → **Routine surveillance or low-priority**
- **≤11** = Minimal risk → **Routine surveillance or low-priority**

8.3 GCP Inspection Planning Process & Schedule

i. **Data Collection**
Data collection from Clinical Trial application

ii. **Risk Calculation through Scoring method**
Apply the scoring matrix across all ongoing/planned trials.

iii. **Prioritization of trials and resources**
Development of Risk-Based GCP inspection lists of trials and assignment resources based on score and nomination of inspectors.

iv. **Inspection Plan Development**
High-scoring trials will be prioritized for on-site inspection
GCP inspection scope can be full-scope (Site & Trial Specific), trial specific/focused, or triggered.

v. **Issuance of GCP Inspection Plans**
After finalization of Risk-Based Inspection plan, it will be uploaded on DRAP official website and all PI/stake holders will be informed accordingly.

vi. **Continuous Review**
Re-score trials bi-annually or with major study changes (e.g., protocol amendments, serious findings) or based on their previous findings.

9. OBJECTIVES OF GCP INSPECTIONS

The DRAP may conduct GCP inspections under the following circumstances:

i. To verify the accuracy and reliability of conduct of clinical trial/research and its data that has been submitted to support registration of the medicine for its Market Authorization.;
ii. To investigate a complaint about the conduct of the study at a particular site;
iii. Before/upon termination of the clinical site/Clinical research;
iv. During ongoing clinical trials/research to providereal-time assessment of the investigator's conduct of the trial/research and protection of human subjects;
v. Monitoring serious adverse events notification reporting frequency;
vi. Monitoring on safety handling of investigational products and other related items;
vii. On request by the investigator/sponsor.
viii. Upon direction of the CSC or the Authority

10. NATURE OF GCP INSPECTIONS:

GCP inspections may be protocol specific inspections or system specific inspections.

10.1 Protocol specific inspections:

This type of inspection will seek to ascertain whether the trial/research protocol meets the standards of GCP e.g. to determine whether the dossier data submitted to regulatory authority are credible and accurate etc.

10.2 System specific inspections:

Clinical trial/research systems that may be inspected include informed consent, process of obtaining the consent, handling of investigational product, biological samples, pharmacovigilance and monitoring etc.

An inspection may be conducted at an investigator site (trial site) which is already approved by DRAP, any laboratory used for clinical trial/research analyses and facility of the Sponsor, Contract Research Organizations/facilities, acting under arrangements with a Sponsor or investigator to perform some or all of the functions of the Sponsor, may also subject to inspection.

Clinical Trial/Research Sites/Centers may be inspected before the regulatory approval, while the trial is on-going, when subjects are currently being enrolled in a trial/research or completed on a routine basis or sometimes when triggers by a complaint or there is a suspicion of serious non-compliance integrity issues and/or scientific/ethical misconduct.

Generally, GCP inspections are announced. However unannounced inspections may also be possible.

11. TYPES OF GCP INSPECTIONS:

The GCP Inspections can either be routine, triggered, or can be conducted in response to an application.

11.1 Routine GCP inspections:

Routine inspections are inspections carried out as a routine surveillance of GCP compliance in the absence of specific trigger elements. These inspections are announced and can be conducted before, during or after completion of Clinical Trial/Research. The duration of the inspection and the number of inspectors present on an inspection will vary depending on the complexity of the Clinical Trial/Research and activities conducted at the site/center and it shall be decided by the CSC.

11.2 Triggered GCP inspections:

These are the inspections prioritized as per "Risk Calculation" or requested/directed by the CSC where there is a concern due to either the actual issues observed or the potential impact of deviations from GCP on the conduct of the study as a whole or at a particular site or when a serious violation or breach of GCP standards has occurred. This type of inspection may be done announced or unannounced and applies to ongoing or completed clinical trials/research and decided by the CSC.

12. GCP INSPECTORS COMPETENCY MATRIX, QUALIFICATION AND NOTIFICATION

12.1 Competency Matrix:

The following Competency Matrix is for guidance to assess and develop skills for GCP Inspectors. It identifies key competency areas, describes each, and outlines the expected behaviors or knowledge at three levels of proficiency: Basic, Intermediate, and Advanced/Expert:

S. NO.	Competency Area	Description	Level 1: Basic (Score-1)	Level 2: Intermediate (Score-2)	Level 3: Advanced/Expert (Score-3)
1	Knowledge of Clinical Research related Rules & Regulations of the DRAP.	Understanding of the Bio-Study Rules, 2017	Reads and understands the Rules	Applies relevant rules during inspections	Trains others and interprets rules/regulation
2	Knowledge of Clinical Research related Guidelines of DRAP.	Understanding of the Guidelines for Conduct of Clinical Research in Pakistan	Reads and understands the guideline	Applies Guidelines during inspections	Trains others and interprets guidelines
3	Knowledge of GCP related Guidelines of DRAP.	Understanding of the Guidelines for Conduct & Reporting of GCP Inspection	Reads and understands the guideline	Applies Guidelines during inspections	Trains others and interprets guideline
4	ICH-GCP Knowledge	Understanding of latest ICH-GCP (E6(R2))	Reads and understands	Applies ICH-GCP guidelines during	Trains others and interprets guideline

		Guidelines	guidance	inspections	
5	Clinical Trial Design	Understanding of trial protocols, phases, design	Can understand trial structure and documents?	Can evaluates protocols for compliance?	Can advises on protocol design and compliance?
6	Inspection Planning	Planning scope, resources, and documentation for inspection	Have a role and participates in GCP inspection planning activities	Can independently plans / propose standard GCP inspections	Can lead complex/multisite inspection plans
7	Risk-Based Inspection	Ability to assess and prioritize inspections using risk-based scores	Familiar with GCP risk-based planning concepts	Applies risk-based scoring system	Develops Risk-Based strategies
8	Ethical Compliance	Ability for reviewing informed consent processes and ethical issues	Understands ethical requirements	Can evaluates informed consent and its processes	Can advise on ethical considerations
9	Data Integrity	Assessing systems, source data verification, audit trails	Can identifies simple data issues	Can audits data trails.	Can identify root causes and system-wide issues regarding data integrity.
10	Communication	Conducting interviews & communication of findings during GCP Inspection.	Uses only scripted communication	Can conduct independent interviews	Can lead communication under a complex conditions
11	Reporting & Documentation	Recording observation, creating and reviewing inspection reports, categorization of risks and CAPA assessments	Can assists in GCP inspection reports drafting	Can generate / writes and finalizes GCP inspection reports	Can reviews and approves GCP inspection reports received from other GCP Inspectors.
12	Clinical Trial Site and CRO/Sponsor's Oversight	Evaluating Sponsor and CRO roles and their oversight effectiveness	Can reviews trial site-level documents	Can reviews multi-sites documents and oversight mechanisms	Can assess sponsor's/CRO's oversight effectiveness

* After competency assessment training need can be analyzed and accordingly, roles in GCP inspection panel can be assigned as per competency scores:

- ≥30 = Trainer/Senior GCP Inspector.
- >25 = Lead Auditor/ GCP Inspector.
- >18 = Coordinator/GCP Inspector.
- >12 = Reviewer/GCP Inspector.
- ≤12 = Junior/Trainee GCP Inspector.

12.2 Training requirements for role progression and roles in GCP inspection panels.

Following table describe roles and professional development trainings for GCP inspectors:

Role in panels	Entry Requirements	Training
Junior / Trainee GCP Inspector	Bachelor's 1-3 years professional experience in clinical research regulation and/or other regulatory functions	GCP Certification, SOPs, Guidelines, nomination in panel with senior GCP inspectors.
GCP Inspector	Bachelor's/Master's 3-5 years professional experience in Clinical Research regulation and/or other regulatory functions along with GCP audit	Certification on ICH-GCP Guidelines, Certified Clinical Research Professional (CCRP), Training on Risk-Based Planning, Safety Reporting & Pharmacovigilance, Communication Skills.

	experience	
Lead GCP Inspector / Junior Trainer	≥7 years on job experience on Clinical Research regulation and/or other regulatory functions with abilities to interpret and incorporate international standards in local guidelines and inspection leadership	Certification on ICH-GCP Guidelines, Certified Clinical Research Professional (CCRP), Training on Risk-Based Planning, Safety Reporting & Pharmacovigilance, Communication Skills, ethics, risk-based inspection.
Trainer / Senior GCP Inspector	≥10 years + leadership	Certified Clinical Research Professional (CCRP) and/or CPI, Training on Risk-Based Planning, Safety Reporting & Pharmacovigilance, Communication Skills, ethics, risk-based inspection. Certification on ICH-E Module Mentoring, international standards

12.3 Minimum eligibility Criteria for GCP Inspectors:

Minimum educational and certification required for consideration to be a DRAP notified GCP inspector is as follows:

i. Educational Background

A Bachelor's degree in Pharmacy, Health Sciences, Medicine, Regulatory Sciences, Public Health, or a related field, from recognized University along with valid certification on ICH-GCP Guidelines.

Advanced degrees (Pharm D, Masters or PhD) along with advanced certification (e.g. CCRP, CPI, MRCT, US-FDA Trial Investigator) will be preferred.

ii. Professional Experience

Minimum 3 years of professional experience in Clinical Research, Pharmacovigilance and/or other related regulatory field.

Certification: Valid Certification on ICH-GCP Guidelines (Mandatory)

iii. Knowledge Requirements

Familiar with the Bio-Study Rules, 2017, the latest ICH-GCP Guidelines, Guidelines for Conduct of Clinical Research in Pakistan (latest edition) and Guidelines for Conduct & Reporting of GCP Inspections (latest edition).

Understanding of clinical trial operations and regulatory approval process.

iv. Other additional technical & soft skills:

Interviewing, conflict resolution, analytical thinking, and report writing

- Professional integrity and independence
- Strong communication skills
- Critical thinking.
- Willingness to travel across country.

13. GCP INSPECTION PROCESS:

The complete process for conduct and reporting of GCP Inspection is described below:

13.1 Nomination/Notification of GCP Inspection Team:

The Authority will notify the GCP Inspectors upon recommendations of the Pharmacy Services Division and the CSC, who fulfill minimum eligibility criteria. A manual of GCP Inspectors certification will be kept in the Pharmacy Services Division.

Notified GCP inspectors shall be nominated by the CSC and/or by the Authority shall perform the inspection. A member of the CSC or any other expert (fulfilling minimum eligibility criteria) nominated by the CSC or the Chairman CSC, may accompany the inspection team. The inspection team will be constituted considering the Risk-Based score, and other variables considered relevant on a case by case basis by the CSC. The inspectors should be well qualified (fulfilling minimum eligibility criteria). The team will have a lead inspector responsible for leading and coordinating the inspection, collating the information from team members, and finalizing the inspection report.

13.2 Notification of schedule of GCP Inspection:

In general, Risk-Based GCP Inspection plan issued bi-annually by the Pharmacy Services Division for information of the Investigator, Sponsor, CROs, Site/Center or Bio-Analytical Laboratory of a Clinical Trial/Research, but they will again be notified at least 7-10 days prior to the scheduled inspection date and advised to confirm availability of inspectee and relevant trial related personnel. The notification of schedule will identify the study, the proposed sites to be inspected and, the proposed date(s) of inspection. In relation to triggered inspections, the CSC/DRAP may provide a shorter notice period or may conduct unannounced/surprise inspection.

The following information may be requested from the inspectee (Investigator, Sponsor, CROs, Site/Center or Bio-Analytical Laboratory of a Clinical Trial/Research) to be submitted to the CSC/DRAP;

- Research participant/enrolment status per trial site (number randomized, drop-out rate, and number of serious adverse events reported per site), at trial initiation or during the trial.
- Copies of study standard operating procedures along with amendments e.g. (monitoring procedure, informed consent procedure, serious adverse event reporting procedure, IPs / drug supply procedure).
- Trial-specific document such as Trial Master File (TMF) or Investigator Site File (ISF), a copy of the current protocol and protocol amendment and informed consent form, source data verification guidelines, IPs/product handling instructions, laboratory manual, randomization code (if it is necessary), breaking procedure (if it is necessary), monitoring plans and reports.
- Updated CV of principal investigator or investigators, and members of the IRB.
- Arrangements for direct access to any computerized systems upon which trial date

or essential documents are stored.

- Any other documentation deemed necessary by the inspectors.

An inspection plan, outlining the sites to be inspected and the schedule of meetings to be held with the Investigator(s) and/or Sponsor will be provided prior to the inspection to the inspectee. The Trial Master File comprising the essential documents which will enable both the conduct of the trial/research and the quality of the data produced, to be evaluated must be available by direct access and shall provide the basis for the GCP inspection.

13.3 Pre – inspection preparation

The inspection schedule/dates will be confirmed with the inspectee (incase of announced GCP inspections only) and the inspectee may be required to submit the aforementioned data/documents to the CSC / Pharmacy Services Division-DRAP on priority but not later than 14 days of the receipt of the notice of GCP inspection, along with relevant essential documents. The inspection plan shall be finalized by the nominated panel coordinator.

Each team member should become familiar with all the relevant documents, including the Study Protocol(s), Informed Consent Forms, Clinical Trial Report(s), Case Report Forms, Adverse Event Reports, Research Study / Site information, and other related documentation.

13.4 Conduct of GCP inspection

13.4.1 Opening Meeting:

GCP inspections will start with an opening meeting, document review, interview sessions, visit to site facilities and a closing meeting as indicated in the inspection plan. An opening meeting will be conducted with Principal Investigator and study team/staff by the inspectors, where the inspectors will explain the GCP inspection plan, and also confirm that the resources, essential documents and facilities required for the inspection are available.

13.4.2 Presentation/Overview of Research:

The inspectee/PI/SI shall be required to present a general overview of the Clinical Trial/Research at this meeting, information regarding the recruitment of subjects, informed consent process, investigational product management, safety reporting, biological sample handing etc.

13.4.3 Interview(s) of Study/Research Team:

During inspection, the inspectors may interview Investigator/Study team/staff and participants to determine how the trial/research is conducted and may ask questions relating to study staff, Institutional Review Board (IRB), Investigator Site Files, Trial Participant Recruitment, Informed Consent, Investigational Product Management Safety Reporting, Biological Samples handling, Source Documents, Case Report Forms, record keeping, monitoring, etc.

13.4.4 Visit of Site/Center Facilities:

The GCP Inspectors shall visit facilities used to conduct Clinical Trial/Research activities.

13.4.5 Document Review:

The activities and documents to be examined during the routine type of GCP inspection undertaken by the CSC/DRAP are outlined below;

Protocol specific inspections may include:	System Inspection may include:
• Trial Master File • Legal and administrative aspects • Communication with the ethics Committee • Communication with the National Bio-Ethics Committee • Communication with the CSC/DRAP • Other Communications • Organizational aspects • Implementation of the trial at the investigator site • Facilities and equipment • Management of biological samples • Organization of the documentation • Monitoring and auditing • Use of computerized systems • Informed consent of trial participants • Details of impartial witness if any • Review of the trial participant data • Adverse event reporting • Management of the investigational product(s) • Protocol deviations • Other, as required by the GCP Inspectors.	○ Organization and personnel ○ Facilities and equipment ○ Sponsor/CRO Operating Procedures ○ Implementation and termination of the clinical trial ○ Monitoring ○ Investigational Product ○ Sample management ○ Safety and adverse events reporting ○ Data handling and clinical trial report ○ Documentation archiving ○ Sponsor audit and quality assurance system ○ Management process for protocol deviations ○ Delegation of duties ○ Other, as required by the GCP Inspectors

All the essential documents concerning a clinical trial must be available for inspection. A TMF/ISF for a clinical trial must contain all documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. The TMF/ ISF must be established from the onset of the trial and kept updated on an ongoing basis as the trial completes different stages. All the essential documents contain a minimum list of documents generated before, during and after the trial, which must be stored in the TMF/ ISF with the Sponsor and Investigator, respectively. If certain documents are assessed not to be of relevance to the TMF/ISF, it must include a reason for omitting these documents in a timely manner.

The inspectee must ensure that a list of source data is available with a description of where source data etc. can be found. Source data may be both electronic and on paper. A list of such data includes medical records, laboratory reports, diaries, dispensing logs, ECG print-

outs, Case Report Forms (CRF), X-ray images, radiological reports, etc. The list of source data must be prepared before the trial/research is initiated. It must be signed and dated by the principal investigator or by a person whom the principal investigator has delegated or assigned this task. The list must be available in the TMF/ISF.

13.4.6 Closing/Exit Meeting:

At the end of GCP inspection, there will be an exit meeting where the inspectors will present the GCP inspection findings and grading (As defined in the guidelines and inspection Checklist) to the inspectee(s) and ensure that results of the inspection are clearly understood.

14. ANNEXURE-I

GCP INSPECTION CHECKLIST

A. DESCRIPTION AND GRADING OF GCP INSPECTION FINDING

Critical (CR)	
Definition	Conditions, practices or processes that adversely affect the rights, safety or wellbeing of the subjects and/or the quality and integrity of data. Critical observations are considered totally unacceptable.
Possible consequences	Rejection of data and/or legal action required.
Remark	Observation classified as critical may include a pattern of deviations classified as major, bad quality of the data and/or absence of source documents. Manipulation and intentional misrepresentation of data belong to this group.
Major (MA)	
Definition	Conditions, practices or processes that may adversely affect the rights, safety or wellbeing of the subjects and/or the quality and integrity of data. Major observations are serious deficiencies and are direct violations of GCP principles.
Possible consequences	Data may be rejected and/or legal action required.
Remark	Observations classified as major, may include a pattern of deviations and/or numerous minor observations.
Minor (MI) / Other	
Definition	Conditions, practices or processes that would not be expected to adversely affect the rights, safety or wellbeing of the subjects and/or the quality and integrity of data. Minor observations are undocumented departure from GCP principles.
Possible consequences	Observations classified as minor, indicate the need for improvement of conditions, practices and processes.
Remark	Many minor observations might indicate a bad quality and the sum might be equal to a major finding with its consequences.
Comments	The observations might lead to suggestions on how to improve quality or reduce the potential for a deviation to occur in the future.
Responsibility for the finding	The responsibility for addressing the finding will be stated. This could be Sponsor/CROs, Principal Investigator, IRB/IEC/ERC etc.

B. GCP INSPECTION CHECKLIST

Names, Designation & role of GCP- Inspector(s)	• • •
Date of GCP-Inspection	
Risk-Based Category & Score of Clinical Trial & Site	
Nature & Type of GCP Inspection	
Name and address of the site	
Trial/Research Protocol Number	
Number of Site(s) involved	
Stage/Status of the Study:	
Timing of GCP-Inspection	• Before trial commencement ☐ • During clinical research conduct ☐ • After completion of trial/research ☐ (Tick/encircle one)
Name of Principal Investigator	
Name(s) of Co-Principal Investigator	
Name(s) of Site-Principal Investigator	
Study Title	
DRAP/CSC Approval / Registration No	
Research/Trial Protocol No. Version & date:	
Amendment(s) approval history: Version & date:	
IRB/ERC Protocol approval Version & date:	
NBC Protocol approval version & date:	
Informed Consent Form Version approved & date:	
ICF Amendment History approval Version & date:	
Screening date of 1st participant	
How many participants enrolled? (till date of GCP-Inspection)	
How many participants withdrew from the study?	
How many participants completed the study?	

Observations are classified into the categories "Critical", "Major", "Minor/ Other" as defined in Section-A above. The recommendations are listed at the end of the report.

A. FACILITY INSPECTION	YES	NO	NA	Observation/Grading
1. Consulting Area				
1.0 Does the area for individual participant informed consenting provide the required privacy to maintain confidentiality?				
1.1 Is the consulting area where the PI/designated person evaluates the participants during visits adequate in size?				
1.2 Are there lock-up cupboards for confidential documents?				
1.3 Is the trial specific equipment available in the consulting room?				
1.4 If not, is the area where procedures are performed adequate and easily accessible?				
1.5 Does the PI manage and maintain the trial visits? To add to inspection training that this could be not applicable in the case of field sites				
2. Procedure Room				
2.1 Is all equipment e.g. sphygmomanometer, scale(s), etc. as required per protocol calibrated and validated?				
2.2 Are SOPs on how to use equipment available?				
2.3 Is the phlebotomy/blood sampling area kept according to infection control procedures?				
2.4 Waste handling according to applicable guidelines.				
2.5 Is the emergency trolley available in the procedure area? As per the requirements for vaccines and medical devices. 2.5.1 Does the facility have emergency power back up to maintain drug temperatures and sample storage? 2.5.2 Is the trolley locked and are the keys available and controlled? 2.5.3 Are expiry dates clearly checked and controlled? 2.5.2 Is the emergency trolley frequently checked and documentation as proof available? 2.5.4 Oxygen and accessories available, checked and signed? 2.5.5 Are PI and sub-investigators ALSS trained?				
2.6 Are clinical staff CPR trained?				
3. Pharmacy (Investigational Product Storage Area)				

3.1 Is the pharmacy access controlled, temperature and humidity controlled?				
3.2 Are vaccines stored as per required temperature and humidity?				
3.3 Is the preparation of investigational product management done according to the approved protocol by suitable qualified staff?				
3.4 In case of vaccines, are a spillage SOP available and the study team trained to handle such an incidence?				
3.5 Are electronic or hand-written temperature logs available?				
3.6 Is an SOP on how to handle electricity or temperature failure in the pharmacy available?				
3.7 Are the different studies Investigational Products kept in separate lock-up cupboards and clearly identified'?				
3.8 Are vaccines transported and handled as per cold chain requirements?				
3.9 Have any temperature deviation occurred? If yes, what was the temperature recorded and estimated duration of exposure?				
4 Archive				
4.1 Is there an agreement between Sponsor and Trial Site / CRO on the archiving of documentation?				
4.2 Is this clause documented in the protocol or contract				
5 Clinical Laboratory				
5.1 Is the clinical laboratory at the same site?				
5.2 If not, are procedures in handling biological samples clearly documented?				
5.3 Are all equipment and testing procedures used in the laboratory validated?				
5.4 Is the laboratory accredited for the tests to be performed?				
6 Waste disposals				
6.1 Is the disposal of biological specimens and sharps appropriate?				

B. DOCUMENTATION

Essential Documents are those documents that 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 GCP and all applicable regulatory requirements. **(ICH GCP Section 8)**

Check the *availability* of the following documents:

(During the planning stage, the following documents should be generated ***before*** the conduct of the trial) **General**	**YES**	**NO**	**NA**	**Observation/Grading**
1.1 Approved, signed and final version of the Protocol (including amendments)				
1.2 Final version of the Investigator's Brochure				
1.3 Information Leaflet, information regarding the trial in lay terms				
1.4 Informed Consent Form (translation) and applicable procedure				
1.5 Sample of the case report forms (CRF) as per protocol requirements				
1.6 Any other written information (e.g. advertisements)				
1.7 IRB / IEC approval				
Financial aspects of the trial as predefined in an agreement between the Investigator and the sponsor				
1.9 Guaranteed indemnity / insurance document / statement				
Signed agreements between involved parties e.g. Investigator / CRO, Investigator/Sponsor				
1.11 Source documents and CRF verification procedure (SOPs) available?				
1.12 Clear documentation of transfer of responsibilities				
1.13 All approval documentation:				
(During the planning stage, the following documents should be generated ***before*** the conduct of the trial) **General**	**YES**	**NO**	**NA**	**Observation/Grading**
Independent Ethics Committee approval (Clearly stated which dated version of protocol and informed consent is approved.) Regulatory approval. (Clearly stated which dated version of protocol and informed consent is approved.)				
1.14 List of Ethics Committee members				
1.15 Latest signed and dated CV's of investigators				
1.16 Proof of GCP training of all study team members				
1.17 Pre-trial GCP site assessment report (only at the Sponsor site)				
1.18 List of DSMB members (if any)				
1.19 Verify the availability of the Local Safety Monitor's CV				
1.20 Trial initiation visit, agenda and study team attendance list				
1.21 Verify the availability of the Serious Adverse Event reporting forms and reporting procedures/timelines (including supporting SOP's)				
Laboratory				
Normal values / ranges for medical / laboratory / technical procedures as supplied by the laboratory /				

contract laboratory				
1.23 Laboratory Certification				
1.24 Laboratory Accreditation				
1.25 Quality Control or quality assessment of laboratory by the sponsor				
1.26 Validation methods where applicable				
Investigational Product				
1.27 Sample labels of IPs				
1.28 All shipping records of IPs (dates, batch numbers, Drug Import License & Clearance certificate etc.)				
Proof that conditions as stated in the protocol have been maintained during shipment and storage of products				
1.30 CoA of IPs (Check stability, expiry dates)				
1.31 Vaccine / IPs accountability records e.g. quantities ordered and received				
1.32 Decoding procedures for blinded trials				
(During the planning stage, the following documents should be generated ***before*** the conduct of the trial) **General**	**YES**	**NO**	**NA**	**Observation/Grading**
1.33 Master randomization list availability				
Instruction for handling of investigational product and trial related materials				
Proof that the correct diluent has been packed according to the correct storage condition and shipped with the vaccine?				
2 ICH GCP section 8.3 (In addition to having on file the aforementioned documents the following documentation should be added to the files ***during*** the conduct of the trial) **Documentation**	**YES**	**NO**	**NA**	**Observation/Grading**
2.1 Updates of Investigator's Brochure e.g. ADRs				
Any approved amendments to protocol informed consent forms and/or any other trial documents				
2.3 IRB/IEC and regulatory approval of any new investigators, and their CVs				
2.4 Proof of GCP training				
2.5 Updates of normal values / ranges for medical / laboratory / technical procedures as supplied by the laboratory / contract laboratory				
2.6 IPs accountability documentation and correct use of the product according to the protocol and IPs management				
2.7 Shipment documentation of any new batches of IPs including CoA, batch release and temperature control.				

Communications other than monitoring visits Letters Meeting minutes and agendas Notes of telephone calls				
2.9 Signed Informed Consents				
2.10 Source documents, e.g. X-rays, serology printout, diary cards etc.				
2.11 Signed and dated CRFs				
2.12 SAE reporting to Sponsor				
2.13 Reporting of any serious unexpected ADR and relevant safety information to DRAP, NBC and IRB where required				
2 ICH GCP section 8.3 (In addition to having on file the aforementioned documents the following documentation should be added to the files ***during*** the conduct of the trial) **Documentation**	**YES**	**NO**	**NA**	**Observation/Grading**
2.14 Progress reports to IRB/IEC				
2.15 Participant screening log				
2.16 Participant identification code list				
2.17 Participant enrolment log				
2.18 Study team signature sheet with delegated functions by PI				
2.19 Retained biological samples (records, storage conditions)				
2.20 All deviations e.g. inclusive/exclusive criteria (waiver)recorded				
3 ICH GCP section 8.4 (Documentation ***after*** completion or termination of the trial)	**YES**	**NO**	**NA**	**Observation/Grading**
3.1 IP accountability at site(s) (final reconciliation)				
3.2 Documentation on disposal of IPs				
3.3 Completed participant identification code list				
3.4 Audit Certificate (if applicable), i.e. if carried out				
3.5 Final trial close-out monitoring report				
3.6 Final report by investigator to IRB/IRC/IEC/REC, NBC and the DRAP (refer to ICH GCP section 4.13)				
3.7 Clinical Study Report (refer to ICH GCP section 5.22)				
3.8 Treatment allocation and decoding documentation that have occurred available.				
3.9 Is a follow up plan available (post-trial period) for participants with adverse events related to the IP as per protocol?				

C. INFORMED CONSENT PROCESS	**YES**	**NO**	**NA**
1 Was the informed consent form version used the same as the one approved by the IEC/IRB?			
2 Was a written SOP used to solicit informed consent?			
3 Were all the participants given a copy of a signed informed consent form?			

4	Did all the participants sign the consent form prior to any study related procedure?			

D. GENERAL INFORMATION

a) Ask for an organogram of the Trial Site/CRO and note the following points:
   a.1 Number and categories of people employed;
   a.2 Description of the qualifications, training and experience of the personnel;
   a.3 Work load of study team;
   a.4 Number of concurrent clinical studies performed on site and identification of participants to avoid confusion and mix-ups of IP's administration.

b) Ask for a description of the quality assurance system set up at the trial site.

c) Check the existence, availability, accessibility and validity of the operating procedures; ask for a list of the Standard Operating Procedures used for the trial.

d) Verify the availability of 100% of all documentation particularly the ICF, CRF and source documents.

e) Perform verification of Informed Consent forms as per DRAP requirements.

f) Perform at least 25% Source documentation versus CRFs verification

g) Perform a100% accountability of IPs

E. Any other Information / Detail as required by panel or provided by inspectee.

F. List of deficiencies:

S. No	Deficiencies	Reference	
1 Critical			
1.1			
1.2			
2. Major			
2.1			
2.2			
3. Minor			
3.1			

G. GCP inspection outcomes:
Initial conclusion:

H. References used:

a) **The Bio-Study Rules, 2017**
b) **Guidelines for Conduct of Clinical Research in Pakistan**
c) **Latest ICH-GCP Guidelines**
d) **Guidelines for Conduct & Reporting of GCP Inspections**

I. Signature of GCP Inspectors

i. Name & Designation
ii. Name & Designation
iii. Name & Designation

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