



STEM CELL LABORATORY (STCL)



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Shipping Cryopreserved Cellular Therapy Products to Transplant Centers

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STCL-DIST-006

SHIPPING CRYOPRESERVED CELLULAR THERAPY PRODUCTS TO TRANSPLANT CENTERS

1 PURPOSE

- 1.1 The purpose of this procedure is to describe the steps involved in preparing, packing, and shipping cryopreserved cellular products in a dry shipper that will potentially be used for transplantation/infusion.

2 INTRODUCTION

- 2.1 Cryopreserved products, including peripheral blood progenitor cells, umbilical cord blood, etc., must remain in a frozen state throughout shipment to the transplant facility. Dry shippers are designed for the safe transportation of biological samples at cryogenic temperatures ($\leq -150^{\circ}\text{C}$). Dry shippers employ a hydrophobic compound which absorbs the liquid nitrogen to ensure spill-free shipping. Due to the hydrophobic nature of the absorbent material, it also repels moisture and humidity. This assures maximum holding time and eliminating the necessity to dry units in between uses. A fully charged dry shipper must be capable of holding a minimum temperature of $\leq -150^{\circ}\text{C}$ for a period of 48 hours beyond the expected time of arrival at the receiving facility.
- 2.2 The transplant center receives the cryopreserved product and stores it in vapor or liquid phase of liquid nitrogen until the day of transplant. On the day of transplant, the product is thawed, sometimes washed (at the discretion of the transplant center), and infused. Reactions to infusion within the subsequent 24 hours are scored and reported to the bank. Recoveries of nucleated cells, viable cells, CD34 cells, and CFUs (if applicable) are enumerated at the transplant center and reported back to the laboratory. Sterility cultures of the infused product are also obtained by the transplant center and reported to the laboratory.

3 SCOPE AND RESPONSIBILITIES

- 3.1 It is required that the cryopreserved products must be labeled, contained in a cryo canister, and maintained at all times at temperatures of $\leq -150^{\circ}\text{C}$ in vapor phase or submerged in liquid nitrogen. This procedure outlines the steps for proper packaging and handling of cryopreserved samples shipped for transplant.
- 3.2 The Stem Cell Laboratory Medical Director, Laboratory Manager, Quality Manager, and the participating laboratory staff are responsible for ensuring that the requirements of this procedure are successfully met.

4 DEFINITIONS/ACRONYMS

- | | | |
|-----|--------------------|--|
| 4.1 | STCL | Stem Cell Laboratory |
| 4.2 | $^{\circ}\text{C}$ | Degrees Celsius |
| 4.3 | ISBT | International Society of Blood Transfusion |
| 4.4 | CCBB | Carolinas Cord Blood Bank |

- 4.5 LN2 Liquid Nitrogen
- 4.6 FACT Foundation for the Accreditation of Cellular Therapy
- 4.7 CBU Cord Blood Unit
- 4.8 TC Transplant Center

5 MATERIALS

- 5.1 Liquid Nitrogen
- 5.2 Courier Airway Bill
- 5.3 ISBT Bar code labels (Minimum of 4)
- 5.4 Cryogenic gloves
- 5.5 Goggles or face shield (*as needed*)
- 5.6 Styrofoam retrieval cartridges
- 5.7 Zip ties

6 EQUIPMENT

- 6.1 Validated dry shipper with polystyrene outer container
- 6.2 Calibrated data logger
- 6.3 Cryo-safe container (*if additional samples are requested with shipment*)
- 6.4 Insulated transport cooler, *if additional sample are requested*
- 6.5 ThermoGenesis BioArchive® and retrieval cartridge (*if appropriate*)
- 6.6 LN2 canisters (*needed to house cellular products during transport*)

7 SAFETY

- 7.1 Wear all applicable personal protective equipment when handling potentially infectious blood and body fluids to include, but not limited to, gloves, lab coat, cryogenic gloves, face shield, etc.

8 PROCEDURE

- 8.1 Quality Control
 - 8.1.1 Validated dry shippers will be used to ship cryopreserved products to transplant centers.
 - 8.1.2 The shipping container will be charged to its full capacity. When fully charged, the shipper should maintain a minimum temperature of $\leq -150^{\circ}\text{C}$ for up to 48 hours beyond the expected time it will take for the dry shipper to arrive (*be delivered*) to the transplant facility.
 - 8.1.3 Shipment will be by overnight courier when shipping to remote transplant centers within the United States. Products shipping overseas will arrive by designated international courier.

- 8.1.4 Transplant center staff will be notified of the expected arrival time, courier service, and tracking number for the unit.
- 8.1.5 Two members of the STCL staff must verify the product's ISBT bar code number before shipment.
- 8.1.6 Transplant center staff will notify STCL staff upon arrival of the shipper and provide a faxed copy of the completed *STCL-FORM-058 Receipt of Cellular Products* form.
- 8.2 Confirm that *STCL-FORM-060 Inter-institutional Physician's Agreement Request to Transfer Patient Product* has been completed by the recipient's transplant center physician, the recipient (or by a legal guardian if the recipient is a minor), and a Duke Medicine physician who is affiliated with the recipient and/or the cellular products being requested for shipment outside the Stem Cell Laboratory.
- 8.3 Confirm that a validated dry shipper and data logger are available and provided by the Carolinas Cord Blood Bank (CCBB) or by the transplant facility requesting the shipment of cellular products from the Stem Cell Laboratory.
 - 8.3.1 Inspect dry shipper and all components to ensure that there is no damage that could impact the performance of the dry shipper. Report any issues to the lab manager or designee immediately.
 - 8.3.1.1 Check the shipper for external damage, including dents or cracks.
 - 8.3.1.2 Check that clamps and hinges are secure and inner shipper rack is present and functional.
 - 8.3.1.3 Inspect the shipper seal to make sure it is intact.
 - 8.3.2 The CCBB will prepare the dry shipper a minimum of 24 hours before shipment is scheduled by filling the inner container of the dry shipper with liquid nitrogen to the top of the silver lining. Replace the lid and allow the dry shipper to stand so liquid nitrogen will soak into the absorbent material. Recheck the dry shipper; if the LN₂ has been completely absorbed, top off the shipper with additional LN₂, if necessary.
 - 8.3.2.1 When a charged, validated, empty dry shipper is provided by a domestic transplant center that has requested that the STCL ship cellular products to their facility, the shipper is routinely delivered to the STCL on a designated day and then packed and returned to the transplant center the same day the dry shipper was received so it can be delivered to the TC the following day.
 - 8.3.3 On the day of the product shipment, the CCBB staff will pour off any remaining unabsorbed liquid nitrogen into another empty dry shipper or into the top of a LN₂ freezer.
 - 8.3.4 The CCBB staff will choose a data logger lid to accompany the dry shipper and will program it for use.

- 8.4 In the event that additional sample vials are requested to ship along with the cellular product(s), samples should be removed from their designated storage location using the following steps:
 - 8.4.1 Determine the storage location of the samples from the patient's lab file.
 - 8.4.2 Fill an insulated transport cooler with dry ice.
 - 8.4.3 Obtain a cryo-safe container (box) to hold the samples during transport (*if needed*) and attach an ISBT barcode and record other patient-related information (ie. name, MRN, DOB, etc) to the outside of the sample container (box).
 - 8.4.4 Place the container in a dry ice filled transport cooler.
 - 8.4.5 Retrieve the frozen sample(s) from their designated storage location.
 - 8.4.6 Confirm with a second technologist that the appropriate vials have been retrieved. Confirmation is obtained by one person reading the ISBT barcode and/or other patient-related information on the sample vials aloud while the other person confirms against the information within the requested lab file.
- 8.5 Remove the product(s) requested for shipment from the respective freezer storage location(s). Working in vapor phase, open the product canister(s) and confirm with a second technologist that the proper product(s) has been retrieved.

NOTE: Confirmation is obtained by one person reading the recipient (*and donor, if applicable*) information located on the attached tie tag(s) and the ISBT barcode and letter designation (*if applicable*) on both the tie tag and affixed demand 128 label aloud from the frozen retrieved product(s) while the other person confirms with the information within the requested lab file.
- 8.6 Visually inspect the product(s) to ensure the product is intact and there are no cracks or tears in the bag(s). Notify the laboratory manager, or designee, immediately if any irregularities are seen.
- 8.7 If the product is stored in the ThermoGenesis BioArchive® freezer, retrieve using the following steps:
 - 8.7.1 Insert a Styrofoam retrieval cartridge into a retrieval cassette and place that cassette in either port 1 or 2 of the BioArchive.
 - 8.7.2 Log on to the BioArchive computer.
 - 8.7.3 Click the retrieval icon and scan the ISBT barcode. Allow the BioArchive to retrieve the unit into the cassette.
 - 8.7.4 Remove the unit, within the Styrofoam insert, from the BioArchive and place in vapor phase of another LN₂ freezer.
 - 8.7.5 Working in vapor phase, remove the metal CBU cassette from the Styrofoam insert. Open the cassette, and confirm with a second technologist that the proper ISBT barcode number has been retrieved.

NOTE: Confirmation is obtained by one person reading the ISBT

- barcode aloud from the frozen retrieved CBU while the other person confirms with the information within the requested file.
- 8.7.6 Visually inspect the unit to ensure the product is intact and there are no cracks or tears in the bag. Notify the laboratory manager, or designee, immediately if any irregularities are observed.
 - 8.7.7 Return the CBU to the Styrofoam retrieval cartridge in preparation for shipment.
 - 8.8 Place the requested product(s) in container(s) and any additional samples into the designated dry shipper. Make sure the cellular products (and additional samples, *if applicable*) are **secured tightly** inside the dry shipper so items don't move around during transport.
 - 8.9 Attach the data logger lid to the dry shipper and activate by pressing the "transit" button twice. The word "transit" will appear in the digital display.
 - 8.10 Secure a zip tie to the data logger lid and dry shipper.
 - 8.11 Obtain completed forms (*if applicable*) and copy the following forms to include in the packet of information being provided to the transplant facility and the lab file:
 - 8.11.1 STCL-DIST-006 FRM1 Courier Chain of Custody Form
 - 8.11.2 STCL-DIST-006 FRM2 Adverse Event Reporting Form
 - 8.11.3 STCL-DIST-006 FRM3 Post Thaw Evaluation Worksheet
 - 8.11.4 STCL-FORM-057 Packing Information
 - 8.11.5 STCL-FORM-059 Cellular Product Summary
 - 8.11.6 STCL-FORM-061 Checklist for Shipping Cryopreserved Cellular Products from STCL
 - 8.11.7 STCL-FORM-058 Receipt of Cellular Products
 - 8.11.8 Current thawing procedure for designated products being shipped to TC (*see documents listed in Sections 9.12 – 9.14*)
 - 8.11.9 Circular of Information (*current version*)
 - 8.12 Obtain copies of all source documentation to include: cell counts, viability, sterility, CD34 testing, CFU (if applicable), copy of freezing graph, lot # worksheet, processing worksheet, summary of donor eligibility, etc. to include in the brochure packet.
 - 8.13 Copy and fax *STCL-FORM-057 Packing Information* to the transplant facility that will be receiving the dry shipper and place the original document in the packet of information being provided inside the lid of the dry shipper and the copy into the lab file.
 - 8.14 Seal the packet (envelope) of information and then secure the packet to the inside of the dry shipper lid.
 - 8.15 Close and lock the dry shipper lid and secure with the necessary zip ties.
 - 8.16 Make sure the CCBB dry shipper is labeled with the following information:

- 8.16.1 CCBB-DIST-027 FRM1 Dry Shipper Outer Label for CBU Shipments
- 8.16.2 CCBB-DIST-027 FRM2 Shipper Permanent Address Label
- 8.16.3 CCBB-DIST-027 FRM3 Shipment Delivery Address Form
- 8.16.4 Air bill for the courier company transporting the dry shipper
- 8.17 Place dry shipper inside the STCL so it is ready when the courier arrives on-site. The courier must complete the chain of custody form *STCL-DIST-006 Courier Chain of Custody* prior to release of the shipper. Non Federal Express couriers must also provide the air bill number for shipment to verify with laboratory staff that they are picking up the correct shipment.
- 8.18 Return of the Empty CCBB Dry Shipper
 - 8.18.1 Upon receipt of the empty dry shipper from the transplant center (TC), all couriers labeling information (*i.e., air bill, etc*) is removed.
 - 8.18.2 The information from the data logger will be downloaded and printed by CCBB and a copy provided to the STCL staff to be filed in the respective lab file. A copy of the temperature tracing should also be provided to the transplant center for their records.
- 8.19 Use of Dry Shipper for Transporting Cryopreserved Cellular Products to N92 (or other local site) for Infusion
 - 8.19.1 Ensure *STCL-FORM-056 Cellular Therapy Infusion Request Form* has been signed by a physician.
 - 8.19.2 Confirm that a validated dry shipper and data logger are available from the Carolinas Cord Blood Bank for use by the Stem Cell Laboratory.
 - 8.19.2.1 The CCBB will prepare the dry shipper a minimum of 24 hours before shipment is scheduled by filling the inner container of the dry shipper with liquid nitrogen to the top of the silver lining. Replace the lid and allow the dry shipper to stand so liquid nitrogen will soak into the absorbent material. Recheck the dry shipper; if the LN₂ has been completely absorbed, top off the shipper with additional LN₂, if necessary.
 - 8.19.2.2 On the day of the product shipment or inpatient infusion, the CCBB staff will pour off any remaining unabsorbed liquid nitrogen into another empty dry shipper or into the top of a LN₂ freezer.
 - 8.19.2.3 The CCBB staff will choose a data logger lid to accompany the dry shipper.
 - 8.19.3 Coordinate with the clinical staff on N92 or other designated inpatient location a tentative arrival time so they can prepare for the infusion of cellular products. Call the courier to arrange transportation to N92 or other local infusion site.

- 8.19.4 Identify and remove the cryopreserved cellular product(s) from its designated freezer location.
- 8.19.5 Confirm the recipient/donor tie tag, ISBT barcode and letter designation with a second technologist and initial completion of this step on *STCL-FORM-043 Thawing and Infusion Worksheet* in the freezer check column.
- 8.19.6 Place cryopreserved cellular products into the dry shipper.
- 8.19.7 Replace the data logger lid and activate the logger by pressing the “transit” button twice. The word “transit” will appear in the digital display.
- 8.19.8 Upon completion of the infusion, and return to the STCL, the empty dry shipper will be returned to the CCBB Laboratory and the information from the data logger will be downloaded and printed by CCBB and provided to the STCL so this documentation can be placed in the patient’s lab file.
- 8.20 Use of Dry Shipper for Transporting Cryopreserved Cellular Products to designated manufacturing / production facility associated with protocol-specific study or trial.
 - 8.20.1 When applicable for specific Duke-related protocols, the Stem Cell Laboratory may be required to ship cellular products to a designated manufacturing / production facility where those cells will be manipulated (*ie. expanded, etc*) and later returned to the STCL for infusion to a Duke patient.
 - 8.20.2 Dry shippers, in this instance, will be provided by the study sponsor and the STCL will be required to follow the specific standard operating procedures provided that are associated with that specific protocol; we may also be asked to complete designated forms or documents that should be referenced in the protocol and/or standard operation procedure.

9 RELATED DOCUMENTS/FORMS

- 9.1 Circular of Information (*current version*)
- 9.2 STCL-DIST-006 FRM1 Courier Chain of Custody Form
- 9.3 STCL-DIST-006 FRM2 Adverse Event Reporting Form
- 9.4 STCL-DIST-006 FRM3 Post Thaw Evaluation Worksheet
- 9.5 STCL-FORM-043 Thawing and Infusion Worksheet
- 9.6 STCL-FORM-056 Cellular Therapy Infusion Request Form
- 9.7 STCL-FORM-057 Packing Information
- 9.8 STCL-FORM-058 Receipt of Cellular Products
- 9.9 STCL-FORM-059 Cellular Product Summary

- 9.10 STCL-FORM-060 Inter-institutional Physician's Agreement Request to Transfer Patient Product
- 9.11 STCL-FORM-061 Checklist for Shipping Cryopreserved Cellular Products from STCL
- 9.12 STCL-PROC-021 Thawing of Peripheral Blood Progenitor Cells -PBPCs- or Bone Marrow for Direct Administration
- 9.13 STCL-SOP-028 Procedure for Manually Thawing Umbilical Cord Blood Units Frozen in Two Compartment Bags Using Dextran-Albumin Solution
- 9.14 STCL-SOP-048 Procedure for Thawing Bone Marrow and Peripheral Stem Cells Using Dextran-Albumin Solution

10 REFERENCES

- 10.1 American Association of Blood Banks. Standards for Cellular Therapy Product Services, Current edition.
- 10.2 NetCord-FACT (Foundation for the Accreditation of Cellular Therapy) International Standards for Cord Blood Collection, Processing, and Release for Administration, Current edition.

11 REVISION HISTORY

Revision No.	Author	Description of Change(s)
02	Barbara Waters-Pick	<ul style="list-style-type: none"> • Changed order of the documents listed in Section 8.11 so they were in alphabetical order • Added “(see documents listed in 9.12 – 9.14)” at the end of Section 8.11.8 • Added CCBB document numbers to Sections 8.16.1 thru 8.16.3 • Changed order of the documents listed in Section 9 so they were in alphabetical order • Corrected typos and formatting throughout the document

Signature Manifest**Document Number:** STCL-DIST-006**Revision:** 02**Title:** Shipping Cryopreserved Cellular Therapy Products to Transplant Centers**Effective Date:** 09 Apr 2021

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Management

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Document Release

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