Title: Continuous improvement: a corrective and preventive action (CAPA) plan

Version: 1.0

Author: Clinical Research and Development Office (CRDO)

Author Signature:  **Date:** 7 March, 2019
The author is signing to confirm the technical content of this document

Institution name: Melbourne Children's

Reviewed and Approved by:
These signatures confirm the reviewers agree with the technical content of the document and that this document is approved for implementation at the RCH Campus.

Andrew Davidson – Medical Director, Melbourne Children's Trial Centre (MCTC)

Signature:  **Date:** 7 March, 2019

This document is effective from the date of the last approval signature and will be reviewed in two years.

Document History

Revision	Modified by	Change No.	Description of Change
1.0	Natalie Rose	N/A	New Issue

Contents

1. PURPOSE

To document the procedure for managing and addressing research-related risks as referred to in ICH E6 R2 section 5.20 and NHMRC's 2018 "Guidance and supplementary guidance: safety monitoring and reporting in clinical trials involving therapeutic goods", and "Reporting of Serious Breaches of Good Clinical Practice or the Protocol for Trials Involving Therapeutic Goods".

2. RESPONSIBILITY AND SCOPE

This standard applies to all Melbourne Children's campus employees (including visiting medical officers, visiting health professionals, contractors, consultants and volunteers) who propose to undertake, administrate, review and/or govern human research involving Melbourne Children's research participants and staff.

3. APPLICABILITY

Principal Investigator/ Investigator, Sub-Investigator(s) research coordinators and other staff involved in trial-related duties for single site, RCH-based trials.

4. BACKGROUND

A Corrective and Preventive Action Plan (CAPA) is a quality system plan used to address a research-related issue that has occurred. It incorporates:

1. Identifying the root cause of the issue;
2. Identifying actions to prevent recurrence of the issue (corrective action) or, identify actions to prevent an issue from occurring (preventive action);
3. Documenting that the required actions were completed.

Some examples of research-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.

The CAPA process is an important part of ensuring quality and ethical research practice and ensuring that systems used in research are continuously improved.

5. PROCEDURE

5.1. Identification of an issue

Potential and/or actual issues that arise during the conduct of research can be identified through several sources. For example:

- A specific incident has occurred;
- Observations/concerns are made by a research staff member about a potential issue;
- Concerns are raised during/after monitoring, auditing, external/third party audits, or regulatory authority inspection of the research;
- A concern raised by another body such as a data safety monitoring committee, HREC or Governance.

Please note that these may or may not be a deviation from the protocol.

5.2. Assessing the risk

A CAPA is required in cases where a corrective action and/or preventive action is necessary to appropriately address a risk. Risk assessments improve quality and compliance. They are a proactive, anticipatory approach to improve quality management. The risk should be determined by assessing (i) the impact on patient rights/safety and the study objectives, and (ii) the likelihood of occurrence/recurrence.

5.3. Developing the CAPA plan

The steps involved are:

1. Initiation of CAPA: The concerned department / individual shall identify and decide who will take overall responsibility for the CAPA plan. This includes development of the CAPA plan, its implementation, training of staff on the CAPA plan, and evaluation of the results of the CAPA plan.
2. Evaluate the extent of the problem: 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 research.
3. Focus on determining the root cause(s): investigate how/why the incident occurred (i.e. are there specific causes or sources of the problem; why is this problem occurring; is the problem due to training, design, manufacture, management, documentation, etc.)
4. After identifying the root cause(s), break the solution into discrete, measurable actions that address the root cause(s) - actions items should include:
    a. What will be done – identify action(s) needed to correct and prevent recurrence (e.g. amending documents, changing systems, staff training)
    b. Who will make amendments/perform the corrective actions and when?
    c. 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.
5. Track progress towards completion of all required actions and evaluate whether the implemented actions have successfully addressed the issues.
6. For Preventive Actions, describe the preventive actions or planned, and who is responsible. Create a list of all tasks that must be completed to prevent the problem.

5.4. Documenting and reporting the CAPA

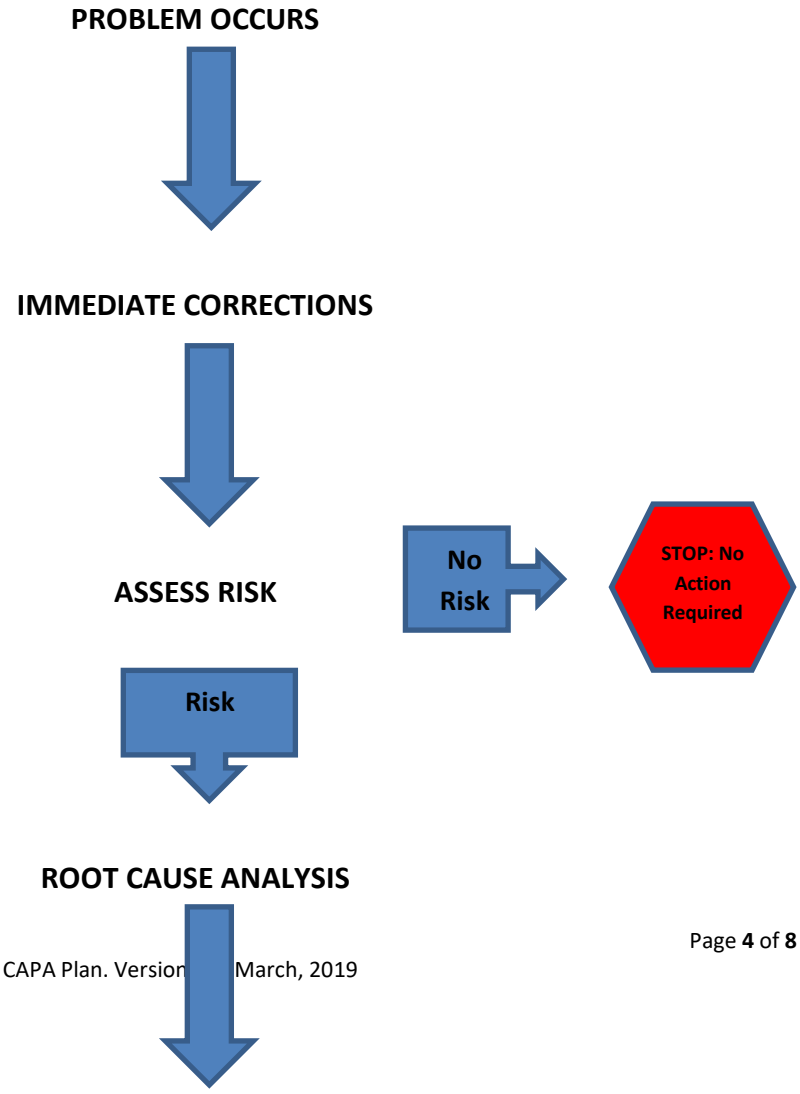
CAPAs should be documented using the CAPA template (see attachment), unless the Sponsor requires the use of their own template. Where the sponsor is not MCRI/RCH (i.e. commercial studies), a copy of the CAPA should be sent to the trial sponsor. Where MCRI acts as the sponsor, and an external coordinating centre is being used, the CAPA should be sent to the external centre. Where MCRI is the sponsor, and coordinating centre, the CAPA should be reviewed by the PI, and stored with other trial related documents in the Trial Master File.

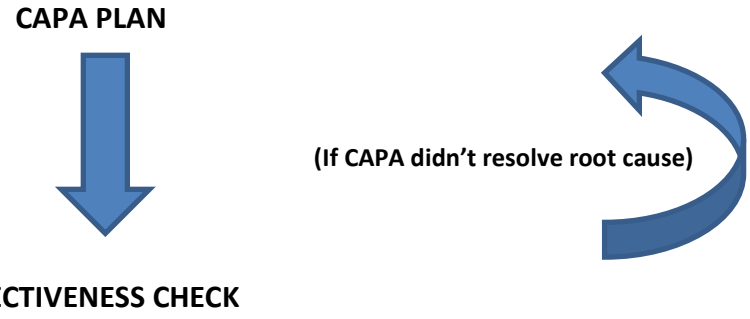
Each issue requires a separate CAPA. All CAPAs should be reviewed, signed and dated by the individual preparing the form and the Principal Investigator.

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, a copy of the CAPA should be submitted to the approving HREC and to RCH Governance Office, in accordance with the REG requirements for addressing protocol violations, deviations and complaints (please refer to REG website for details).

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

A summary of all CAPAs (in progress and completed) should be maintained in a CAPA tracking log (see attachment), and stored with other trial related documents in the Trial Master File. 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.





6. GLOSSARY

Corrective and Preventive Action (CAPA) Plan – actions taken to collect information and identify a problem, determine root cause, identify and implement a corrective and/or preventive action to prevent further recurrence.

CAPA Owner- Individual that ensures that a corrective and/ or preventive action(s) is managed, documented, completed, modified and verified as effective.

Correction – immediate remedial actions taken to repair, rework or adjust the effect of an existing deviation or other undesirable situation.

Corrective Action – immediate action to a problem that has already occurred or has been identified.

Preventive Action – taken to eliminate the root cause of a potential problem, including the detection/identification of problems.

Responsible Department – The area owner / management of dedicated equipment, facilities, personnel or processes.

Responsible Person – Department or personnel accepting responsibility for the completion of assigned corrective and preventive actions.

Root Cause – factor that caused a non-conformance and should be permanently eliminated through process improvement.

Root Cause Analysis – a class of problem solving methods used to identify the root causes of problems or events.

7. REFERENCES

Note for Guidance on Good Clinical Practice (CPMP/ICH/135/96, annotated with TGA comments).

RCH Research Ethics and Governance: Safety Report Form, August 2017.

8. APPENDICES

DOCUMENT END

Appendix 1: Corrective and Preventive Action Plan Template

A CAPA is written to identify a discrepancy/problem in the conduct of a clinical research study, note the root cause of the identified problem, identify the corrective action to prevent the recurrence of the problem, and document that the corrective action has resolved the problem. In general, the tone of CAPA should be forward-looking and not seek to explain an error discovered in the conduct of a clinical research study.

Date:	*Date that the CAPA is written*
To:	*Sponsor, HREC, etc*
From (Person responsible for overall CAPA):	*Name, Title, the site/institutional affiliation of the person authoring the CAPA, including their signature*
Protocol Title / Research Study:	
HREC Number:	
Issue / Deficiency Identified:	*Brief description or outline of the topic/process/problem being documented. This can be formatted as a paragraph, numbered list, or bulleted items.*
Root Cause:	*The reason(s) that the issue arose. Root-cause analysis is a class of problem solving methods used to identify the root causes of problems or events.*
Corrective Action Plan:	*Description of the correction action(s) taken or planned by the site. If the site was instructed to perform these corrective actions (i.e. by the sponsor or monitor), indicate by whom and as of what date. If status of reports, records or data will remain incomplete or unavailable, make a statement regarding your failed attempts or describe when/how the records will be retrieved or completed.*
Implementation:	*Description of the procedures used to document resolution of the problem, the persons who are responsible for the procedures, etc.*
Effective Date of Resolution:	*Effective date for corrective action*
Preventive Action:	*Description of the preventive actions taken or planned by the site. If the site was instructed to perform these preventive actions, indicate by whom and as of what date. Preventive actions are taken to eliminate the root-cause of a potential problem, including the detection/identification of problems*
Evaluation/Follow up:	*Any plan/procedure to evaluate the implementation and completion, persons who are responsible for the evaluations, timeframe for the evaluation, etc.*

Comments: *Any additional comments or information not noted above. Document any relevant observations here.*

Principal Investigator Signature

Date

Principal Investigator Printed Name

Appendix 2: CAPA Tracking Log

CORRECTIVE ACTION REPORT NO.	OPEN DATE	ISSUED TO	DESCRIPTION	DUE DATE	CLOSEOUT DATE

Verified By: _____

Date: _____