MINISTRY OF HEALTH
NATIONAL PHARMACEUTICAL REGULATORY AGENCY

MALAYSIAN GUIDELINE FOR GOOD CLINICAL PRACTICE (GCP) INSPECTION

THIRD EDITION (2026)

NATIONAL PHARMACEUTICAL REGULATORY AGENCY (NPRA)

MALAYSIAN GUIDELINE FOR GOOD CLINICAL PRACTICE (GCP) INSPECTION

National Pharmaceutical Regulatory Agency

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4. EMA. (2007). *Annex IV to Procedure for conducting GCP inspections requested by the EMEA: Sponsor and/or Contract Research Organization (CRO)*. (INS/GCP/3/IV)
5. US FDA. Code of Federal Regulations, *Title 21 Parts 11: Electronic records; electronic signatures.* (21CFR11)
6. US FDA. Code of Federal Regulations, *Title 21 Parts 50: Protection of human subjects*
7. US FDA (2014) *Guidance for Industry Circumstances that Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection*
8. CANADA. Health Canada. (2008). *Classification of observations made in the conduct of inspections of clinical trials.* (GUIDE-0043)
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FOREWORD

Clinical research has been identified as one of the key entry-point projects under the National Economic Transformation Program since 2010. With the increasing number of clinical trials conducted in Malaysia, a concerted effort is crucial to ensure compliance with Good Clinical Practice (GCP) to safeguard the rights, safety, and well-being of trial participants, as well as to uphold the integrity and reliability of clinical trial data.

To this end, GCP inspections are conducted by NPRA Inspector to verify that trials are carried out in accordance with the Malaysian Guideline for Good Clinical Practice, applicable ethical principles, and relevant regulatory requirements. The first edition of the Malaysian Guideline for GCP Inspection was published in 2010. The subsequent revision has been comprehensively revised to serve as the latest reference for the coordination, preparation, conduct, and reporting of GCP inspections.

The revised guideline provides detailed information on inspections at clinical trial sites, sponsor sites, and contract research organization (CRO) facilities. It also incorporates updated guidance on the classification and handling of inspection findings, including the appropriate corrective and preventive actions (CAPA). The examples provided are intended for illustrative purposes only and should be interpreted contextually on a case-by-case basis.

Importantly, this revision reflects Malaysia's commitment to harmonizing with global regulatory standards and incorporates the latest requirements in line with ICH E6(R3).

Finally, I would like to extend my sincere appreciation and congratulations to the dedicated working committee for their valuable contributions to the development of this second edition of the Malaysian Guideline for GCP Inspection.

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1.0 INTRODUCTION

The National Pharmaceutical Regulatory Agency (NPRA) is responsible for conducting inspections and investigations in all clinical trials related to medicinal products for human use.

Following the decision made by Ministry of Health on the National Medicines Policy, there should be an established requirement for compliance with Good Clinical Practice for all clinical studies pertaining to medicinal products for human use to determine whether the clinical studies were conducted in accordance with applicable regulatory requirements which include regulations, ethical standards, the Malaysian Guidelines for Good Clinical Practice and the Declaration of Helsinki.

The Drug Control Authority (DCA) had endorsed the Guideline for Good Clinical Practice inspection in accordance with Regulation 29 under the Control of Drugs and Cosmetics Regulation 1984 in the 221 meeting on the 29th October 2009. The Malaysian Guidelines for Good Clinical Practice Inspection will integrate the principles of GCP as described in the Malaysian Guidelines for Good Clinical Practice, regulations and also ensure that the clinical trials are carried out in accordance with the ethical principles that are reflected, for example, in the Declaration of Helsinki. This may include but may not be limited to conducting clinical trials in accordance with the approved protocol, that the data generated are accurate; that participants enrolled in clinical trials are not subjected to undue risks and that the trial is conducted in accordance with the generally accepted principles of GCP.

Clinical trials may be inspected while the trial is still on-going, when participants are currently enrolled in a trial or when the trial has been completed. An inspection may also be conducted when triggered by a complaint or when there is a suspicion of serious non-compliance, integrity issues and/or scientific or ethical misconduct.

An inspection may be conducted at the qualified investigator (clinical trial site), facility of the sponsor, Contract Research Organisation's (CRO) facilities, clinical laboratories and other establishments deemed appropriate by NPRA. While NPRA typically conducts on-site inspections, remote inspections may be performed when deemed necessary, taking into consideration specific circumstances such as public health emergencies, travel restrictions, or other factors that may impact the feasibility of on-site inspections.

The objectives of a GCP inspection are to:

- Ensure the rights, safety and well-being of trial participants have been protected.
- Determine whether the trial was conducted in accordance with applicable regulatory requirements, ethical standards and Malaysian Guidelines for Good Clinical Practice.
- Determine whether the data submitted in the dossier are credible and accurate.
- Assure the integrity of scientific testing and study conduct.

- Take corrective action to ensure compliance and enforcement actions when deemed necessary.

2.0 TERMS AND DEFINITIONS

Adverse Events and Adverse Reaction-Related Definitions:

Adverse Event (AE)
Any unfavourable medical occurrence in a trial participant administered the investigational product. The adverse event does not necessarily have a causal relationship with the treatment.

Adverse Drug Reaction (ADR)
- In the pre-approval clinical experience with a new investigational product or its new usages (particularly as the therapeutic dose(s) may not be established): unfavourable and unintended responses, such as a sign (e.g., laboratory results), symptom or disease related to any dose of a medicinal product where a causal relationship between a medicinal product and an adverse event is a reasonable possibility. The level of certainty about the relatedness of the adverse drug reaction to an investigational product will vary. If the ADR is suspected to be medicinal product-related with a high level of certainty, it should be included in the reference safety information (RSI) and/or the Investigator's Brochure (IB).
- For marketed medicinal products: a response to a drug that is noxious and unintended and that occurs at doses normally used in humans for prophylaxis, diagnosis or therapy of diseases or for modification of physiological function.

Serious Adverse Event (SAE)
Any unfavourable medical occurrence that is considered serious at any dose if it:
- Results in death,
- Is life-threatening,
- Requires inpatient hospitalisation or prolongation of existing hospitalisation,
- Results in persistent or significant disability/incapacity, or
- Is a congenital anomaly/birth defect.

An important medical event that may not be immediately life-threatening or result in death or hospitalisation, that may jeopardise the participant or that may require intervention to prevent serious outcomes should generally be considered as serious.

Suspected Unexpected Serious Adverse Reaction (SUSAR)
An adverse reaction that meets three criteria: suspected, unexpected and serious.
- Suspected: There is a reasonable possibility that the drug caused the adverse drug reaction.
- Unexpected: An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator's Brochure or alternative documents according to applicable regulatory requirements; see **RSI**).
- Serious: See above for **SAE.**

Agreement
A document or set of documents describing the details of any arrangements on delegation or transfer, distribution and/or sharing of activities and, if appropriate, on financial matters between two or more parties. This could be in the form of a contract. The protocol may serve as the basis of an agreement.

Applicable Regulatory Requirement(s)
Any law(s) and regulation(s) addressing the conduct of clinical trials of investigational products.

Approved Training in Good Clinical Practice
Training which is approved by the National Committee for Clinical Research. The content of the training must incorporate the curriculum as stipulated by the committee.

Assent
Affirmative agreement of a minor to participate in clinical trial. The absence of expression of agreement or disagreement should not be interpreted as assent.

Audit
A systematic and independent examination of trial-related activities and records performed by the sponsor, service provider (including contract research organisation (CRO)) or institution to determine whether the evaluated trial-related activities were conducted and the data were recorded, analysed and accurately reported according to the protocol, applicable standard operating procedures (SOPs), Good Clinical Practice (GCP) and the applicable regulatory requirement(s).

Audit Certificate
A declaration of confirmation by the auditor that an audit has taken place.

Audit Report
A record describing the conduct and outcome of the audit.

Audit Trail
Metadata records that allow the appropriate evaluation of the course of events by capturing details on action (manual or automated) performed relating to information and data collection and, where applicable, to activities in computerised systems. The audit trail should show activities, initial entry and changes to data fields or records, by whom, when and, where applicable, why. In computerised systems, the audit trail should be secure, computer-generated and time stamped.

Blinding/Masking
A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single-blinding usually refers to the participant(s) being unaware, and double-blinding usually refers to the participant(s) and investigator(s) and, if appropriate, other investigator site staff or sponsor staff being unaware of the treatment assignment(s).

Case Report Form (CRF)
A data acquisition tool designed to record protocol-required information to be reported by the investigator to the sponsor on each trial participant (see **Data Acquisition Tool**).

Certified Copy
A copy (irrespective of the type of media used) of the original record that has been verified (i.e., by a dated signature or by generation through a validated process) to have the same information as the original, including relevant metadata, where applicable.

Clinical Trial
Any interventional investigation in human participants intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic 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 Trial Site(s)
The location(s) where trial-related activities are conducted and/or coordinated under the investigator's/institution's oversight.

Clinical Study Report (CSR)
A written description of a trial of any investigational product conducted in human participants, 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).

Comparator
An investigational or authorised medicinal product (i.e., active control), placebo or standard of care used as a reference in a clinical trial.

Compliance (in relation to trials)
Adherence to the trial-related requirements, GCP requirements and the applicable regulatory requirements.

Computerised Systems Validation
A process of establishing and documenting that the specified requirements of a computerised system can be consistently fulfilled from design until decommissioning of the system or transition to a new system. The approach to validation should be based on a risk assessment that takes into consideration the intended use of the system and the potential of the system to affect trial participant protection and the reliability of trial results.

Contract Research Organisation (CRO)
See **Service Provider.**

Confidentiality
Prevention of disclosure to other than authorised individuals of a sponsor's proprietary information or of a participant's identity or their confidential information.

Coordinating Investigator
An investigator assigned the responsibility for the coordination of investigators at different investigator sites participating in a multicentre trial.

Data Acquisition Tool (DAT)
A paper or electronic tool designed to collect data and associated metadata from a data originator in a clinical trial according to the protocol and to report the data to the sponsor.

The data originator may be a human (e.g., the participant or trial staff), a machine (e.g., wearables and sensors) or a computer system from which the electronic transfer of data from one system to another has been undertaken (e.g., extraction of data from an electronic health record or laboratory system).

Examples of DATs include but are not limited to CRFs, interactive response technologies (IRTs), clinical outcome assessments (COAs), including patient-reported outcomes (PROs) and wearables devices, irrespective of the media used.

Data Integrity
Data integrity includes the degree to which data fulfil key criteria of being attributable, legible, contemporaneous, original, accurate, complete, secure and reliable such that data are fit for purpose.

Direct Access
Permission to examine, analyse, and verify records that are important to the evaluation of a clinical trial and may be performed on-site or remotely. 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 participants' identities and their data and sponsor's proprietary information.

Drug
Includes any substance, product or article intended to be used or capable, or purported or claimed to be capable, of being used on humans or any animal, whether internally or externally, for medicinal purposes.

Essential Records
Essential records are the documents and data (and relevant metadata), in any format, associated with a clinical trial that facilitates the ongoing management of the trial and collectively allow the evaluation of the methods used, the factors affecting a trial and the actions taken during the trial conduct to determine the reliability of the trial results produced and the verification that the trial was conducted in accordance with GCP and applicable regulatory requirements.

Good Clinical Practice (GCP)
A standard for the planning, initiating, performing, recording, oversight, evaluation, analysis and reporting of clinical trials that provides assurance that the data and reported results are reliable and that the rights, safety and well-being of trial participants 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 participant or the participant's legally acceptable representative cannot read, and who reads the informed consent form and other documented information supplied or read to the participant and/or their legally acceptable representative.

Independent Data Monitoring Committee (IDMC)
An independent data monitoring committee (e.g., data safety monitoring board) that may be established by the sponsor to assess at intervals the progress of a clinical trial, the safety and relevant efficacy data, and to recommend to the sponsor whether to continue, modify or stop a trial.

Independent Ethics Committee (IEC)/Institutional Review Board (IRB)
An independent body (a review board or a committee, institutional, regional, national, or supranational), constituted of medical/scientific professionals and non-medical/non-scientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human participants involved in a trial and to provide public assurance of that protection, by, among other things, reviewing and approving/providing favourable opinion on the trial protocol, the suitability of the investigator(s), the facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial participants. The legal status, composition, function, operations and regulatory requirements pertaining to IRBs/IECs may differ among countries, but should allow the IRB/IEC to act in agreement with GCP as described in the Malaysian Guideline for GCP.

Informed Consent
A process by which a participant or their legally acceptable representative voluntarily confirms their willingness to participate in a trial after having been informed and been provided with the opportunity to discuss all aspects of the trial that are relevant to the participant's decision to participate. Varied approaches to the provision of information and the discussion about the trial can be used. This may include, for example, providing text in different formats, images and videos and using telephone or video conferencing with investigator site staff. Informed consent is documented by means of written paper or electronic), signed and dated informed consent form. Obtaining consent remotely may be considered when appropriate.

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 trial that may be accessed at the investigator site, at the sponsor's and/or service provider's (including CRO's) facilities, or at other establishments deemed appropriate by the regulatory authority(ies). Some aspects of the inspection may be conducted remotely.

Inspector/Drug Enforcement Officer (DEO)
Any person appointed to be an inspector under Section 3 of Dangerous Drugs Act 1952, Section 31 of Poisons Act 1952, Section 21 of Registration of Pharmacists Act 1951, Section 6A of Medicines (Advertisement and Sale) Act 1956, Section 3 (1) and Section 3 (2) of Sale of Drugs Act 1952.
Throughout this guideline, the term inspector and DEO shall be construed as synonymous and used interchangeably.

Inspected Party/ Inspectee
The inspected party referring to the trial site, service providers, sponsor or any organisations who involved in the conduct of the clinical trials. Inspected party can be used interchangeably with inspectee.

Institution
Any public or private entity or agency or medical or dental organisation in whose remit clinical trials are conducted.

Investigator
A person responsible for the conduct of the clinical trial, including the trial participants for whom that person has responsibility during the conduct of the trial. If a trial is conducted by a team of individuals, the investigator is the responsible leader of the team and may be called the principal investigator. Where an investigator/institution is referenced in this guideline, it describes expectations that may be applicable to the investigator and/or the institution in some regions. Where required by the applicable regulatory requirements, the "investigator" should be read as "investigator and/or the institution.

Investigator Site
The location(s) where trial-related activities are conducted and/or coordinated under the investigator's/institution's oversight.

Investigational Product
A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation 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. Investigational products should be considered synonymous with drugs, medicines, medicinal products, vaccines and biological products.

Investigator's Brochure (IB)
A compilation of the clinical and nonclinical data on the investigational product(s) that is relevant to the study of the investigational product(s) in human participants.

Legally Acceptable Representative
An individual or juridical or other body authorised under applicable law to consent, on behalf of a prospective participant, to the participant's participation in the clinical trial. When a legally acceptable representative provides consent on behalf of a prospective participant, activities related to the consenting process (and re-consent, if applicable) and, where relevant, activities associated with the withdrawal of consent described in this guideline are applicable to the participant's legally acceptable representative.

Metadata
The contextual information required to understand a given data element. Metadata is structured information that describes, explains or otherwise makes it easier to retrieve, use or manage data. For the purpose of this guideline, relevant metadata are those needed to allow the appropriate evaluation of the trial conduct.

Monitoring
The act of overseeing the progress of a clinical trial and of ensuring that the clinical trial is conducted, recorded and reported in accordance with the protocol, SOPs, GCP and the applicable regulatory requirement(s).

Monitoring Report
A documented report following site and/or centralised monitoring activities.

Multicentre Trial
A clinical trial conducted according to a single protocol but at more than one investigator site.

Drug Control Authority (DCA)
An authority set up under the Control of Drugs and Cosmetics Regulations 1984 and as such its responsibility, role and mandate are defined by law.

Finding
A deviation or deficiency noted by an Inspector during an inspection.

Product
a. A drug in a dosage unit or otherwise, for use wholly or mainly by being administered to one or more human beings or animals for a medicinal purpose.
b. A drug to be used as an ingredient for a preparation for a medicinal purpose.

Protocol
A document that describes the objective(s), design, methodology, statistical considerations and organisation of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents.

Protocol Amendment
A documented description of a change(s) to a 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 in compliance with GCP and the applicable regulatory requirement(s).

Quality Control (QC)
The operational techniques and activities undertaken to verify that the requirements for quality of the trial-related activities have been fulfilled.

Randomisation
The process of deliberately including an element of chance when assigning participants to groups that receive different treatments in order to reduce bias.

Reference Safety Information (RSI)
Contains a cumulative list of ADRs that are expected for the investigational product being administered to participants in a clinical trial. The RSI is included in the Investigator's Brochure or alternative documents according to applicable regulatory requirements. Refer to ICH Guideline Development Safety Update Report for more information about RSI.

Regulatory Authorities
Bodies having the power to regulate, including those that review submitted protocols and clinical data and those that conduct inspections. These bodies are sometimes referred to as competent authorities.

Remote Inspection
The process of conducting inspections at a distance or virtually, supported by technology for communicating, sharing, reviewing, and developing documents and accessing systems, without the inspectors being physically present at the sites where the activities subject to an inspection have taken place or where the inspection would routinely be hosted.

Serious Breach
Any deviation of the approved protocol version or the clinical trial regulation that is likely to affect the safety, rights of trial participants and/or data reliability and robustness to a significant degree in a clinical trial.

Service Provider
A person or organisation (commercial, academic or other) providing a service used by either the sponsor or the investigator to fulfil trial-related activities.

Signature
A unique mark, symbol or entry executed, adopted or authorised by an individual, in accordance with applicable regulatory requirements and/or practice to show expression of will and allow authentication of the signatory (i.e., establish a high degree of certainty that a record was signed by the claimed signatory). A signature may be physical or electronic.

Source Records
Original documents or data (which includes relevant metadata) or certified copies of the original documents or data, irrespective of the media used. This may include trial participant's medical/health records/notes/charts; data provided/entered by trial participants (e.g., electronic patient-reported outcomes (ePROs)); healthcare professionals' records from pharmacies, laboratories and other facilities involved in the clinical trial; and data from automated instruments, such as wearables and sensors.

Sponsor
An individual, company, institution or organisation which takes responsibility for the initiation, management, and arrangement of financing of a clinical trial. A clinical trial may have one or several sponsors where permitted under regulatory requirements. All sponsors have the responsibilities of a sponsor set out in the relevant GCP guidelines. In accordance with applicable regulatory requirements, sponsors may decide in a documented agreement setting out their respective responsibilities. Where the documented agreement does not specify to which sponsor a given responsibility is attributed, that responsibility lies with all sponsors.

Sponsor-Investigator
An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to or used by a participant. The term does not include any person other than an individual (e.g., the term does not include a corporation or an agency). The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator.

Standard Operating Procedures (SOPs)
Detailed, documented instructions to achieve uniformity of the performance of a specific activity.

Sub-Investigator
Any individual member of the clinical trial team designated and under the oversight of the investigator to perform significant trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research fellows).

Trial Participant
An individual who participates in a clinical trial who is expected to receive the investigational product(s) or as a control. In this guideline, trial participant and participant are used interchangeably.

Trial Participant Identification Code
A unique identifier assigned to each trial participant to protect the participant's identity and used in lieu of the participant's name when the investigator reports adverse events and/or other trial-related data.

Vulnerable Participants
Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental and nursing students; subordinate hospital and laboratory personnel; employees of the pharmaceutical industry; members of the armed forces; and persons kept in detention. Other vulnerable participants may include persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors and those incapable of giving consent.

3.0 CONDUCT OF GCP INSPECTION

3.1 Categories of GCP Inspection

The inspections of clinical trials are typically initiated in close collaboration with the Centre of Product and Cosmetic Evaluation, NPRA. These inspections may be conducted as part of a routine process or may be triggered by specific concerns, such as issues identified during the evaluation of the product dossier. Inspections may occur during an ongoing clinical trial or after its completion. In some instances, for-cause inspections may be initiated in response to reports or concerns of serious non-compliance, such as data integrity issues or ethical/scientific misconduct. Typically inspection days will be 3 to 4 days.

Descriptions of the inspection categories are as follows:

3.1.1 Routine inspection

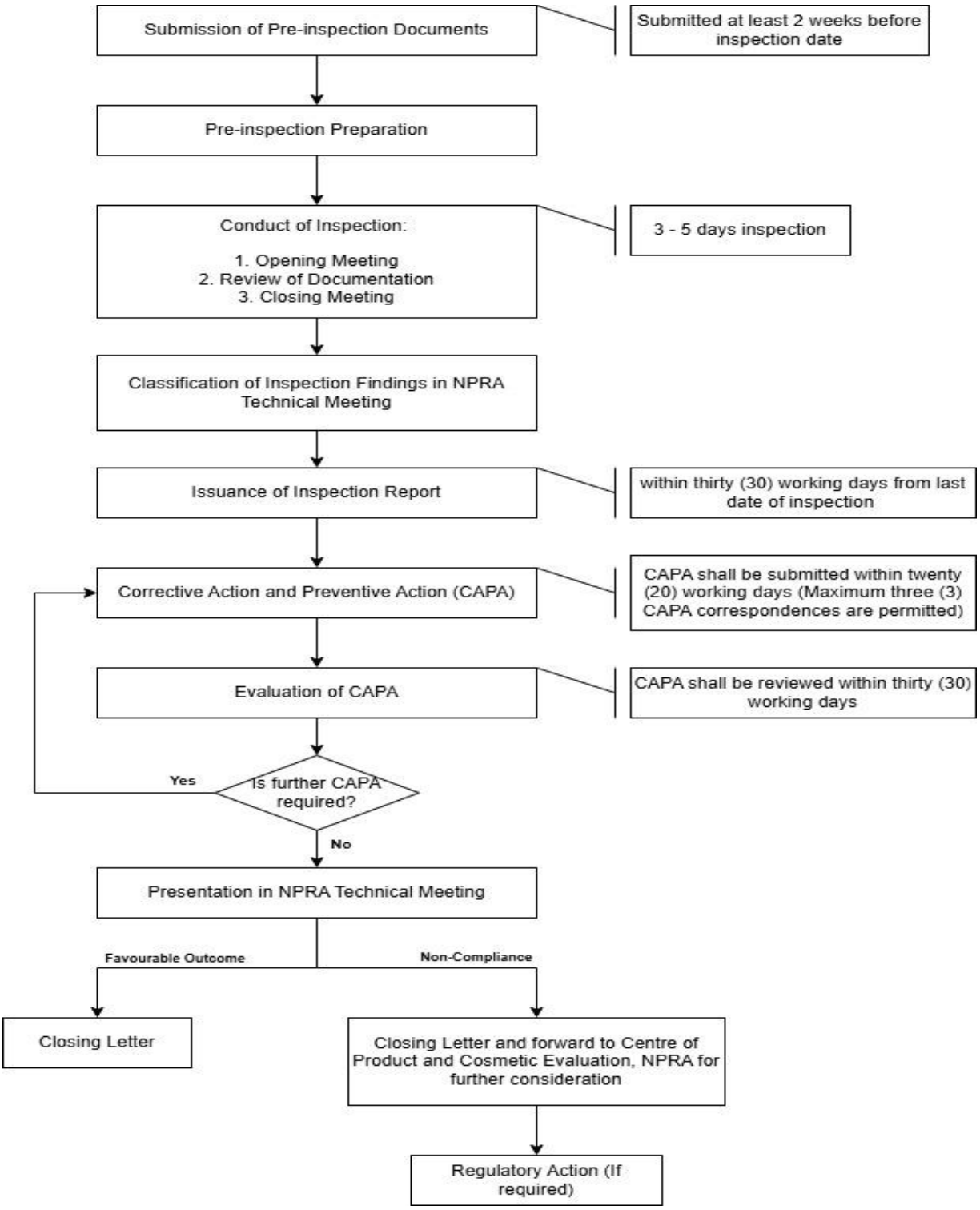
Routine inspections, conducted in connection with a product registration application, may apply to both ongoing and completed clinical trials. Site selection is based on a risk-based approach, taking into account factors such as the significance of the data (e.g., pivotal trials), the characteristics of the target population, the nature and complexity of the investigational product, and other criteria relevant to trial integrity and participant safety.

3.1.2 For-Cause inspection

For-cause inspections are conducted in response to specific indicators of potential non-compliance with regulatory standards or concerns regarding quality and data integrity. Such inspections may occur at any stage of a clinical trial, whether it is ongoing or completed, with the aim of safeguarding participant welfare and ensuring the validity and reliability of clinical data. These inspections may be triggered by:

- Suspected or identified serious breaches of GCP or significant deviations that could impact participant safety or compromise the integrity of clinical trial data.
- Complaints or credible information suggesting non-compliance or quality issues, including information from other regulatory oversight areas such as Good Manufacturing Practice (GMP).
- The need to evaluate the adequacy and effectiveness of corrective actions following previous inspection findings.

3.2 Flow Chart of GCP Inspection



3.3 Conduct of GCP Inspection

An inspection shall be conducted based on an established inspection plan. The plan will be based on the type and scope of the inspection.

3.3.1. Initiation of Inspection

NPRA typically initiates communication with the CTIL/CTX licence holder to coordinate and arrange an inspection. NPRA GCP inspections are typically conducted on an announced basis. For announced inspections, an official announcement letter will be issued to the inspected party, detailing the inspection date, objectives, duration of inspection, names of inspectors, inspection agenda, and a list of pre-inspection documents to be submitted to NPRA. Under normal circumstances, the inspected party is expected to submit the requested pre-inspection documents at least two (2) weeks before the agreed inspection date.

3.3.2. Opening Meeting

The inspection commences with an opening meeting between the inspectors and representative(s) of the inspected party. The lead inspector shall chair the meeting and highlight the objectives, which include, but are not limited to:

- Introducing the inspection team
- Highlighting the scope and objectives of the inspection
- Explaining the regulatory framework governing the inspection
- Informing the inspected party of the delegation of duties among the inspectors
- Briefly explain the methods and procedures to be used during the inspection
- Confirming the availability of resources, documents, and facilities required by the inspector(s)
- Confirming the time and date for the closing meeting and any interim meetings, if applicable.

Following this, a representative of the inspected party will provide an overview presentation of the current activities, workload, and functions of each department involved in the conduct of the clinical trial. The inspected party is also requested to maintain attendance records for both the opening and closing meetings.

3.3.4. Conduct of Inspection

The inspection activities will be outlined in the inspection agenda. During the inspection, the inspector(s) reserve the right to adjust the inspection agenda as necessary to ensure all the inspection objectives are achieved.

Inspector(s) shall be granted direct access to all relevant source data/documents, books, records and reports, whether in hardcopy or electronic format. In the event that the inspectors are denied direct access to documents and/or facilities to which the inspector

has legal access, such refusals will be documented and included in the inspection findings. These refusals may result in the data being deemed unacceptable by the NPRA for product registration purposes.

Detailed checklists for the conduct of inspection and different types of inspection are available on NPRA's webpage.

The inspected party shall ensure that management and other key study personnel are available throughout the inspection to provide input, if requested by the inspectors. Additionally, the inspected party shall make available a designated and suitable room for document review and other inspection-related activities. The inspected party should also ensure that appropriate arrangements are in place to facilitate inspectors' access and permissions to any electronic systems used in the trial.

3.3.5. Closing Meeting

The lead inspector shall chair for the closing meeting, which should include the participation of the inspected party. During this meeting, all inspection findings will be verbally communicated to the inspected party. At the end of the session, the inspected party will be given the opportunity to seek clarification on any findings raised. A list of attendees for both the opening and closing meetings, as well as a record of the evidence collected during the inspection, shall be maintained by the inspected party.

3.4 Inspection Report and CAPA

The inspection report will be issued to the inspected party within 30 working days from the last date of the inspection.

All inspection finding will be classified according to the definitions in *Section* 6.0 and detailed in a written inspection report, which will be communicated to the inspected party via email. The inspected party shall respond and provide an electronic Corrective and Preventive Actions (CAPA) response, addressing the findings within twenty (20) working days from the inspection report date. Subsequent CAPA responses should be submitted within twenty (20) working days.

CAPA correspondence will be reviewed by the inspection team within **30 working days** from the date of receipt. This timeline applies to initial and follow-up CAPA responses

A maximum of three (3) CAPA correspondences are permitted. The Committee (comprising the inspection team, Head of Section for Good Clinical Practice and Good Laboratory Practice, and NPRA Internal Committee) will consider the necessity of a fourth CAPA on a case-by-case basis. Additional CAPA requested by the inspection team must be submitted no later than 20 working days from the date of request.

All communications related to the inspection process shall be conducted exclusively via email.

4.0 OUTCOME OF GCP INSPECTION

4.1 Favourable Outcome

Once all findings have been satisfactorily addressed with the necessary CAPAs, the lead inspector shall recommend closure of the inspection in the NPRA Internal Meeting. The inspection outcome memo will be forwarded to the Centre of Product and Cosmetic Evaluation. A closing letter will then be issued to notify the inspected party that the inspection has been officially closed.

4.2 Non-Compliance

When the CAPAs are not satisfactorily addressed or significant findings remain unresolved, the lead inspector shall present the non-compliance issues in the NPRA Internal Meeting. The non-compliance issues will be forwarded to the Centre of Product and Cosmetic Evaluation for further consideration. A closing letter will be issued to the inspected party. Regulatory actions in response to non-compliance are subject to approval by the DCA.

5.0 REFUSAL OF INSPECTION

Inspector(s) have the right to enter any sites involved to carry out inspections, take samples, require the production of books and documents, and to take copies of, or copies of entries in, such books and documents which inspector (s) reasonably believes would furnish evidence of the inspection and findings without any redaction. Obstructing an inspector(s) intentionally during the conduct of an inspection may result in the non-acceptance of studies for registration purposes.

The circumstances that may be deemed as delaying, denying, limiting, or refusing an inspection are as follows:

5.1. Delay of inspection

Delays may occur for various reasons, some of which are beyond the control of the facility. Delays in scheduling pre-announced inspections, delays during an inspection and delays in producing records without a reasonable explanation are considered obstruction of inspection.

5.2. Denial of inspection

NPRA interprets the word deny to include active behaviour by the owner, operator or service provider to prevent GCP inspectors from conducting an inspection or to prevent GCP inspectors from completing an inspection. This includes statements or physical actions intended to avoid inspection or to mislead, deceive or impede the GCP inspectors.

5.3. Limiting of inspection

Any personnel who prevents GCP inspectors from conducting an inspection to the extent allowable under the applicable regulatory guidelines may be reviewed as limiting inspection.

5.4. Limiting access to facilities

Preventing GCP inspectors from having reasonable access to an area of the site that the inspector is entitled to inspect may be considered limiting an inspection.

5.5. Limiting photography

Photographs are an integral part of GCP inspection because they present an objective and contemporaneous representation of facility conditions. Impeding or resisting photography by GCP inspectors may be considered a limitation if such photographs are determined by the inspectors to be necessary to effectively conduct that particular inspection.

5.6. Limiting access to or copying of records

Ability to have direct access and copy records is a critical aspect of GCP inspection. Not allowing GCP inspectors access to or copying of records may be considered limiting an inspection.

5.7. Refusal to permit entry or inspection

Refuses to permit entry or inspection includes active and passive behaviour and non-action by the owner, operator or service provider i.e. drug facility/institution/site that results in GCP inspectors not being able to enter or fully inspect the facility.

Refusal to permit entry to any inspection site would be written in the inspection report.

6.0 CLASSIFICATION OF INSPECTION FINDINGS

The classification of inspection findings is intended to help classify the severity of findings noted during inspections of clinical trials. The overall evaluation will commensurate with the nature and extent of the deviations (i.e. severity) observed. The inspection findings should be categorised as critical, major and minor, based on the following definitions.

6.1. Critical

Conditions, practices or processes that adversely affect the rights, safety or well-being of the participants and/or the quality and integrity of data.
Critical findings are considered totally unacceptable.

Possible consequences: rejection of data and/or legal action may be required.
Remark: Findings classified as critical may include a pattern of major deviations, poor data quality and/or absence of source documents, fraud, manipulation and/or intentional misrepresentation of data.

6.2. Major

Conditions, practices or processes that might adversely affect the rights, safety or well-being of the participants and/or the quality and integrity of data.
Major findings are serious deficiencies and constitute direct violations of GCP principles.

Possible consequences: data may be rejected and/or legal action may be required.
Remark: Findings classified as major may include a pattern of deviations and/or numerous minor findings.

6.3. Minor

Conditions, practices or processes that would not be expected to adversely affect the rights, safety or well-being of the participants and/or the quality and integrity of data.

Possible consequences: Findings classified as minor indicate areas where improvement of conditions, practices and/or processes is needed.
Remark: A large number of minor findings may reflect poor overall quality, and collectively could be considered equivalent to a major finding with similar consequences.

7.0 FORMULATING RESPONSE TO INSPECTION FINDINGS

Only findings detailed in the inspection report require responses. Each finding should be carefully reviewed to understand the issue raised by the inspector. The inspector will typically cite evidence(s) to support the finding, which may present opportunities for correction and prevention. The finding pertains to, at minimum, the cited evidence.

Upon reviewing the evidence, the inspected party should decide whether the issue can be addressed through corrective action, preventive action, or if it requires documentation only. Issues responded to must be supported with appropriate evidence. Responses to inspection findings shall be submitted electronically using the template outlined in Appendix A – *CAPA Evaluation Form*.

7.1. Analysis of the Finding

The inspected party should thoroughly review the finding to determine its root cause. The following questions may guide the analysis:

- Is the finding systematic (i.e. could other trials be affected) or isolated?
- What was the cause of the finding?
- Was it due to a genuine error or oversight?
- Was there a lack of training (individual or group)?
- Was there an absence of a documented procedure?
- If a documented procedure existed, was it not followed or was it inadequate?

7.2. Corrective Action

Provide a clear explanation of the corrective action.

7.3. Preventive Action

Preventive action should include details of any planned amendments to the referenced documented systems or procedures, e.g. training to be undertaken and methods for assessing the effectiveness of the preventive measures implemented.

7.4. Timelines

Both corrective and preventive actions should be accompanied by appropriate timelines for completion.

APPENDIX A: CAPA EVALUATION FORM

Inspection & Organisation Information	
Inspection Reference Number	
Category/Scope	
Type of Inspection	
Organisation Inspected Name & Address	
Principal Investigator	
Date of Inspection	
Lead Inspector	
Inspector(s)	
Observer(s)	
Inspection report date	

Clinical Trials Reviewed	
Protocol No.	
Study Title	
Product Name / Test Compound	
Clinical Trial Import Licence	
Clinical Trial Import Licence/ Clinical Trial Exemption (CTIL/CTX) Applicant Name & Address	
Product Registration Holder Name & Address	
Sponsor Name & Address	

Background Information	
Announcement of inspection	
Pre-inspection documents received	
Date of Pre-Inspection Discussion	
Background and General Information <Scope of inspection> <Highlight background if for-cause inspection >	

Summary of Findings					
No	Inspection Findings	CAPA 1	CAPA 2	CAPA3	CAPA4
Critical					
Major					
Minor					
Date of CAPA Received	[redacted]	<date>			
End Date of CAPA Review		<date>			

NPRA's finding and comment		Inspected Party's Response
Critical		
<i.e: Area of finding> (filled by the NPRA)		
1	Finding	Correction: Root cause: CA1: PA1:
	Inspector's Response: Correction: CA1: PA1:	CA2: PA2: (if applicable)
	Inspector's Response: (if applicable) CA2: PA2:	CA3: PA3: (if applicable)
	Inspector's Response: (if applicable) CA3: PA3:	<if there this multiple CAPA, may summarize here for presentation in meeting>
Major		
i.e: <area of finding> (filled by the NPRA)		
	Finding	Correction: Root cause: CA1: PA1:

	Inspector's Response: Correction: CA1: PA1:	CA2: PA2: (if applicable)
	Inspector's Response: (if applicable) CA2: PA2:	CA3: PA3: (if applicable)
	Inspector's Response: (if applicable) CA3: PA3:	<if there this multiple CAPA, may summarize here for presentation in meeting>
Minor		
i.e: < area of finding (filled by the NPRA)		
	Finding	Correction: Root cause: CA1: PA1:
	Inspector's Response: Correction: CA1: PA1:	CA2: PA2: (if applicable)
	Inspector's Response: (if applicable) CA2: PA2:	CA3: PA3: (if applicable)
	Inspector's Response: (if applicable) CA3: PA3:	<if there this multiple CAPA, may summarize here for presentation in meeting>

The inspected party shall provide all the evidence of implementation as described in the CAPAs in the appendices. Please submit the CAPAs in electronic format.

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