WITS RHI

STANDARD OPERATING PROCEDURE

TITLE	**Supply and handling of trial medication for the RECOVERY trial in South Africa.** (Based on Protocol V27.0 13-Sep-2023 and RECOVERY Trial Pharmacy FAQ V24.5 09-Jan-2025.)
VERSION	1.0
SOP NO.	R1
DIVISION/SCOPE	WITS RHI RESEARCH CENTRE (HILLBROW, JOHANNESBURG)
COMPILED BY	ROLE: PHARMACIST MOHAMMED SEEDAT _____ 13 MAY 2025 NAME SIGNATURE DATE (DD MMM YYYY)
REVIEWED BY	Pharmacist
REVIEW RESPONSIBILITY	Pharmacist

DOCUMENT HISTORY		
VERSION	**DATE**	**DETAILS OF CHANGES**
1.0	21 April 2025	New SOP
1.1	13 May 2025	4.1 Removed "hard copies" 4.1 Added documents can be saved electronically if according to site specific SOPs. 4.7 Removed storage conditions from labelling requirements. 4.13.1 Removed preparation of high dose corticosteroids (Covid-19 arm) 4.14 Added 'ward stock"

USAGE BY	☒ RECOVERY PHARMACY STAFF

APPROVED BY	ROLE: RECOVERY NATIONAL CO-PI Jeremy Nel _____ _____ 13 May 2025 NAME SIGNATURE DATE (DD MMM YYYY) 13 May 2025 EFFECTIVE DATE (DD MMM YYYY)
NEXT REVIEW DATE	WITHIN 3 YEARS OF LAST APPROVAL

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1.0 Background

The correct and accurate management of study products and documentation is a minimum standard of requirement by the South African Health Products Regulatory Authority (SAHPRA), and is of paramount importance to any clinical trial as per Good Clinical Practice (GCP), Good Pharmacy Practice (GPP) and International Conference on Harmonization (ICH) Guidelines. It is therefore necessary to have generic procedures in place for the handling and documentation of study and related drugs.

2.0 Purpose & Principle

The purpose for this Standard Operating Procedure (SOP) is to describe the management and accountability of study products in the RECOVERY TRIAL for sites in South Africa. This SOP is to be used in conjunction with the study specific protocol and manuals of operation.

Study products (Oseltamivir 75mg capsules and Dexamethasone 4mg/ml ampoules) will be procured by the local trial centre (WITS RHI research centre) from local suppliers while Baloxavir tablets will be shipped to the local trial centre by ROCHE, thereafter all products will be distributed to clinical trial sites.

This SOP will outline the requirements and procedures for clinical trial sites in the supply and handling study products for the RECOVERY trial in South Africa.

3.0 Responsibilities

It is the responsibility of the Principal Investigator (PI) to ensure that study procedures are conducted according to the study protocol, study manual (SSP Manual or Manual of Operations), study SOPs and GCP requirements. The PI may delegate this responsibility to other study staff. This delegation is recorded in the Delegation of Authority log.

The delegated Pharmacist will be responsible for maintaining the day-to-day activities of the pharmacy, i.e. stock management, creating source documents, accountability, and temperature monitoring according to protocol and good pharmacy practice. These responsibilities may be delegated to other pharmacy staff members registered with the South African Pharmacy Council (SAPC) and recorded on the study delegation of authority log.

The sponsor will be aware of, and in agreement that the person who has been delegated responsibility for receipt, management and storage of clinical trial supplies is appropriate. Only the Study Pharmacist, site pharmacist and pharmacist assistant will handle study drug on a daily basis. Should there be any changes in personnel, such persons will be included on the Delegation of Authority Logs and the sponsors will be notified.

4.0 Procedures

4.1 Study Product ordering

After site activation, IP will shipped to sites automatically and quantities will be determined by the Pharmacist at local trial centre.

Thereafter , where low stock levels are detected during inventory checks after study initiation, study products will be ordered from the pharmacist at the local trial centre via email
All correspondence with regards to orders will be filed in the protocol specific pharmacy file under shipment documentation or saved electronically if site SOPs allows.

Orders should be placed timeously and allow for estimated delivery to occur within 1-2 weeks after placing orders.

4.2 Receipt of study drugs

All study products may only be received and signed for by pharmacy personnel who have signed onto the protocol Delegation of Authority log.
Upon receipt of study product, the following procedures are carried out:

- Check the number of shippers received, quantity of study products and delivery address against the documentation before accepting receipt.
- IP will be shipped with a min/max thermometer inside the container for deliveries carried out by Wits RHI. If courier is used the min/max readings are not required.
- Pharmacy staff should record min/max values on the packing slip confirming IP was received within temperature range. (Appendix 1)
- The shipping log receipt (packing slip) and letter confirming the inventory details is completed, then scanned and emailed to the local trial centre Pharmacist and/or designated person upon receipt of drug.
- Should there be any discrepancies, quarantine the shipper with the discrepancy and report to local trial centre pharmacist immediately. The shipper is then quarantined until such time a response is received as to what action needs to be taken.
- The received and inventoried study product is then recorded on the Study Product Accountability Record using a separate page for each batch. (Appendix 2) Sites are to create own source documents.
- Once drugs have been inventoried, they are appropriately stored in the temperature-controlled pharmacy.

4.3 Inventory of study drugs

Study products are inventoried upon receipt and balances are checked and documented at least once a month by the pharmacy personnel. The frequency of this inventory may vary depending on the requirements of the protocol.
Each study product has an accountability log that is completed on receipt, dispensation, return and quarantine of any study product.
During the Inventory process the following is verified:

- Quantities and lot numbers of study products on hand if applicable

- Expiry date of each batch of study product.

4.4 Records to be kept by pharmacy

The following protocol-specific records are kept in the pharmacy/site (unless otherwise advised by sponsor);

- Current IRB approved version of the protocol; protocol amendments/Letters of Amendments, clarification memo's.
- Regulatory Documents i.e., Ethics, SAHPRA, and RCC; a signed copy of the FDA Form 1572 or IoR Form (for a non-IND Study) and VAT Exemption documents (if applicable).
- Drug Supply Statement (if applicable); Subject Randomization Log, Study Product Requisition forms and transfer forms, Packing Slips, Waybills & Shipping Documents and Drug Destruction certificates and Correspondence.
- Protocol Summary and/or a protocol specific pharmacy SOP, participant treatment assignment list (if available) and the Study Product Accountability Logs including drug return records.
- Individual Participant Records, i.e., Prescriptions, Study Product repeat requests, Consent signature page copies and participant randomization sheet.
- Monitoring visit reports, Pharmacy quality assurance logs.
- Package inserts and/or investigator brochures
- Calibration of equipment records
- All pharmacy staff training records

4.5 Storage of study drugs

- Study products are stored in the temperature-controlled site pharmacy.
- Storage of study product is separated per protocol if more than one study is being conducted at the site. Each protocol area is clearly demarcated and labelled. Similarly, different study products for the same study are stored separately with each area clearly marked.
- Shelves are clearly marked with the study/protocol details and kit numbers where applicable.
- Study products are also kept separate from other medication stocked by the site, i.e. concomitant medications.
- Access to the pharmacy is restricted to pharmacy personnel only.

4.6 Temperature Monitoring and Recording

- Although temperature excursion reporting is not required for this study, sites must ensure that all study products are kept at required temperature as per GPP.
- The pharmacy temperature is maintained by electronic air conditioning systems (heating and cooling). The ambient/room temperature is maintained at a temperature of approximately 15-25° Celsius.
- Digital Min-Max thermometers are used to manually measure the ambient/room temperature as per site specific SOPs.
- The temperature readings are recorded on temperature logs (Appendix 3) by designated pharmacy personnel. They are named according to the point of temperature monitoring. The serial number of the thermometer used for that month is recorded on the log to keep a record of the equipment used and can be referenced for calibrations and maintenance.

- The ambient temperature is continually monitored (at 10-minute intervals) by the electronic pharmacy temperature and humidity monitoring and alarm system. Weekly summaries of the continual ambient temperature recordings will be printed out, reviewed, initialed, and dated by a pharmacy staff member, and filed.
- All air conditioning systems will be serviced according to site specific SOPS. Servicing documents will be filed in the Pharmacy
- The electronic system will be calibrated/verified annually. All Calibration documents will be filed in Pharmacy if applicable.

4.7 Labelling and repackaging of study drugs

- Labelling of study drugs will be done as per protocol specific guidelines. The minimum requirements for a label as per SA guidelines (Act 101) will be adhered to.
- The label will include:
  - Name of the product
  - Participant trial number/PTID
  - Dispenser's name/initials
  - Prescriber's name/initials
  - Date of dispensing
  - Expiry date
  - Quantity
  - Instructions for use
  - Special warnings
- Protocol specific labels may be used depending on the specific requirements of the protocol.
- The label will be placed on the container so as not to obscure any important information like expiry dates.

4.8 Dispensing of study drugs to participants

- Study Products may only be dispensed upon receipt of a written prescription from an authorized prescriber (as indicated on the Protocol Specific Delegation of Authority Log), for a specific participant.
- When dispensing a study product, the "first in first out rule" will apply. That is, the study product that is received first for a particular sub-lot/batch will be issued first according to the randomization list. However, in the event that study product is received with a shorter expiry date than the study product on hand, the product with the shorter expiry date will be dispensed first.

4.8.1 The Prescription

Sites to create own prescription (Source) but the prescription must include:

- Study/protocol number/name
- Participant screening and/or study numbers (PTID)
- Participant's weight if prescribing weight dependent dosing
- The date the prescription was issued and the date of dispensing
- Name and Quantity of study products to be dispensed

- Name and quantity of concomitant medication (con-med) to be dispensed (if desired at that visit) - The con-med Prescription may be used for this purpose.
- Comments, if necessary
- A tick box to verify that informed consent has been correctly completed and signed at enrolment (if applicable)
- Adress, signature and MP number of authorized prescriber
- Prescriptions will be filed in participant records.

4.8 Supply of Study Product

- Study product will only be supplied to study participants as per randomization lists/envelopes.
- Study product will only be dispensed upon receipt of a valid prescription or request slip.
- Study product may be dispensed directly to participants except where study requirements necessitate that study product be dispensed to the study clinician or nurse. Study products may also be dispensed to clinical staff for distribution to the participant, as in the case of home visits, offsite visits or participant hospitalization or whereby requested by the sponsor.

4.10 Drug Accountability/Monitoring

- The pharmacists are responsible for maintaining detailed records of all study product accountability, including how much product has been received, stored and dispensed at each visit for a specific protocol/study.
- The pharmacists will perform an inventory of all study products in the pharmacy on a minimum monthly basis.
- The Pharmacy Files will be maintained by the pharmacists as detailed in 4.4
- Pharmacy records will be monitored by external monitors as per sponsor requirements, and all pharmacy records to be available or scanned to appropriate person on request.

4.11 Unused and Expired study products

- All unused or expired IP should be sent back to the local trial centre Pharmacy (Wits RHI Research Centre)
- Approval to send IP to local trial centre pharmacy must first be obtained from the local trial centre Pharmacist so arrangements can be made (collection of IP if applicable).

4.12 Destruction of study products

- All unused or expired IP that is on hand al local trial centre or IP collected from trial sites, will be destroyed/discarded by local trial centre Pharmacist as per site SOP.

4.13 PREPARATION INSTRUCTIONS OF IV DEXAMETHASONE

4.13.1 Low-dose corticosteroids (Influenza and Community acquired pneumonia arms)

- Dexamethasone **6mg** once daily given orally or intravenously for ten days or until discharge (whichever happens earliest)

  Preparation of 6 mg dexamethasone IV:

  Consumables:
  - 1 x 50 mL 0.9% NaCl or 5% Dextrose IV bag
  - 2 x 4 mg/mL dexamethasone ampoules
  - 2 x 5 mL syringes
  - needles
  - alcohol swabs

  Instructions:
  - Check that the solution in each ampoule is clear and free of particles.
  - Disinfect the port of the 50 mL IV bag with an alcohol swab.
  - Withdraw 1.5 mL NaCl or dextrose from the bag and discard.
  - Withdraw 1.5 mL dexamethasone between the two ampoules and inject the 1.5 mL dexamethasone into the IV bag.
  - Invert the bag gently.
  - Label the prepared IV bag.

4.14 Ward Stock

If dexamethasone vials from the site pharmacy cannot be obtained during weekends or after hours etc, ward stock dexamethasone may be used and any vials used will be replaced by the site pharmacist and added to the accountability log.

5.0 Definitions/Abbreviations

Definitions:
Local trial centre: Registered institutional pharmacy, located at the Wits RHI Hilbrow Research Centre. This pharmacy services as the central pharmacy for the RECOVERY study.

Study Pharmacist: A licensed/registered Pharmacist who is responsible for overall site study drug management and accountability. She/he will ensure that other pharmacy staff are adequately trained and receive new information as it becomes available. She/he will also be responsible for generating reports, and meeting with sponsors and regulatory authorities as required.

Responsible Pharmacist (RP): Including the responsibilities outlined above (if applicable), this pharmacist will also be responsible for the management of overall pharmacy related duties and delegated duties.

Abbreviations:
IP - Investigational Product
GCP - Good Clinical Practice
GPP - Good Pharmacy Practice
PoR - Pharmacist of Record
PI - Principal Investigator
SAHPRA - South African Health Products Regulatory Authority

6.0 References

- ICH 5.14 Supplying and handling Investigational Product(s)
- ICH 8.2.14 Instructions for handling of Investigational Product(s) and trial-related materials (if not included in protocol or Investigator's Brochure)
- ICH 8.4.2 Documentation of Investigational Product(s) Destruction
- The Medicines and Related Substances Act, 1965 (ACT NO. 101of 1965) Section 27: Destruction of Medicines.
- South African Good Clinical Practice Guidelines, Second Edition, 2006
- Good Pharmacy Practice in South Africa, 2010
- Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks
- RECOVERY Protocol V27.0 13-Sep-2023
- RECOVERY Trial Pharmacy FAQ V24.5 09-Jan-2025
- RECOVERY pharmacy manual v1.0 19 NOV 2021 FARMOVS

7.0 Ethical Issues

All processes conducted by pharmacy personnel will adhere to GCP, GPP and any other relevant standards or regulations

8.0 Document Management, Filing and Archiving

All study information must be stored in accordance with the study protocol, documentation ethical and GCP/GPP requirements and any other relevant regulations or standards

9.0 Document control

9.1 Confidentiality Statements

- All information contained in this document is provided in confidence for the sole use of Wits RHI Research Centre staff and shall not be published or disclosed wholly or in part to any other party without prior permission.

9.2 Distribution

- The document owner detailed below controls the distribution of this document. Any paper copies generated are to be treated as UNCONTROLLED and destroyed when a new issue is made available.

9.3 Document configuration

Title:	SOP R1: Supply and handling of trial medication for the RECOVERY trial in South Africa
Format:	Microsoft word
File Location:	Research Centre Pharmacy

10.0 Appendices

Appendix 1: Packing Slip
Appendix 2: Study Product Accountability Log
Appendix 3: Temperature Log

Appendix 1: Packing Slip

Packing List: Recovery trial

From: Mohammed Seedat / Lethukuthula Manyaka	To:
WITS RHI Hillbrow Health Precinct 7 Esselen street Hillbrow 2001 Johannesburg	

Description	Batch	Expiry	QTY

Acknowledgement of receipt:

Have the contents been received in good order and as per the information in the table above?

☐ Yes ☐ No. Describe:

Thermometer serial number :				
	Min	Max	Time	Initials
Temperature reading at dispatch (Wits RHI)				
Temperature reading at receipt (CMJAH)				

Received By: _____

Signature: _____

Date: _____

Job Title: _____

Appendix 2: Study Product Accountability Log

(To be adapted to suit protocol-specific requirements)

Product: _____ Site: _____

Batch/Lot: _____ Expiry: _____

Date (DD-MMM-YY)	Participant ID	Quantity Dispensed (-) or Received (+)	Balance Forward	Dispensed or Received by Initial	Comments

Appendix 3: Temperature Log

[Temperature monitoring point] – [month and year]

	Morning reading					Afternoon reading				
	Temp			Time	Initials	Temp			Time	Initials
Date	Min	Actual	Max			Min	Actual	Max		

Thermometer Serial Number: _____

Comments: _____

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SIGNATURE LOG

This signature log indicates that you have been trained on this SOP and are aware of the required procedures. Signed copies must be kept in the Regulatory Binder.

I hereby certify that I have read this SOP and will follow the said SOP to maintain standardisation of quality. I know that if any of the material is unclear, I must discuss it with my supervisors until I fully understand all of the content covered in this SOP.

	Name and Surname	Role in Study	Date	Signature
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