Title	**Shipping of plasma samples for PK**
SOP Code	2R2 SOP24_01Sep2021
Effective Date	

1.0 Purpose(s)

The objective of this standard operating procedure (SOP) is to define the procedures to prepare the shipments of frozen plasma samples for the population pharmacokinetic component of the $2R^2$ trial. The SOP will ensure:

- that handling and shipment of samples are in compliance with the standards of Good Clinical Practice and Good Laboratory Practice;
- safety of the samples;
- the quality of the data produced by the study

2.0 Scope: Persons/Areas affected

This SOP concerns the co-investigators, their respective research teams and the laboratory personnel who were involved in conducting research with human subjects for population pharmacokinetic component of the study "$2R^2$: *Higher dose Rifampin for 2 months vs Standard dose Rifampin for Latent TB: a 3-arm randomized trial*".

3.0 Responsibilities

The trial coordinating center is responsible for developing and maintaining this SOP and for making it available at the clinical research site. At the clinical trial site, the site principal investigator is responsible for adoption of the processes described in the SOP and for making this SOP available at the laboratories where PK samples are stored.

4.0 Definition(s)

CTC: The site Clinical Trial Coordinator

PK: Pharmacokinetic study (note this is a component of $2R^2$ trial)

Population PK: sparse pharmacokinetic sampling in 2R2 trial.

5.0 Procedures

Population PK samples are collected during the entire duration of the trial, until one month after the last randomization occurs at site. Collection and storage of samples for PK are described in **SOP11_Population PK.** Once samples collection at site is completed, coordinating center will organize the shipment of samples for all $2R^2$ studies sites.

Coordinating center will confirm with CTC the date of last PK sampling at site. Once last PK sample has been collected, coordinating center will work with site CTC to gather information needed to prepare Waybill and Commercial Invoice for all sites.

Coordinating center will lease with an authorized shipping company (Marken) to organize the shipments of samples from all study sites.

5.1. Procedures at study sites:

When instructed by coordinating center, sites will prepare the shipping of samples.

In Canada: all samples (i.e. boxes A and B, see SOP11_Population PK for information on samples in each box) from Canadian sites will be shipped to Montreal. In Montreal, samples of boxes A will be consolidated and shipped to Bandung in one shipment. Samples from boxes B will be stored in Montreal and kept (in case needed as replacement) until the samples of boxes A have been received and all pharmacokinetic analysis are completed in Bandung.

In Vietnam: all samples collected in Vietnam at Ha Noi sites, will be shipped to Ho Chi Minh City first (i.e. boxes A and B). Only boxes A for all Vietnamese sites, will then be shipped from Ho Chi Minh City to Bandung, Indonesia. Boxes B will be stored in Ho Chi Minh City and kept (in case needed as replacement) until the samples of boxes A have been received and all pharmacokinetic analysis are completed in Bandung.

Documentation: with samples, sites will also send a paper **copy** of the map of samples in the boxes. An e-copy of the samples map will also be sent by email to coordinating center. The original map will be kept at site, with study documents in $2R^2$ master binder.

5.2. Shipping procedure

The shipping of the samples complies with the international regulations for shipping biological specimens, i.e., proper classification, packing, labeling and declaration of Biological specimen shipment.

At the site laboratory:
Trained personnel at the laboratory where the PK frozen samples are stored, will prepare samples for pick up by Marken, the company used as carrier in $2R^2$. Before shipping, laboratory personnel must ensure that packaging of plasma in cryovials and boxes is done according to the instructions and that one copy of the box map is with shipping. A shipping log needs to be filled at samples pick up (**Appendix 1, Log 1**).

In Montreal, the CIM laboratory will also be in charge of receiving samples from other Canadian sites and in Ho Chi Minh City, the Phoi Viet Clinic lab will be also be in charge of receiving the samples from other Vietnamese sites. In Bandung, samples will be received from Vietnam and Canada. A delivery log needs to be filled at samples reception (**Appendix 1, Log 2**).

Laboratory address, pick up/delivery hours and contact person will be provided by each laboratory ahead of time to site coordinator or coordinating center.

Shipping company: Marken will provide outer packaging, labelling and dry ice needed for the shipping. Marken will also provide temperature monitoring device and will send to the coordinating center the reports of temperatures, once the samples are delivered.

Coordinating center: The Waybill and Commercial Invoice for Marken will be prepared by the coordinating center and sent to the laboratory at sites before shipping takes place.
The date of the shipment will be communicated to the laboratories by the coordinating center with 5-7 days notice.

5.3. Packing

Clinical specimens must be tripled packaged, primary container, secondary container and outer container. The maximum quantity for a primary container is 500 ml and outer packaging must not contain more than 4 L. Clinical specimens must be assigned to "UN3373".

For laboratory personnel:

5.3.1. Primary container

The primary containers are cryovials containing plasma samples. Before packing the cryovials, make sure that the tubes are

- Properly Labeled: i.e. ensure each cryovial has these essential information: participant ID, 1st of 2nd samples (i.e. 2h or 4h sample);
- Are packed in a way to prevent breakage
- In the event of breakage, transfer the sample to a new tube (primary container)

5.3.2. Secondary container

The secondary container is a Ziplock sealable bag in which to put the freezer box. Make sure that

- The boxes are intact
- The boxes are labeled
- Once removed from freezer, the boxes are put in a sealable Ziplock bag.
- The bag is sealed properly, there is no leakage
- There is a copy of the box map that is sent with samples (Note : the original box map has to be kept with $2R^2$ documents at site, lab personnel needs to give it to site research coordinator once samples shipment has taken place). Please send an electronic copy (as a picture, a scanned version etc) of the box map to CTC.

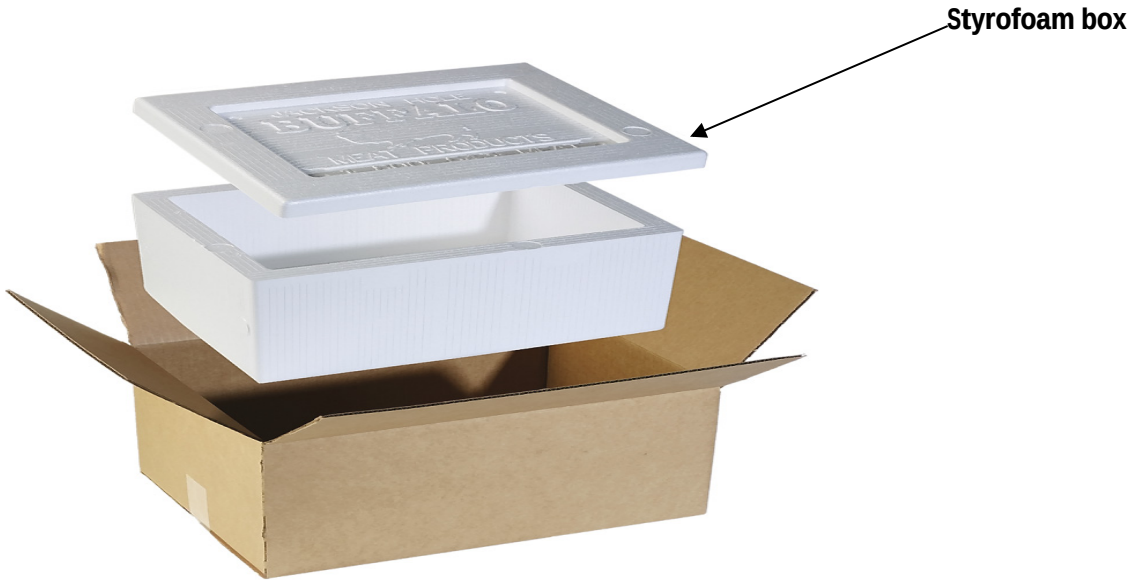
For shipping company:

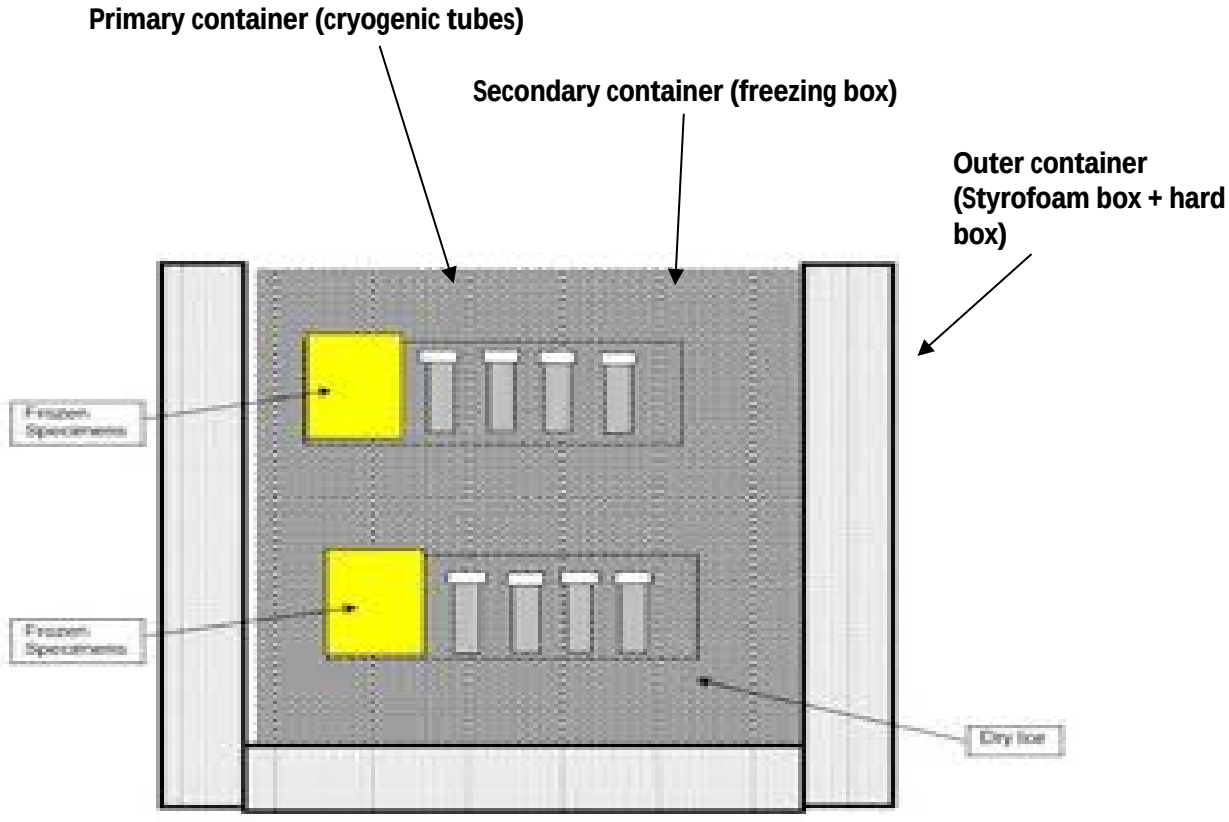
5.3.3. Outer container

The outer container will be provided by Marken. Once the laboratory personnel at sites give to Marken the boxes containing the frozen samples in cryovials, Marken personnel will put them in an outer container.
The outer container is a box with Styrofoam inside. The outer container

- Must be made of durable material and be able to withstand a 1.2 m drop test
- One side must be at least 10X10 cm to fit the required labels

Example of outer container.





5.4. Shipping with Dry ice

Dry ice for the shipping will be provided by Marken, which will be in charge of using the dry ice to prepare the box at pick-up and to replace the dry ice, as needed, during transportation to the final destination.

Dry ice is carbon dioxide kept solid at the extremely low temperature of -109.5 degrees Fahrenheit, cold enough to freeze skin cells and cause an injury similar to a burn. If needed to handle dry ice, always do it with protective gloves or a towel. Store dry ice in an insulated container. Do not store ice in a container that is completely airtight. As the ice changes to CO_2 (carbon dioxide) gas, it will cause an airtight container to expand and possibly explode. Dry ice gives off CO_2 into the air, so if dry ice has been in a closed room for more than 10 minutes, opens the doors and windows before entering. Otherwise, you will experience difficulty breathing. Leave the area immediately if you start to breathe quickly or have any difficulty breathing.

Specimens shipped with dry ice may be classified as hazardous and thus need secure packaging.

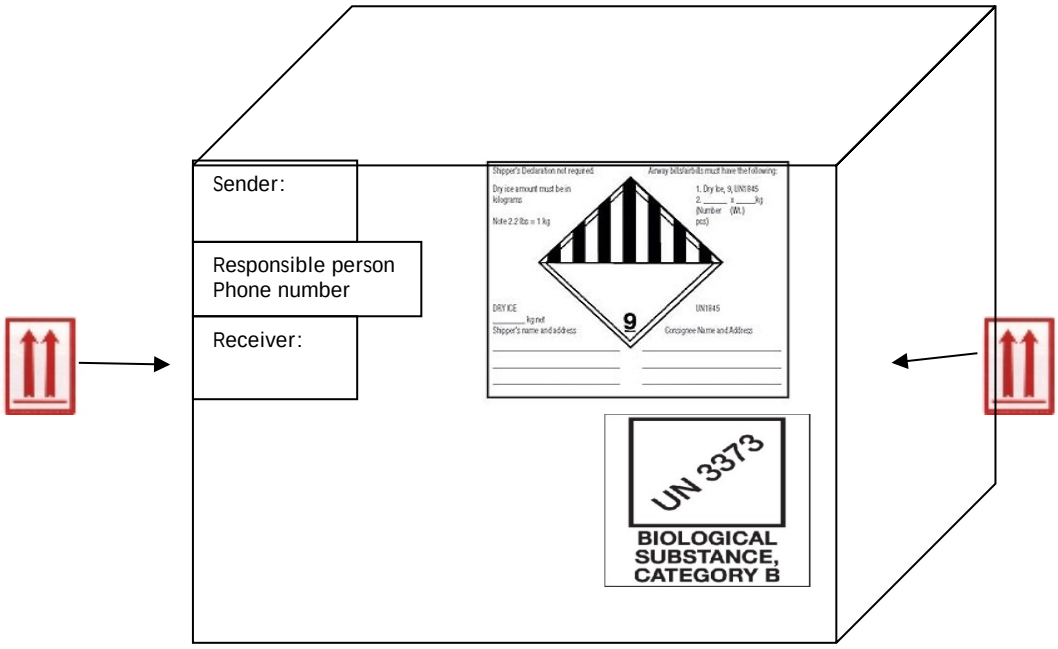
- Do not tape around the edges of the lid of the package containing the dry ice (Styrofoam box)
- Place the dry ice between the outer and secondary container (Styrofoam box and freezing box)
- Secure the primary and secondary container as the dry ice sublimates
- Weight of the dry ice does not exceed 200kgs

5.5. Labeling

Marken will be in charge of labelling the outer container.

The outer container of all diagnostic/clinical specimen packages must display the following on two opposite sides:

- Sender's and Recipient's name and address
- The words "Biological Substance, Category B"
- UN 3373 label
- Up right sign, put on both opposite sides
- Class 9 label, including UN 1845, and net weight if packaged with dry ice



6.0. References

Transport Canada, Transportation of Goods Act (1992) and Regulations (and subsequent amendments). https://laws-lois.justice.gc.ca/eng/acts/T-19.01/page-1.html

Transport Canada: Transportation of dangerous goods in Canada https://tc.canada.ca/en/dangerous-goods/transportation-dangerous-goods-canada

MUHC-RI, SOP011 07 Management of Biological Specimens, 15-May-2017.

Air Transportation Association (IATA) https://www.iata.org/en/programs/cargo/dgr/

7.0 SOP Revision history

SOP code	Effective date	Summary of changes
SOP24	<date>	NA (original version)

Appendix 1- Shipping log for 2R^2 plasma samples.

Log 1- To complete at pick-up:

Site: _____

Shipping to:_____

Sample type (box A or B)	Removed from freezer: Date and time	Packaged: date and time	Is dry ice used?	Pick up on: date and time	Staff preparing shipping	Courier Waybill N:	Comments

Note: all samples are frozen plasma samples for PK study, stored at -80C.

Log 2- To complete when receiving a delivery:

Site: _____

Delivery from:_____

Sample type (box A or B)	Was dry ice used?	Received: Date and time	Was put in freezer: Date and time	Staff receiving shipping	Courier Waybill N:	Comments

Note: all samples are frozen plasma samples for PK study, stored at -80C.