STANDARD OPERATING PROCEDURE

Storage of Clinical Trial Drugs

1 Scope

This procedure documents the requirements for the activities associated with storage and temperature monitoring of clinical trial materials (CTM) in the Royal Children's Hospital (RCH) pharmacy department. This procedure also describes the actions to be taken in the event of a temperature excursion. The handling of clinical trial materials (CTM) must comply with Good Clinical Practice (GCP) principles, protocol specific requirements and local legislation regarding the storage of drug poisons and controlled substances.

2 Responsibilities

2.1 Pharmacist/Pharmacy Technician

(i) Ensure that staff involved in processes associated with the storage of CTM have completed Good Clinical Practice training meeting Minimum Criteria v.2.0 for ICH E6 (R2) GCP Investigator Site Personnel Training identified by TransCelerate BioPharma, Inc., as necessary to enable mutual recognition of GCP training among trial sponsors.

(ii) Ensure that all equipment and consumables required are assembled prior to storing and monitoring the storage conditions of CTM.

(iii) Complete all necessary records associated with storage and monitoring of storage conditions of clinical trial products according to Institutional, Study Protocol and Regulatory requirements.

3 Procedure

3.1 Storage of clinical trial drugs should comply with the following conditions:

- CTM should be stored in a designated separate area with separation from non-trial pharmacy stock
- CTM for specific protocols should be stored in a designated separate area with separation from CTM for different protocols and be clearly identified and labelled with the protocol identity.
- CTM should preferably be stored in the pharmacy until dispensed for use.
- CTM stored outside of the clinical trials pharmacy should be regularly reviewed to ensure appropriate storage and drug accountability recording.
- CTM storage should be as per conditions specified by the manufacturer or clinical trial sponsor.
- CTM should be stored in accordance with regulatory requirements. When the CTM is not a registered drug or poison it should be stored in accordance with the storage of an equivalent or similar registered drug.
- Contingency storage plans in case of disruption to the storage conditions are detailed in this procedure, including timely notification to trial sponsors regarding any disruption to the storage of CTM.

3.2 Temperature monitoring should be undertaken as follows:

3.2.1 Room temperature areas

- CTM will be stored in temperature controlled area of the pharmacy
- The temperature will be maintained as close to 22°C as possible.
- The temperature will be monitored with a calibrated temperature monitoring data logger.
- The temperature monitoring data logger will be programmed to measure the temperature every 30 minutes.
- The temperature monitoring data logger will be downloaded, filed electronically, printed and filed.
- It will be reviewed as indicated by a clinical trial pharmacist's signature and date on the filed paper copy. This will occur on an approximately weekly basis.
- The temperature monitoring data logger paper and electronic records will be retained for at least 25 years.
- The temperature monitoring data logger is visually checked daily (M-F) but not logged as being checked.
- If the temperature is recorded above 25°C or below 15° C the RCH Engineering Department will be advised and corrective steps taken.
- Upon triggering the alarm, the pharmacist on call will receive notification of the alarm and an engineer will attend the pharmacy in the presence of the pharmacist.
- During weekday working hours CTM subjected to the temperature excursion will be managed by the clinical trials pharmacist(s) on site.
- Out of weekday working hours the CTM subjected to the temperature excursion will initially be managed by the on call or after-hours pharmacist.
- If the temperature is recorded above 25°C or below 15° C the details of the temperature excursion will be communicated to sponsors as per their requirements and the event will be reported in a Note to File to be filed with the paper logs and electronically.

3.2.2 Refrigerator

- The temperature will be maintained between 2-8°C.
- The temperature will be monitored with a calibrated temperature monitoring data logger.
- The temperature monitoring data logger will be programmed to measure the temperature every 15 minutes.
- The temperature monitoring data logger will be downloaded, filed electronically, printed and filed.
- It will be reviewed as indicated by a clinical trial pharmacist's signature and date on the filed paper copy. This will occur on an approximately weekly basis.
- The temperature monitoring data logger paper and electronic records will be retained for at least 25 years
- In addition to the above the RCH Engineering Department centrally monitors the RCH pharmacy refrigerators 24 hours a day with an audible alarm system in place.
- The RCH Engineering Department temperature monitoring system is continuous and records every 15 minutes.
- The alarm is triggered when a temperature excursion occurs when the temperature is outside the 2-8°C temperature range continuously for more than 20 minutes.
- Upon triggering the alarm, the pharmacist on call will receive notification of the alarm and an engineer will attend the pharmacy in the presence of the pharmacist.
- During weekday working hours CTM subjected to the temperature excursion will be managed by the clinical trials pharmacist(s) on site.
- Out of weekday working hours the CTM subjected to the temperature excursion will initially be managed by the on call or after-hours pharmacist.

- If the reason resulting in the temperature excursion is unable be rectified immediately, the CTM will be transferred to a backup refrigerator.
- The details of the temperature excursion will be recorded on the Relocation of CTM due to FRIDGE temperature excursion (RCH SOP JAN 2023) form.
- The temperature monitoring data logger located within the fridge will be moved as per the process detailed within the Relocation of CTM due to FRIDGE temperature excursion (RCH SOP JAN 2023) form.

3.2.3 Freezer: -25 - -15°C

- The RCH Engineering Department centrally monitors the RCH pharmacy freezer 24 hours a day with an alarm system in place.
- The RCH Engineering Department temperature monitoring system is continuous and records every 15 minutes.
- The temperature monitoring data is emailed to the clinical trials pharmacy weekly. The data is downloaded, filed electronically, printed and filed.
- It will be reviewed as indicated by a clinical trial pharmacist's signature and date on the centrally filed paper copy.
- The temperature monitoring data logger paper and electronic records will be retained for at least 25 years.
- The alarm is triggered when a temperature excursion occurs when the temperature is outside the -25 - -15°C temperature range continuously for more than 20 minutes.
- Upon triggering the alarm, the pharmacist on call will receive notification of the alarm and an engineer will attend the pharmacy in the presence of the pharmacist
- During working hours CTM subjected to the temperature excursion will be managed by the clinical trials pharmacist(s) on site.
- After working hours the CTM subjected to the temperature excursion will initially be managed by the on call pharmacist or after-hours pharmacist.
- If the reason resulting in the temperature excursion is unable be rectified immediately, the CTM will be transferred to a backup freezer or refrigerator depending on the requirements of the CTM.
- The immediate details of the temperature excursion will be recorded on the Relocation of CTM due to OP Freezer temperature excursion (RCH SOP Aug 2022).
- The temperature monitoring data logger within the back-up freezer will be started if the CTM is moved to the back-up freezer as per the Relocation of CTM due to OP Freezer temperature excursion (RCH SOP Aug 2022).

3.2.4 Ultra Cold Freezer: -80°C

- Murdoch Children's Research Institute (MCRI) centrally monitors the Ultra Cold freezer 24 hours a day with an alarm system in place.
- The MCRI temperature monitoring system is continuous and records every minute.
- The temperature monitoring data is emailed to the clinical trials pharmacy weekly. The data is downloaded, filed electronically, printed and filed.
- It will be reviewed as indicated by a clinical trial pharmacist's signature and date on the centrally filed paper copy.
- The temperature monitoring data logger paper and electronic records will be retained for at least 25 years.
- The alarm is triggered when a temperature excursion occurs when the temperature is outside the temperature range set for the CTM stored within the freezer.
- Upon triggering the alarm, during working hours CTM subjected to the temperature excursion will be managed by the clinical trials pharmacist(s) on site. The clinical trial pharmacy staff will receive

an email notification that the freezer has experienced a temperature excursion and will attend the freezer farm.

- Upon triggering the alarm, after working hours the CTM subjected to the temperature excursion will initially be managed by an on call pharmacist or a clinical trials pharmacist dependent on availability. The pharmacist will attend the freezer farm accompanied by an engineer.
- If the reason resulting in the temperature excursion is unable be rectified immediately, the CTM will be transferred to a backup freezer or refrigerator depending on the requirements of the CTM.
- The immediate details of the temperature excursion will be recorded on Relocation of CTM due to ULTRA COLD -80 Freezer temperature excursion (RCH SOP SEP 2022) form.

3.2.5 Record keeping

- Paper printouts of the temperature monitoring logs that apply to all protocols are kept in dedicated temperature monitoring folders in the RCH Clinical Trials Pharmacy.
- Compliance certificates and any relevant records are filed in the dedicated folders, and electronically.
- Paper and all online records will be retained for at least 25 years.
- Separate temperature monitoring records are not kept within individual protocol binders. Specific requests to do so will not be completed. Sponsors requiring paper logs filed in the protocol specific pharmacy binder will need to liaise with their contract research associate or monitor to perform this requirement.
- Contract research associates and monitors are provided with remote access to online records; paper records are made available at on-site monitoring visits.

3.3 The following actions should be taken if an alarm is triggered indicating a temperature excursion in any storage locations:

- Review the temperature data logger readings for deviations.
- Quarantine the CTM and if appropriate transfer CTM to the back-up storage facility as per the SOP specific to that storage location.
- The times of transfer are recorded and a temperature data logger is present in the back up facility.
- Notify sponsors or their delegates, as soon as practicable according to the study specific site temperature excursion reporting requirements. If a protocol specific temperature excursion reporting form is not available, complete and submit Appendix 1 located at the end of this SOP.
- Notify study coordinators and the investigator for future protocol appointments that may be impacted by the temperature excursion.
- When large numbers of protocol's CTM are impacted by a temperature excursion; prepare a tabulated listing of the protocols impacted and their quarantine status as per Appendix 2 in this SOP. This table will be prominently displayed or easily accessed online and updated according to the current status of CTM affected by the temperature excursion. The table will be reviewed BEFORE any CTM listed is dispensed in the period after the temperature excursion.
- Do not dispense CTM until authorization of fit for use is provided in writing by the sponsor. Once fit for use is received the CTM is no longer quarantined.
- Ensure the appropriate technician is contacted to investigate the alarm incident and/or to repair equipment.
- If available obtain and file the technician's report which may include preventative measures for future incidents.
- Complete a File Note detailing the alarm incident, file it with the relevant temperature record, online and in paper.
- Prepare protocol specific File Notes for completion once authorization of fit for use or NOT fit for use is provided in writing by the sponsor. File in the Storage section of each protocol's folders.

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Approved by:	Kate Richichi	
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Appendix 1

Clinical Trials Outside Temperature Range Form

Do NOT use this form if a protocol-specific temperature excursion reporting form is available

This form may be used to record details of temperature excursions for CTM.

Attach to this form the data points from the Temperature data logger(s) for the period immediately before the excursion, during the excursion and immediately after the excursion has been corrected.

Protocol Title:

Protocol Number: **HREC Number:** **Site:**

Description of IP:					
Start Date of excursion ddmmmyyyy	**Storage location** Fridge, ambient, freezer, ultra-cold freezer	**Start time of excursion (24 hr)**	**End time of excursion (24 hr)**	**End Date of excursion ddmmmyyyy**	**Comments**

Appendix 2

HREC	Protocol number	Date excursion communicated to the sponsor	Sponsor Contact details	Pharmacist Reporting the excursion	Date and outcome of excursion