Standard Operating Procedure

Title: **Management of Temperature controlled storage**

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Applicability: Temperature controlled storage in Melbourne Children's Research Unit

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Document History

Revision	Modified by	Date of Release	Description of Change
1.0	Carolyn Stewart	18/04/2023	New Issue

CONTENTS

1. PURPOSE

To document the procedure for the management of the storage of biological samples and other temperature sensitive clinical trial products in the Melbourne Children's Research Unit (MCRU) temperature-controlled storage units (freezer(s) and refrigerator(s)). The purpose of the procedure is to ensure the integrity of the stored items.

1.1. Quality Improvement

This SOP works towards ensuring the integrity of the biological samples and other temperature sensitive clinical trial products and compliance with the study protocol, associated procedures, ICH-GCP and local/national requirements.

2. SCOPE

This SOP applies to the **short-term** temperature-controlled storage of biological samples from the time of collection from clinical trial participants until shipment to laboratory for analysis. This SOP also applies to the storage of temperature sensitive clinical trial products. This SOP does not apply to the long term or indefinite storage of biological samples.

3. RESPONSIBILITY

All temperature-controlled storage within MCRU, and this SOP are the responsibility of the MCRU team.

It is the responsibility of the MCRU team to ensure that all users of the temperature-controlled storage units in MCRU, are familiar with and adhere to this SOP.

It is the responsibility of all users of the temperature-controlled storage units in MCRU to adhere to this procedure and to notify the MCRU team of any:

- issues identified with the temperature-controlled storage units
- concerns with the feasibility of this SOP
- suggested improvements to the temperature-controlled storage in MCRU and/or this SOP

4. PROCEDURE

4.1. Process Map Temperature out of Range/Equipment Failure Flow Chart (see appendix 1)

4.2. Equipment Use

4.2.1. The -80°C Freezer is to be used only for the storage of biological samples. Ice packs will be placed in the -20°C Freezer in preparation for sample packing/shipping.

4.2.2. Temperature controlled storage unit should be checked daily for any visible issues (For example, build-up of ice, rubber seals, freezer door not shut properly, and samples not stored appropriately) by the MCRU Clinic Coordinator and followed up as required.

4.2.3. Temperature-controlled storage unit will be kept in a locked room, accessible only by authorised personnel.

4.2.4. Temperature sensitive clinical trial products include medications sensitive reagents for sample preparation, tubes for blood collection and in some cases dispensed Investigational Product.

4.2.5. Biological samples to be placed in the temperature-controlled storage unit will be appropriately packaged and clearly labelled with the participant identifier (i.e. study ID), date of collection & study HREC number.

4.2.6. A list of approved studies with study identifiers and contact details of the study team (PI and study personnel) will regularly be updated by the MCRU Clinic Coordinator. It is a responsibility of the study team member to update the MCRU Clinic Coordinator of any changes.

4.2.7. The MCRU temperature-controlled storage units are not appropriate for long term storage. If samples need to be stored for greater than 1 month, an alternative location needs to be arranged by the study team.

4.3. Temperature Monitoring

4.3.1. The temperature of the storage units will be monitored continuously by the RCH Spotless Building Automated System (BAS) and alarms raised for any failure or temperature excursion.

4.3.2. The -80°C and -20°C freezers and the 2 - 8°C refrigerator are all identified within BAS as 'priority' response when activated.

4.3.3. Alarms are managed by RCH Spotless Security who will contact either the CNC Research and Trials, MCRU Clinic Coordinator or the after hours MCRI Engineering (See Alarm Contact List).

4.3.4. The Alarm Contact list will be updated by the MCRU Clinic Coordinator who will check the details with Spotless quarterly. This information will be documented on both Florence and Microsoft Teams

4.3.5. Monthly temperature logs will be provided to MCRU by RCH Spotless.

4.3.6. MCRU Clinic Coordinator will be responsible for maintaining central files of monthly temperature logs on both Florence and Microsoft Teams.

4.3.7. A portable temperature logger will be kept alongside samples/temperature sensitive products in each of the temperature-controlled storage units. These will be used for backup temperature recording and in case of out of range temperature.

4.3.8. The data on the portable temperature logger will be downloaded and cleared monthly by the MCRU Clinic Coordinator.

4.3.9. Portable temperature loggers must stay with samples at all times.

4.4. Temperature Out of Range Actions

Follow Process Map for Temperature Out of Range/Equipment Failure (Appendix 1) which is also found laminated and on the wall behind the -80 freezer in MCRU.

4.4.1. SPOTLESS (BAS Alarm)

When BAS issues an alarm notification, RCH Spotless Security will:

- Within hours: Notify Contact List personnel in the order they appear on the Alarm Contact List.
- Out of hours: Attend MCRU and inspect the unit and check for cause and remedy and notify Contact List personnel in the order they appear on the Alarm Contact List.

4.4.2. RCH/MCRI Staff (audible alarm)

When RCH/MCRI staff member is alerted by an audible alarm they will:

- Record the time of the alarm
- Respond and check for cause (e.g. door open, ice build up, power outage) and attempt to resolve.
- Contact the CNC Research and Trials and MCRU Clinic Coordinator who will attend MCRU and the affected storage unit to assess.
- If temperature is not stabilising, CNC Research and Trials and/or MCRU Clinic Coordinator will contact MCRI Engineering to attend and assess storage unit.
- Note: Once out of range the –80C freezer can take up to 3 hours to return to temperature.

4.4.3. If/when temperature returns to range, note the time and provide detail of the event to the MCRU Clinic Coordinator.

4.4.4. If alarm continues and/or temperature does not return to range, then CNC Research and Trials and/or MCRU Clinic Coordinator will contact MCRI Engineering to immediately arrange for the relocation of samples/products to an alternate temperature monitored storage unit (see section 4.5).

4.4.5. The MCRU Clinic Coordinator will:

- Arrange for urgent maintenance/vendor assessment of the storage unit (if required) and;
- Prepare an Out of Range Temperature Report and;
- Circulate report to affected study team members.

4.5. Relocation of Biological Samples and Temperature Sensitive Clinical Trials Products

4.5.1. Biological Samples and Temperature sensitive products will be relocated if the affected storage unit has failed or if the temperature cannot be reliably maintained within the required range. Samples/products will remain at a back-up temperature monitored storage provided by MCRI Engineering until affected storage unit is restored. If affected storage unit has failed the MCRU Clinic Coordinator will contact MCRI Engineering for transfer of samples and portable temperature logger to an alternative backup location.

4.5.2. The MCRU Clinic Coordinator will be responsible for contacting study team members whose samples have been affected.

4.5.3. The study team members will be responsible for arranging for the shipping of affected samples from the backup location to the study specific laboratory at the earliest opportunity.

4.5.4. The study team member will be responsible for preparing the study specific file note and reporting the storage unit failure and any associated temperature excursions to the study sponsor.

4.5.5. Samples/product may be returned to the affected storage unit only after it is confirmed that the unit is fully and reliably operational by MCRI Engineering.

4.6. Preventative Maintenance

The management and maintenance of temperature-controlled storage will follow RCH/MCRI Preventative Maintenance procedures.

4.7. Routine Audit of Stored Inventory

The MCRU Clinic Coordinator will review the storage units on a monthly basis to ensure:

- That biological samples are being shipped regularly (primary and backup biological samples)
- That biological samples are not being stored for extended periods of time.
- That temperature sensitive clinical trial products are for active trials and that they are in-date.

4.8. Maintenance of Alarm Contact List

4.8.1. The Alarm Contact List (listed in order that they will be contacted in); The MCRU Clinic Coordinator, CNC Research and Trials and MCRI Engineering.

4.8.2. This list will need to be updated and checked quarterly by the MCRU Clinic Coordinator to ensure that there hasn't been changes in staff roles and contact details. This information will be documented on both Florence and Microsoft Teams.

4.8.3. The current Alarm Contact List will be stored on both Florence and Microsoft Teams.

5. CORRECTIVE ACTIONS

MCRU is responsible for ensuring that any deviation from this SOP that results in a potential risk to the integrity of biological samples and other temperature sensitive clinical trial products or safety of staff are included in breach notifications, refer to MCTC061 SOP CAPA Plan. The Principal Investigator is then responsible for reporting any deviations that may present a risk to the Sponsor/HREC/DTS if the event requires a report.

6. GLOSSARY

Clinical Trial

The World Health Organization (WHO) definition for a clinical trial is: 'any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes'.

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.

Investigational Medicinal Product (IMP)

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.

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.

Participant

A participant is a person that is the subject of the research.

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.

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.

Study Team

Refers to the extended group of people involved in a research study. This includes the investigator team and any additional members of staff who are involved in the set-up or conduct of the study e.g. research nurse, research assistants.

Study Team Member

A research worker works at a clinical research site under the immediate direction of a Principal Investigator, whose research activities are conducted under Good Clinical Practice guidelines. May also be called "Clinical Trial Coordinator" or "Research Coordinator" or "study coordinator". (ARCP Definition.)

Temperature Sensitive Clinical Trial Products

Include but not limited to concomitant medications (non-study specific and study specific), laboratory or pathology kits (non-study specific and study specific), biological samples (study specific).

Temperature Logger

A Temperature Logger is a single-use temperature data logger which can be easily downloaded to produce a .pdf report of temperature records over a given period of time. A Temperature Logger will be used to record the temperature at which the samples were exposed once removed from continuously monitored temperature controlled storage and until the samples are placed back in continuously monitored temperature controlled storage. It will also be used to monitor room temperature storage.

Trial Coordinator

A Trial Coordinator has a significant role in the management of the clinical trial at the Sponsor level and provides leadership in clinical trial activities to ensure that the trial is completed within budget, on time and of the highest quality. A Trial Coordinator is responsible for managing the planning, implementation, and tracking of the clinical monitoring process, administration, and start-up of the clinical trial at the participating site and maintaining an overview of the conduct of the trial at sites. Some common roles and responsibilities performed by the Trial Coordinator include:

- Participate in protocol development, CRF design and clinical study report writing
- Guide in the creation and development of important study documents and manuals
- Conduct feasibility assessments
- Develop study budgets
- Oversee participant recruitment
- Oversee overall trial conduct
- Ensure compliance of site-staff with the trials Standard Operating Procedures
- Ensures compliance to all regulatory requirements both at a local and international level
- Ensures compliance to all data protection requirements both at a local and international level
- Ensures compliance to all safety reporting requirements both at a local and international level
- Conduct team meetings and site-staff training programs
- Overall responsibility of the trial
- Supervise in-house clinical trial staff

7. REFERENCES

Note for guidance on Good Clinical Practice (CPMP/ICH/135/96) annotated with TGA comments DSEB, July 2000, sections 1 and 5

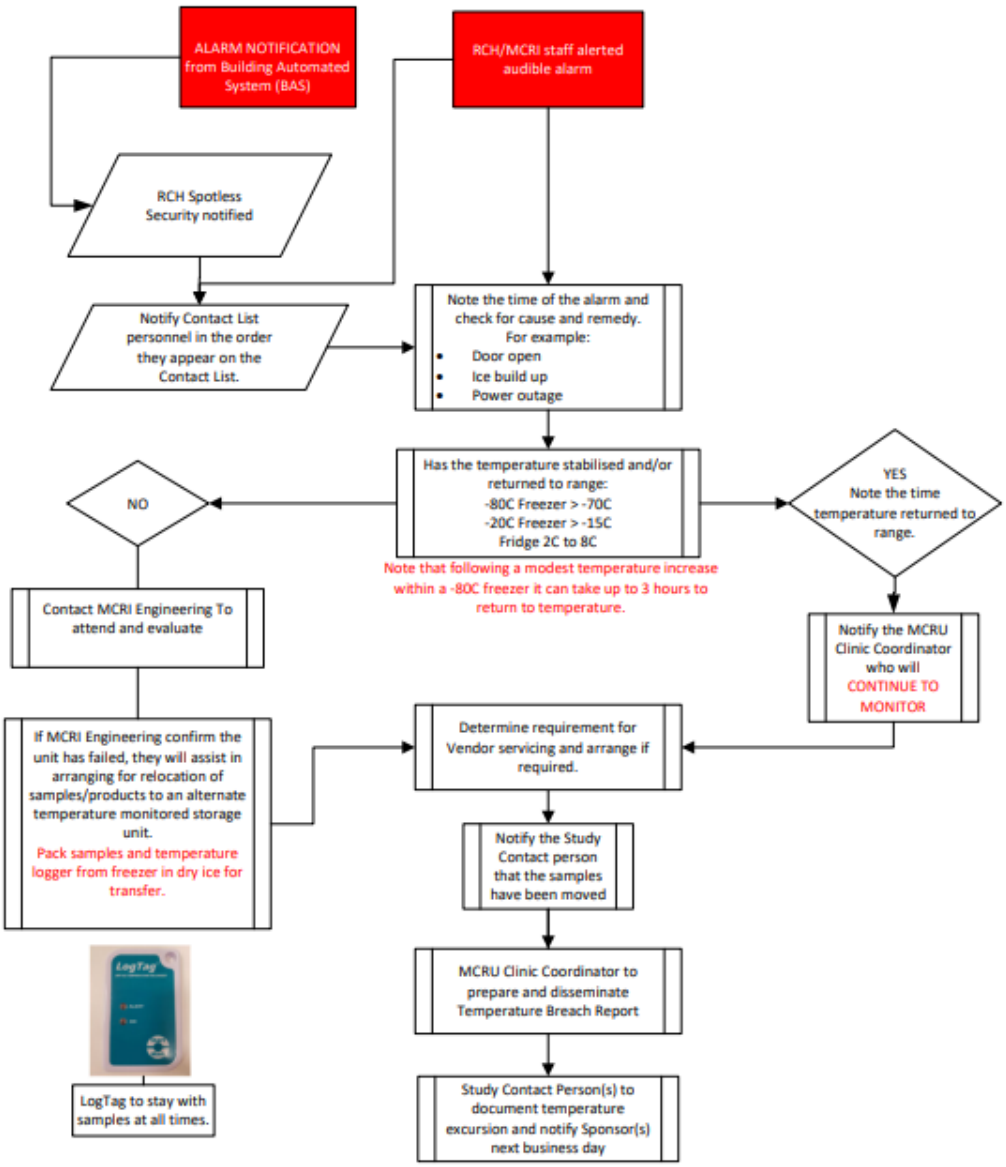
8. COLLABORATORS

Name/Role	Department/Group	Affiliation
Kaya Gardiner	RCH Operations	RCH
Barisa Kedir	Melbourne Children's Research Unit	RCH

9. APPENDICES

9.1. Appendix 1: Process Map for out of Range Temperature/Equipment Failure

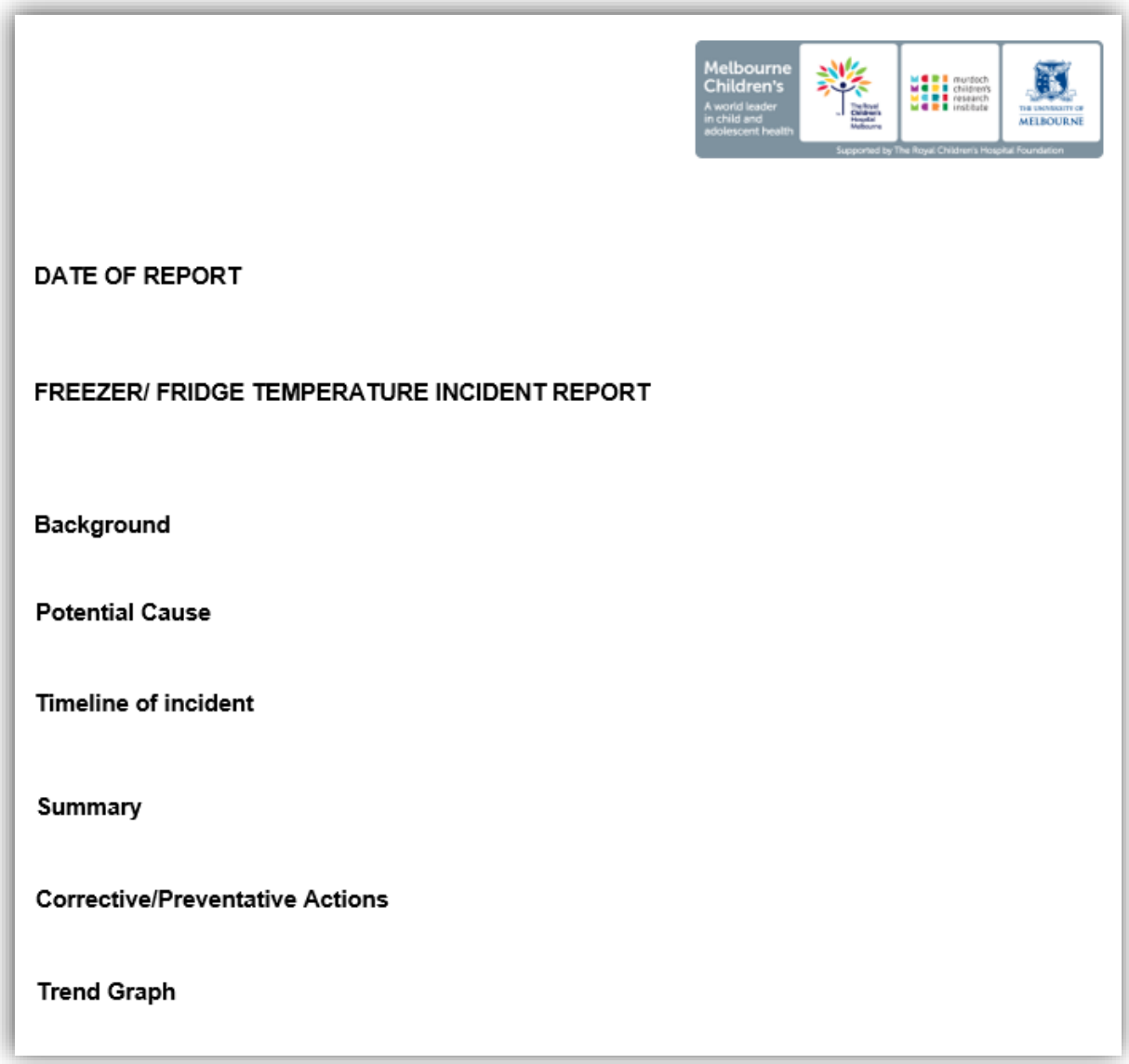
Standard Operating Procedure MCTC164
Management of Temperature Controlled Storage
Process Map for Temperature Out of Range/Equipment Failure



ALARM CONTACT LIST	Name	Phone Number
MCRU Clinic Coordinator		
CNC Research and Trials		
MCRI Engineering 1		
MCRI Engineering 2		

Version 1.0 Dated 27MAR2023

9.2. Appendix 2: Out of Range Temperature Report Template



DATE OF REPORT

FREEZER/ FRIDGE TEMPERATURE INCIDENT REPORT

Background

Potential Cause

Timeline of incident

Summary

Corrective/Preventative Actions

Trend Graph

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