Standard Operating Procedure

Title: **MCRI Sponsorship Application Process for Investigator Initiated Trials (IITs)**

Document ID: **MCTC037b**

Version: **1.0**

Applicability: MCRI Investigator-initiated trials

Author

NAME and TITLE: Iona Walton, MCTC

The author is signing to confirm the technical content of this document

Signature: Signed Electronically by:
Iona Walton - iona.walton@mcri.edu.au
27-Jun-2023 @ 02:39 PM AEST Reason: Authorship

Institution/Department name: Melbourne Children's

Reviewed and Approval

These signatures confirm the reviewers agree with the technical content of the document and that this document is approved for implementation at the Melbourne Children's.

NAME and TITLE: Andrew Davidson, Medical Director of MCTC

Signature: Signed Electronically by:
Andrew Davidson - Andrew.Davidson@rch.org.au
03-Jul-2023 @ 08:53 AM AEST Reason: Approval

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

Document History

Revision	Modified by	Date of Release	Description of Change
1.0	Iona Walton	27/06/2023	New Issue. Separation of MCTC037 into an internal and external SOP for Sponsorship application and approval process. Update and review of procedure was undertaken. Key changes to application process includes: • Clarification of trials requiring sponsorship • Specification of required documents for submission • Removal of appeal processes

CONTENTS

1. PURPOSE

This Standard Operating Procedure (SOP) describes the process and activities taken by the Sponsor-Investigator and trial team seeking Murdoch Children's Research Institute (MCRI) sponsorship of an Investigator Initiated Trial (IIT).

The MCRI Sponsorship Committee (SC) is the body responsible for the review of IITs seeking sponsorship. The SCs primary goal is to ensure governance and management of risk of MCRI-Sponsored trials so that they are conducted appropriately and efficiently, and will be completed to a high quality and achieve maximum impact. The SC does not primarily assess scientific quality, research merit or ethical acceptability of the trial design, as this is the responsibility of the reviewing Human Research Ethics Committee (HREC). The SC submission and review process does not duplicate the Research Ethics and Governance (REG) process for MCRI; it exists in parallel. It is strongly recommended that all IIT protocols be reviewed by the SC prior to or at the same time as submission to RCH HREC to ensure that the SC approval process does not slow down the ethics approval and research governance authorisation process. RCH HREC will no longer approve any IITs without evidence of Sponsorship Committee approval by the MCRI or an external collaborative network, company or organisation.

All applicable SOPs produced by MCRI are to be used in conjunction with the relevant applicable NHMRC policies and procedures when conducting a MCRI sponsored IIT.

This SOP is consistent with the requirements set out in the ICH Topic E6 (R2) Integrated addendum to ICH E6 (R1): Guideline for Good Clinical Practice (ICH E6 R2) with TGA annotations, herein referred to as Good Clinical Practice (GCP).

2. BACKGROUND

All clinical trials conducted in Australia must have an Australian entity as the Sponsor. This includes external Sponsors based overseas who wish to conduct a trial in Australia.

The trial Sponsor is responsible for the initiation, management and financing of the trial and carries the medico-legal responsibility associated with its conduct. All aspects of which must be in accordance with GCP, the National Statement, the protocol approved by the approving Human Research Ethics Committee (HREC) and any external funding body.

For trials conducted under the Clinical Trial Notification (CTN) and Clinical Trial Approval (CTA) schemes, the trial Sponsor has additional responsibilities for managing the supply and administration of therapeutic goods.

When an investigator leads the initiation and conduct of a trial, i.e. it is not externally sponsored, they will take on the role of Sponsor-Investigator, reflecting their dual role as Sponsor and Investigator. In this circumstance, the Investigator must first seek documented approval. This will most commonly be:

a) MCRI-led IITs
b) International IITs seeking a local Australian Sponsor.

3. SCOPE

This SOP applies to all MCRI/RCH Investigators seeking/maintaining sponsorship from MCRI for an IIT of a clinical trial. Clinical trials can involve investigating new or existing medicines, medical devices and other medical or non-medical interventions. For example, a clinical trial could involve new drugs, medical devices, biologicals, vaccines, surgical and other medical treatments and procedures. Psycho-therapeutic and behavioural therapies help service changes, preventative care strategies and educational interventions are also examples of clinical trials. Researchers might also conduct clinical trials to evaluate diagnostic or screening tests and new ways to detect and treat disease.

Investigators requesting sponsorship for an IIT must be employees of, or have honorary appointments with, MCRI.

Since January 1, 2020, all IITs led by MCRI or RCH staff have been required to receive formal sponsorship approval from the MCRI SC before commencing recruitment. Trials initiated prior to 2020 are not required to obtain retrospective sponsorship approval. However, at the recommendation of the approving HREC or MCRI SC, or at their own discretion, Investigators for trials commenced prior to January 1, 2020, may seek formal MCRI SC approval.

This SOP does NOT Apply to:

- Observational studies
- Trials which have been designed by an organisation external to MCRI and have an external Australian commercial or collaborative group sponsor*.

If Investigators are unsure if the sponsorship process applies to them – they are advised to contact the MCRI SC Chair via mctc@mcri.edu.au for clarification and guidance. It is advised that if a study is intending to register as a clinical trial, intervention drug/device or non-drug/device that it will need to get Sponsorship approval – whether it will be approved by the SC Chair or whole Committee will be decided upon submission.

**If funding of a trial belongs to another organisation or institute (e.g. University of Melbourne), MCRI may still be an appropriate sponsor for this trial. Please contact the grants team at grants@mcri.edu.au to discuss.*

4. RESPONSIBILITY

This SOP applies to the intended Sponsor-Investigator of an IIT that is seeking MCRI Sponsorship. For Investigator-Initiated research, the PI or CPI leading the research takes on certain responsibilities of the Sponsor and hence is called the "Sponsor- Investigator".

5. PROCEDURE

5.1. Submission Process for Sponsor-Investigators

5.1.1. Submission

The Sponsor-Investigator needs to submit the application for MCRI Sponsorship at least ten working days prior to the next SC meeting. The schedule of meeting dates can be found here.

The submission must be emailed to mctc@mcri.edu.au and include the following:

- A completed MCRI Sponsorship Committee Application Coversheet and Risk Management Table
- The current draft of the protocol with a version no and date.
- A current trial budget
- Evidence of the source of trial funding (e.g. Grant approval letter, email from department head, etc.)
- A Division of Responsibilities Matrix showing role of the international Sponsor and local Coordinating Principal Investigator – *Applicable to IITs sponsored by an overseas company/organisation/institution, where MCRI is acting as the local Sponsor only*
- A Risk Assessment and Risk Management - *Applicable to IITs requiring a CTN*
- Data Manage Plans and Data Sharing Plans - *Applicable to IITs requiring a CTN*
- Clinical Monitoring Plans - *Applicable to IITs requiring a CTN*

5.1.1.1. SC Chair Approval

The SC Chair will review all documents submitted by the Sponsor-Investigator and determine whether the trial is of greater than negligible risk to the institute. If the SC Chair deems the trial low risk the Chair may approve the trial without having the whole SC review. IT is at the discretion of the SC Chair if this trial approved outside of the committee will require annual reviews until completion or will only need to submit a final report upon completion.

The SC Chair must notify the SC at the following committee meeting of any trials approved by the Chair.

5.1.2. SC Meetings

If the SC Chair decides the submitted trial will need to be reviewed be the whole SC, the Sponsor-Investigator will be notified of the requirement of their presence. The

Sponsor-Investigator, or delegate, will then attend the meeting considering their trial. At the meeting, the Sponsor-Investigator (or delegate) will be asked to provide an overview of their trial, highlight any risks they have identified in their Sponsorship Application and completed Risk Management Table and answer any questions from the SC.

Note: *The SC Chair may excuse the Sponsor-Investigator from attending the meeting in exceptional circumstances. In these cases, the SC will discuss the application and send any questions and/or recommended action to the Sponsor-Investigator following the meeting. The Sponsor-Investigator must provide a response prior to receiving Sponsorship Approval. This process may delay SC approval.*

During the meeting, the SC will determine:

- The overall risk rating of the trial
- The degree of SC (or delegate) oversight required
- Any further actions required for mitigating and/or monitoring the risks identified by the SC and Sponsor-Investigator (or delegates)
- If the SC will require the Sponsor-Investigator to submit any of the following documents for further review:
    - Data Sharing Plan
    - Data Management Plan
    - Clinical Monitoring Plan

    If these documents are required, the committee will also determine a due date for their submission.

5.1.3. Response to SC Feedback

If any revisions/concerns are recommended by the SC, the Sponsor-Investigator needs to address these and re-submit the revised documents to the SC. The Sponsor-Investigator is required to address the concerns from the SC in writing and provide a management plan/solution.

5.1.4. Approval Post SC Feedback

Once the SC/SC Chair is satisfied the Sponsor-Investigator has addressed all comments/concerns, the IIT will begin the MCRI sponsorship approval steps.

A Certificate of Sponsorship, MCTC027, will be sent to the Sponsor-Investigator to complete. This involves completing a Responsibilities checklist of sponsor responsibilities being delegated to the Sponsor-Investigator for the trial. Once filled out this form needs to be returned to the Admin Assistant. The agreed upon responsibilities taken on by the Sponsor-Investigator will be reviewed by the SC Chair. If these are accepted, the SC Chair will also sign the Certificate of Sponsorship. This

confirms full MCRI Sponsorship of the trial, as of the date of the Sponsor-Investigator's signature.

MCRI Sponsorship Committee will re-evaluate decision to Sponsor trials if new information becomes available related to the initial ethics/governance approval.

5.1.5. Issue of Certificate of Sponsorship

Once the IIT is approved for MCRI sponsorship, the MCRI SC Chair (or delegate) will send a "Certificate of Sponsorship" to the Sponsor-Investigator to state that the trial will be sponsored by MCRI. The Sponsor-Investigator will be sent a blank certificate to sign and specify details of trial and responsibility delegations. This will then be returned to the SC Chair before a final copy is signed and sent back. . The Sponsor-Investigator may then proceed to complete their REG Application if not already done so.

Note: *The Certificate of Sponsorship is not the confirmation to commence recruitment. It is an approval document certifying MCRI is willing to sponsor the trial. RCH HREC will not provide ethical approval and/or governance authorisation for MCRI Sponsored trials until receipt of the SC signed Certificate of Sponsorship.*

5.2. Protocol Amendments post SC Approval

5.2.1. Assess impact on SC Risk Assessment

If changes are made to the protocol or trial that substantially impact the sponsorship application risk assessment at any time after approval by the SC, then the SC should be notified at the same time as the reviewing HREC and RCH Research Ethics Governance Office (for trials where RCH/MCRI is a participating site), and the Risk Management Table should be updated and re-submitted.

Note: *While the Sponsor-Investigator holds the primary responsibility for determining whether a protocol amendment substantially increases the trial risks, REG staff reserve the right to reject an amendment without prior review by the SC where REG considers that the proposed amendment substantially changes the trial's risk.*

5.2.2. Re-issue of Certificate of Sponsorship

The "MCRI Certificate of Sponsorship" must be updated and re-signed by the SC Chair or delegate each time a significant change is made to the protocol/trial design (including protocol amendments);

5.2.3. RCH HREC and Governance Approval

For studies that have received RCH HREC approval and RCH Research Governance authorisation, where the amendment is deemed to change the trial's risk, REG will provide approval only after receipt of the updated and signed Certificate of Sponsorship, demonstrating the changes to the trial/protocol amendment have been sighted, considered, and approved by the SC Chair and/or SC.

5.3. Oversight of MCRI Sponsored Trials

Apart from protocol amendments as detailed in section 5.2 Protocol Amendments post SC approval, the SC must be notified as soon as possible of any other events (internal or external) which may impact the risk assessment of the trial. The Risk Management Table must also be updated and re-submitted within one month of the Sponsor-Investigator becoming aware of the event.

5.3.1. Expedited Safety and Non-compliance event reporting

The Sponsor-Investigator must report to the SC the same subset of safety and non-compliance events that must be reported to the reviewing HREC and local research governance office in real time. This includes:

- Serious Breach reports (Sponsor-level and Melbourne Children's site), within 7 calendar days of confirmation
- SSIs, within 72 hours of becoming aware of the event
- USMs, within 72 hours of becoming aware of the event
- SUSARs, within 72 hours of becoming aware of the event

For all serious breaches both at the Sponsor and Trial Site level, the Sponsor-Investigator must provide a Corrective and Preventive Action plan (CAPA) to both the reviewing HREC and the SC as soon as possible.

5.3.2. Periodic Reviews

MCRI sponsored clinical trials will be reviewed by the SC Chair(or delegate) at regular intervals as determined by the SC, based on the risk and recruitment status of the trial. This will typically be half-yearly for high-risk clinical trials, and yearly for medium risk clinical trials. Studies deemed by the SC to be low risk will typically not require review and only be required to submit a SC annual report, as detailed in section 5.3.3.

The aim of the periodic review is to ensure the trial is being conducted in a manner consistent with the most recently submitted Risk Assessment and Management Matrix.

Depending on the risk profile, the following updated documents, with 'Tracked Changes', must be provided to the MCTC Medical Director (or delegate) one week prior to the next scheduled meeting:

- Sponsorship Risk Assessment
- Current Protocol
- Trial budget
- Any other previously submitted documents

5.3.3. SC Annual Progress Report

5.3.3.1. *Submission*

The Sponsor-Investigator must annually submit for SC review:

- A Sponsorship Committee Annual Progress Report Form [MCTC 137]
- An updated Risk Management Table with 'tracked changes' since the last submitted risk assessment
- Central non-compliance log
- SAE / AE Line Listing (if applicable)
- Current Protocol
  - Data Management Plan (if previously required or request from SC and updated since last review)
  - Data Sharing Plan (if previously required or request from SC and if updated since last review)
  - Clinical Monitoring Plan (if previously required or request from SC and if updated since last review)
- Current Trial Budget

5.3.3.2. *SC Feedback*

The Sponsor-Investigator will be provided with the Sponsorship Committee's assessment and recommendations within 7 days of the SC meeting's discussion of their submission. The Sponsor-Investigator must address feedback as per the process in section 5.1.6

5.3.3.3. *Reissue of Certificate of Sponsorship*

The Certificate of Sponsorship must be reissued as per the process detailed in section 5.2.2.

5.4. Submission Deadlines

Applications and updates submitted for MCRI sponsorship to the SC must be made at least 10 working days prior to the next SC meeting. This is to ensure that any revisions and changes requested by the SC can be made prior to the SC meeting.

If the submission deadline is missed the project will be reviewed at the next scheduled meeting. If an application is submitted on time but deemed to be invalid, the project will be discussed at the next meeting after the application is confirmed to be valid.

5.5. Decisions not to Sponsor a Trial

Should the SC determine that risks to the MCRI are inadequately addressed by the Sponsor-Investigator, the SC may decline to grant MCRI sponsorship. The reason for rejecting an application will be provided to the Sponsor-Investigator in an email from the SC Chair.

As the RCH HREC require evidence of Sponsorship prior to approving clinical trials, this may also prevent the trial from receiving HREC approval.

Where appropriate, the Sponsor-Investigator may discuss the decision with the SC Chair.

5.6. Termination of Sponsorship

Any trials that have been increased in its risk rating since starting as per the Risk Management Table must be re-assessed by the SC. The SC may decide to withdraw sponsorship, if needed, and will notify the reviewing HREC of this decision. This may then trigger the reviewing HREC to withdraw Ethical Approval and/or Governance Authorisation. The TGA may also need to be notified.

The Sponsor-Investigator will be given clear notice, in writing from the SC, to cease all trial activities other than those deemed necessary for participant safety. The SC, in consultation with REG and the approving HREC, will advise the Sponsor-Investigator of the reason for sponsorship termination and the next steps for the trial. Sponsor-Investigators will also be directed to contact MCRI grants and MCRI legal for implications of the termination of sponsorship.

6. GLOSSARY

Clinical Monitoring Plan (CMP)

In accordance with the Integrated Addendum to ICH E6 (R1) Guideline for Good Clinical Practice E6 (R2) Section 5.18.7 (that was formerly adopted by the TGA with annotations on 8 February 2018), the Sponsor should develop a monitoring plan that is tailored to the specific human subject protection and data integrity risks of the trial. This plan must describe the monitoring

strategy, the monitoring responsibilities of all the parties involved, the various monitoring methods to be used, and the rationale for their use.

Clinical Trial

Clinical trials can involve investigating new or existing medicines, medical devices and other medical or non-medical interventions. For example, a clinical trial could involve new drugs, medical devices, biologicals, vaccines, surgical and other medical treatments and procedures. Psycho-therapeutic and behavioural therapies help service changes, preventative care strategies and educational interventions are also examples of clinical trials. Researchers might also conduct clinical trials to evaluate diagnostic or screening tests and new ways to detect and treat disease.

Corrective and Preventive Action (CAPA) Plan

A Corrective and Preventive Action (CAPA) plan is a quality system plan and incorporates:

1. Identifying the issue, including scope and impact
2. Identifying the root cause of the issue – how/why it occurred
3. Identifying actions to prevent recurrence of the issue (corrective action) or, identify actions to prevent an issue from occurring (preventive action)
4. Documenting that the corrective actions/preventive actions were completed
5. Documenting that the corrective/preventive action has resolved the problem

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 that the rights, integrity, and confidentiality of trial participants are protected.

Human Research Ethics Committee (HREC)

A body which reviews research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines. The National Statement requires that all research proposals involving human participants be reviewed and approved by an HREC and sets out the requirements for the composition of an HREC.

International Conference on Harmonisation (ICH)

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) is unique in bringing together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of drug registration.

Investigator

A person responsible for the conduct of the clinical trial at a trial site. There are four types of Investigator roles used to describe Investigators with different levels of responsibility for the conduct of clinical trials. These are described below.

Associate 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). May also be referred to as sub-investigator.

Coordinating Principal Investigator (CPI)

If a study is conducted at more than one study site, the Principal Investigator taking the additional responsibility for coordination of the study across all sites in a region is known as the Coordinating Principal Investigator (CPI). This role applies to externally sponsored studies where the Sponsor may be a collaborative research group, commercial Sponsor or an institution. The Principal Investigator at each site will retain responsibility for the conduct of the study at their site.

Principal Investigator

The PI is the person responsible, individually or as a leader of the clinical trial team at a site, for the conduct of a clinical trial at that site. As such, the PI supports a culture of responsible clinical trial conduct in their health service organisation in their field of practice and, is responsible for adequately supervising his or her clinical trial team.

The PI must conduct the clinical trial in accordance with the approved clinical trial protocol and ensure adequate clinical cover is provided for the trial and ensure compliance with the trial protocol.

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 (eg, it 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.

Investigator-Initiated Trials (IITs)

A clinical trial which is initiated and organised by an Investigator i.e. an individual rather than a collaborative group, company, or organisation. In these cases, the Investigator will take on the role of the trial sponsor and will then be responsible for the extensive GCP and regulatory requirements associated with both the management and conduct of the trial.

Melbourne Children's

The campus encompassing all staff from The Royal Children's Hospital, Murdoch Children's Research Institute and Department of Paediatrics University of Melbourne who initiate or carry out research under one or more of these institutional affiliations.

Melbourne Children's Trials Centre (MCTC)

Melbourne Children's Trials Centre (MCTC) is a collaboration between the Royal Children's Hospital, The Murdoch Children's Research Institute, The Royal Children's Hospital Foundation and The University of Melbourne. This Centre brings together expertise in research, clinical practice, and education and incorporates anyone who initiates or carries out research under one or more of these institutional affiliations.

Monitor

A person appointed by the Sponsor to undertake the role of monitoring for the trial. Monitors should be appropriately trained and should have the scientific and/or clinical knowledge needed to monitor the trial adequately.

Murdoch Children's Research Institute (MCRI)

An Australian paediatric medical research institute located in Melbourne, Victoria, affiliated with the Royal Children's Hospital and the University of Melbourne. The institute has six research themes: cellular biology, clinical sciences, genetics, infection and immunity, population health, and data science.

National Health and Medical Research Council: (NHMRC)

An independent statutory body within the portfolio of the Australian Minister for Health and Ageing responsible for allocating funding for, and directing, health and medical research, ethics and advice.

Non-Compliance Report Form

Used by sites participating in MCRI-sponsored IITs to report non-compliance with protocol or GCP to the Sponsor-Investigator/CPI when their assessment suggests a serious breach has occurred.

Non-Compliance Review Form

Used by Sponsor-Investigator/CPI to review non-compliance report Forms submitted by participating sites. This form documents the review and assessment of whether the Sponsor-Investigator/CPI determines the non-compliance to meet the definition of a serious breach.

Protocol

A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial.

Protocol Deviation

A protocol deviation is any breach, divergence or departure from the requirements of GCP or the clinical trial protocol.

Research Ethics and Governance Office (REG)

REG supports the HREC and institutional research governance processes at MCRI.

Research Governance Office (RGO)

The Office or coordinated function within Melbourne Children's which is responsible for assessing the site-specific aspects of research applications, make a recommendation to the CEO / delegate as to whether a research project should be granted authorisation at that site, and overseeing that authorised research at the site meets appropriate standards (research governance).

Royal Children's Hospital (RCH)

The Royal Children's Hospital is major specialist paediatric hospital in Victoria, the Royal Children's Hospital provides a full range of clinical services, tertiary care, as well as health promotion and prevention programs for children and young people. Its campus partners are the Murdoch Children's Research Institute and The University of Melbourne Department of Paediatrics, which are based on site at the hospital.

Serious Adverse Event (SAE)

An adverse event is defined as serious if it:

- results in death
- is life-threatening
- requires hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability or incapacity
- is a congenital anomaly or birth defect

Other important medical events will be considered an SAE when, based upon appropriate medical judgment, they may jeopardise the research participant safety and may require medical or surgical intervention to prevent one of the outcomes listed in the above definition. This can include diagnosis of cancer.

Serious Breach

A breach of Good Clinical Practice or the protocol that is likely to affect to a significant degree: a) The safety or rights of a trial participant, or b) The reliability and robustness of the data generated in the clinical trial. Note: this guidance's definition of serious breach differs from the definition in the Australian Code for the Responsible Conduct of Research and is about deviations from the requirements of Good Clinical Practice or the clinical trials protocol.

Significant Safety Issue (SSI)

A safety issue that could adversely affect the safety of participants or materially impact on the continued ethical acceptability of the trial.

Sponsor

An individual, organisation or group taking on responsibility for securing the arrangements to initiate, manage and finance a study. For investigator-initiated trials, MCRI or RCH will act as the Sponsor but delegate many sponsor responsibilities to the Coordinating Principal Investigator. In this case the CPI has the role of both Sponsor and Investigator and hence the MCTC has adopted the term **Sponsor-Investigator** to reflect the dual role of the CPI in investigator-initiated trials.

Standard Operating Procedure (SOP)

Detailed, written instructions to achieve uniformity of the performance of a specific function.

Suspected Unexpected Serious Adverse Reaction (SUSAR)

This is a serious adverse event:

- Where there is at least a reasonable possibility of a causal relationship between an intervention and an adverse event (in other words the relationship of the SAE to the trial drug/device/other intervention cannot be ruled out)

and

- That is unexpected, meaning that the nature or severity of the reaction is not consistent with the known scientific information (e.g. Investigator's Brochure for an unapproved investigational product or product information document or similar for an approved, marketed product)

Therapeutic Good

In relation to the evaluation, assessment and monitoring done by the TGA, therapeutic goods are broadly defined as products for use in humans in connection with:

- preventing, diagnosing, curing, or alleviating a disease, ailment, defect, or injury
- influencing inhibiting or modifying a physiological process
- testing the susceptibility of persons to a disease or ailment
- influencing, controlling, or preventing conception
- testing for pregnancy

This includes things that are:

- used as an ingredient or component in the manufacture of therapeutic goods
- used to replace or modify of parts of the anatomy

Therapeutic Goods Administration (TGA)

The Therapeutic Goods Administration (TGA) is Australia's regulatory authority for therapeutic goods.

Urgent Safety Measure (USM)

A measure required to be taken to eliminate an immediate hazard to a participant's health or safety.

Quality Assurance (QA)

Covers all policies and systematic activities implemented within a quality system. QA ensures that data are recorded, analysed, and recoded in accordance with the protocol and GCP. The use of GCP guidelines ensures ethical and scientific quality standards for the design, conduct, recording, and reporting of HREC approved clinical trials that involve research participants.

7. REFERENCES

TGA

Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice ICH E6 (2) 2016 – Annotated with TGA comments available at

https://www.tga.gov.au/publication/note-guidance-good-clinical-practice

Note for Guidance on Clinical Safety Data Management: Definitions and Standards for Expedited Reporting (CPMP/ICH/377/95) annotated with TGA comments, available at https://www.tga.gov.au/sites/default/files/ich37795.pdf

TGA Guidance: Australian Clinical Trial Handbook: Guidance on conducting clinical trials in Australian using "unapproved" therapeutic goods, Version 2.2 October 2018, available at https://www.tga.gov.au/publication/australian-clinical-trial-handbook

Department of Health and Human Services Victoria, Coordinating Office for Clinical Trial Research

Information on requirements for trials can be found in "Research governance and Site specific assessment – process and practice" available at http://www.health.vic.gov.au/clinicaltrials/site-specific.htm

NHMRC

NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods (EH59, Nov 2016, available at: https://nhmrc.gov.au/about-us/publications/safety-monitoring-and-reporting-clinical-trials-involving-therapeutic-goods

8. COLLABORATORS

This Guidance document was reviewed by:

Name/Role	Department/Group	Affiliation
Kate Scarff / CRDO Lead	Clinical Research Development Office	MCRI
Andrew Davidson / MCTC Medical Director	Melbourne Children's Trials Centre	MCRI
Iona Walton / Administrative Assistant	Melbourne Children's Trials Centre	MCRI
Nitya Philipson / Research Governance Lead	Office of Research	MCRI
Jennifer Luplow / Research Ethics	Research Ethics and Governance Office	RCH
Kirsten Perrett / Principal Research Fellow	Population Allergy	MCRI

9. APPENDICES

9.1. Appendix 1: Terms for Risk Assessment and Management

The objective for the institution is for each trial to run to completion, with adequate resources, and generate high quality evidence which will change clinical practice. The risk management plan is to ensure these objectives are met for all clinical trials conducted by MCRI.

RISK

A risk is defined as the effect of uncertainty on objectives. A risk is often assessed in terms of a combination of the consequences of an event and the associated likelihood of occurrence.

RISK IDENTIFICATION (SOURCE)

The purpose of risk identification is to find, recognise and describe risks that might prevent a trial achieving its objectives, and/or other risks eventuating for the institution that may emerge due to the trial activity. When identifying risks the following questions should be considered;

- What event(s) can happen that will have an adverse effect on the trial or the institution?
- How can it happen?

CONSEQUENCE

The impact identifies the significance of each risk (i.e. what are the effects to your trial if it risk does happen?). The impact may vary for each risk (for example the impact of funding shortfalls will vary depending on the magnitude of the shortfall)

RISK MITIGATION

Risk mitigation is an activity developed or planned to manage and/or reduce the risk.

LIKELIHOOD

Likelihood is the chance that something might happen. Likelihood is rated at: *Almost certain, Likely, Possible, Unlikely or Very unlikely*.

RISK MONITORING PLAN

This is the process whereby the risks would be identified when they materialise.

IMPACT LEVEL

The Committee or delegate (i.e. MCTC Medical Director (or Acting Director)) to complete what they believe is the impact level, based in the information provided and the type of risk and likelihood to occur. A rating of LOW, MED, HIGH for each risk will be assigned. The Sponsor–Investigator needs to explain in significant detail the mitigation and management plan for risks considered Medium and High Impact.

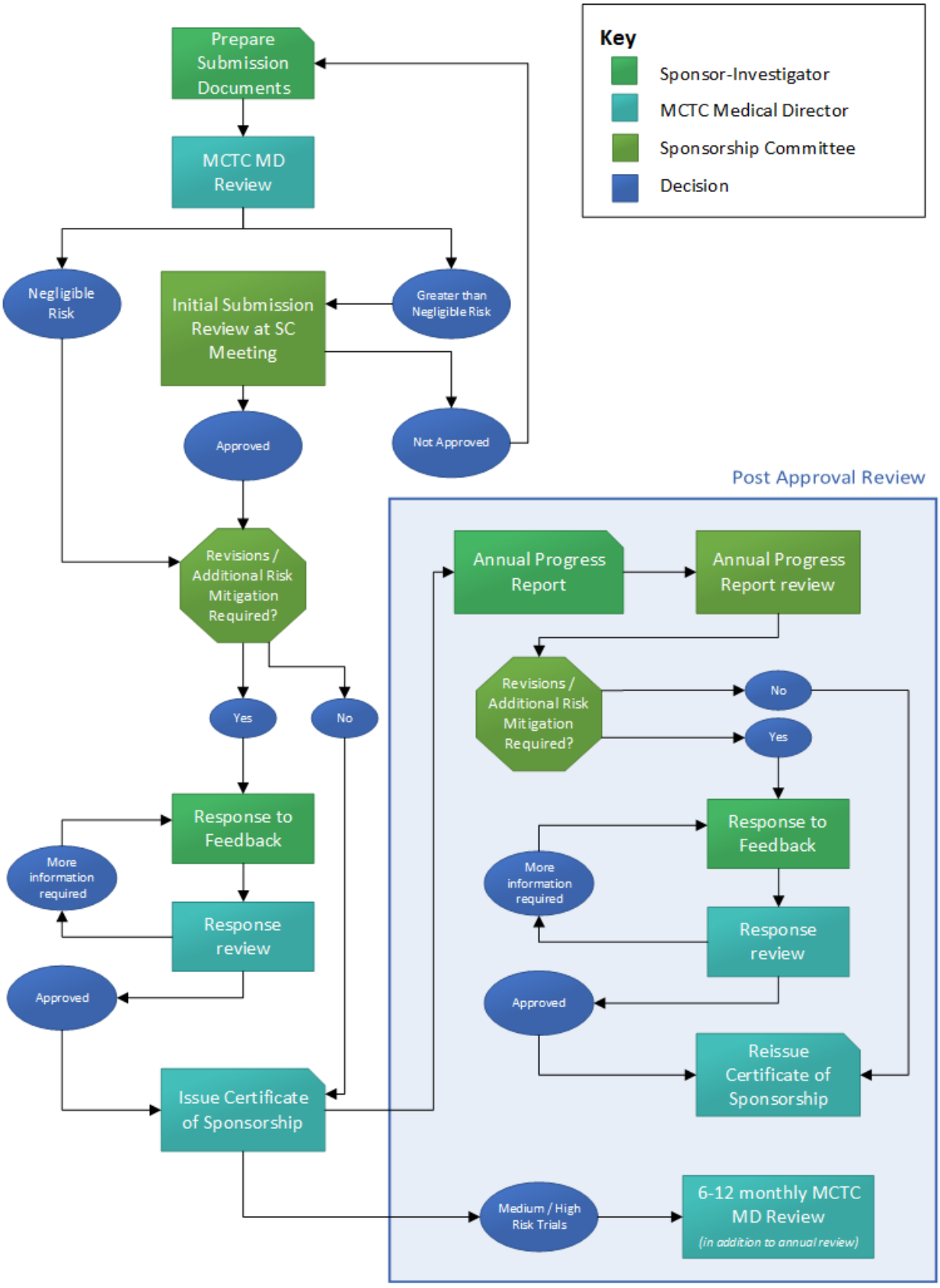
The number and type of risks with a HIGH impact level will determine the level of oversight required by the SC for each trial.

9.2. Appendix 2: Risk Management Table

The table below, "Table A: RISK IMPACT", helps the SC to make an Impact Level Assessment for each risk detailed for the trial. It is used to complete the last column of "MCTC006: Risk Assessment and Management Table". For example, a risk that has a possible likelihood of occurring and major consequences for the study outcome and/or for the organisation if it was to occur, is categorised as a HIGH (Red) RISK IMPACT.

Likelihood	Insignificant Consequences	Minor Consequences	Moderate Consequences	Major Consequences	Catastrophic Consequences
Almost Certain	Low	Medium	High	High	High
Likely	Low	Medium	High	High	High
Possible	Low	Medium	Medium	High	High
Unlikely	Low	Low	Medium	Medium	High
Rare	Low	Low	Medium	Medium	Medium

9.3. Appendix 3: Sponsorship Approval Process Flow



10. RELATED DOCUMENTS

MCTC007 Form | Sponsorship application risk matrix
MCTC137 Form | Sponsorship Committee Annual Progress Report
MCTC027 Form | Certificate of Sponsorship and Investigator Responsibilities
MCTC083 Charter | MCRI Sponsorship Committee
MCTC168 Form | Roles and Responsibilities Matrix
MCTC182 SOP | Sponsor-Investigator Responsibilities in MCRI-Sponsored IITs
MCTC183 SOP | Delegation of Sponsor Responsibilities in MCRI-Sponsored IITs
MCTC035 Template | Risk Assessment and Risk Management Tool for Clinical Trails

DOCUMENT END