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Corrective and Preventative Action Plans

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	Written by	Approved by	Approved by
Name	Erfan Jaberiyanfar	Sally Beresford-Harvey	Les Bokey
Job Title	SWSLHD Clinical Trials Manager	Head of Clinical Trials Operations Ingham Institute & SWSLHD	Director of Research, Ingham Institute & SWSLHD
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Signature	On file	On file	On file

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1.0 Introduction / Background

A Corrective Action and Preventative Action (CAPA) Plan is a quality system used to address clinical trial related issues that have occurred and incorporates identifying the root cause of the issue, actions to address the issue (corrective) as well as preventing recurrence (preventative) and documentation that the required actions were completed. The CAPA process is an important part of ensuring quality and ethical research practice and ensuring that systems used in research are continuously improved.

International Council for Harmonisation (ICH) Good Clinical Practice (GCP) requires non-compliance that significantly affects or has the potential to significantly affect human subject protection or reliability of trial results to be identified and reported. The sponsor in collaboration with the site should perform root cause analysis and implement appropriate corrective and preventive actions.

Some examples of clinical trial related issues include: injury of clinical trial participants or a high potential for this to occur; repeated violations of the protocol; serious breaches of privacy and significant data integrity problems. Any incident (any event resulting in or with the potential for injury, damage or other loss, including near misses) that meets the PD2020_047 NSW Health Incident Management Policy needs to be reported in IMS plus in accordance with this policy.

Any non-compliance from GCP or the protocol should lead to prompt action by the site Principal Investigator (PI) and Sponsor. This action is required to mitigate any risk associated with the site management of the clinical trial or safety of the recruited participants. The requirements for a CAPA processes in clinical trials is guided by the Australian Code for the Responsible Conduct of Research (2018) and the National Safety and Quality Health Service Standards. Refer also to SOP_CTSU_01_Risk Assessment for Clinical trials and SOP_CTSU_20 Non-Compliance for guidance.

2.0 Objective

To explain the process for completion of a CAPA plan after a non-compliance event at the clinical trial site has been identified.

3.0 Scope

This Standard Operating Procedure (SOP) applies to all staff involved in clinical trials at South Western Sydney Local Health District (SWSLHD) and the Ingham Institute.

4.0 Ownership and Responsibility

The Principal Investigator (PI) and clinical trial Sponsor are responsible for the recording, reviewing, and reporting of study non-compliance. The task may be delegated to another suitably trained individual, but the responsibility remains with the PI and Sponsor.

All staff are responsible for reporting incident that occurs according to PD2020_047 NSW Health Incident Management Policy.

Where applicable the Clinical Trial Support Unit will engage and provide support to the PI and the clinical trials team in the completion of CAPA plans and implementing and amending processes in accordance with the root cause analysis.

5.0 Associate Documents

SOP_CTSU_01_Risk Assessment for Clinical trials

SOP_CTSU_02_Investigator responsibilities

SOP_CTSU_03_Communication with Human Research Ethics Committee, Trial Sponsor and Insurer

SOP_CTSU_23_Sponsor Audits and Regulatory

FM_018_Corrective and Preventative Action (CAPA) Plan

FM_027_Non-Compliance Log

6.0 Procedure

Once a non-compliance is detected, the need for corrective and preventative actions are evaluated. The evaluation and determination of planned corrective action is based upon the potential impact on participant safety, and level of failure to meet ICH GCP guidelines, the protocol and Regulatory requirements. Not all non-compliance events require corrective and/or preventive actions. This decision is made following discussions with the Sponsor or initiated by the PI. Please refer to SOP_CTSU_20 Non-Compliance for guidance.

6.1 Guidance on CAPA completion

CAPA reports provide a unified system where incidents or anticipated risks are identified. It ensures that both corrective and preventive actions are taken to reduce or eliminate the problem. One primary function of a CAPA report is to ensure a clinical trial site complies with regulatory and local quality standards. The process helps sites implement changes in

work practice that meet compliance and standard requirements. CAPA reports also provide proactive solutions by lowering their risk of recurrences. The process provides a framework for problem solving and quality improvement.

The PI will evaluate the extent of the problem including identify/characterise the problem; determine the scope and impact; investigate data, process, operations and other sources of information; investigate the impact of the issue on the overall clinical trial. Refer to FM_018 Corrective and Preventative Action (CAPA) plan and complete the following components listed below.

6.1.1 Description of the event

The description of the non-compliance event should be as accurate and complete as possible. Key factors including who, what, when, where, how and why the event occurred. Another important component is to determine the level of risk in the situation, as this will drive CAPA timelines for resolution.

6.1.2 Proposed immediate action (Correction)

This is the action taken to immediately address the existing problem. Correction and control actions should be completed as soon as possible to mitigate any further risk. The immediate action taken which could be an immediate change in a work process is required to be accurately documented in the CAPA document. More importantly, the change in process needs to be effectively communicated to the clinical trial team to ensure collaboration and compliance.

6.1.3 Find the Root Cause

An investigation that results in the identification of the actual cause, or cause(s) of the problem that resulted in the non-compliance. Root Cause Analysis (RCA) is a method or methodology used to investigate an incident to assist in the identification of health system failures that may not be immediately apparent at initial review. The purpose of an RCA is to identify system issues that contributed to or resulted in the incident occurring and to provide recommendations on actions to be taken to prevent or minimise a recurrence of a similar incident. It is interdisciplinary in nature and uses a structured process which endeavours to answer three questions:

- What happened?
- Why did it happen?
- How can it be prevented from occurring again?

Importantly, an RCA is not to be used as a prosecutive tool, but the intent is for learning and improving the quality at the site.

After identifying the root cause(s), break the solution into discrete, measurable actions that address the root cause(s):

- What will be done – identify action(s) needed to correct and prevent recurrence (e.g. amending documents, changing systems, staff training)
- Who will make amendments/perform the corrective actions and when?
- Establishing an achievable target date for completion. Describe the procedures implemented to resolve the problem and indicate who is responsible for the procedure. Indicate an achievable date for the corrective action.

6.1.4 Proposed action for long term solution (Corrective and Preventative Action)

Corrective and preventive actions are considered long-term solutions to resolve or eliminate the cause of the non-compliance. This process is initiated to address the root cause, which can include the following;

- Review of workplace procedures that align with NSW health policy
- staff training as appropriate
- work process modifications that align with the clinical trial protocol requirements
- review of resource allocation and/or requirements
- staff review and acknowledgement of SWSLHD SOP for clinical trials
- Use of standardised forms and templates to manage clinical trial activity and regulatory processes

The PI or Delegate will track the progress towards completion of all required actions and evaluate whether the implemented actions have successfully addressed the issues.

6.1.5 Comments on effectiveness taken

This is the last phase of the CAPA process. The effectiveness plan phase is used to establish and define pre-determined criteria to verify that corrective and/or preventive actions were indeed effective. A CAPA should only be closed once the verification of effectiveness has been successfully completed. If a CAPA was found to be ineffective, a revised plan is required until the preventive strategy has been verified as successful.

6.2 Documentation, collaboration, and storage

The CAPA should be submitted to the appropriate authority or sponsor's nominee within a timely fashion from identification of the issue, unless otherwise specified by the Sponsor. If

the CAPA is required in response to a protocol deviation and serious breach, a copy of the CAPA should be submitted to the approving Human Research Governance Committee (HREC) and the Research Governance Office (RGO) in accordance with the requirements for addressing protocol deviations and breaches.

If the CAPA is unacceptable, the PI will be notified and will need to provide an appropriate response within the given timelines.

The CAPA Owner/ Responsible Person must ensure that corrective and/or preventive actions are managed, documented, completed, modified, verified as effective, and closed as required per this procedure. All Non-compliance events, including CAPA documentation is required to be stored within the specific Investigator Site File.

CAPA reporting assists each department to build a database of corrective and preventive actions against common and anticipated issues. The documentation of action plans, aside from helping prevent similar problems in the future, assist with risk mitigation and employee accountability. Refer to SOP_CTSU_01_Risk Assessment for Clinical Trials.

Any incident that meets the PD2020_047 NSW Health Incident Management Policy will be reported in the IMS Plus system. A copy of this report should be filed in the Investigator Site File.

All CAPAs and IMS Plus Reports relating to clinical trials should be provided to the Clinical Trial Support Unit for review and assessment for quality improvement across the SWSLHD and Ingham Institute.

7.0 References

ICH GCP (E6 R2): Good Clinical Practice Guidelines - Annotated by TGA

National Statement on Ethical Conduct in Human Research (2023)

Australian Code for the Responsible Conduct of Research (2018)

National Safety and Quality Health Service Standards

8.0 Amendment History

Version	Date	Amended by	Details of Amendment
2.0	22-Feb-2023	Erfan Jaberiyanfar	• Updated list of associated documents. • Update policy reference numbers. • Grammatical changes. • Update of reference links.

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