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Procedure: Packaging, Shipment, Receipt & Thawing for EXCEL Study

I. PURPOSE

This SOP details the steps for the packaging, shipment, receipt and thawing of the hematopoietic cell transplant products to a manufacturing facility for preparation of cells for the "A Phase II Pilot Study of Donor-Derived Ex-Vivo Expanded Natural Killer Cell Infusions in Children and Young Adults with High-Risk Acute Myeloid Leukemia Receiving Myeloablative HLA-Haploidentical Hematopoietic Cell Transplant: A Multicenter Pediatric Transplantation and Cellular Therapy Consortium (PTCTC) Study (EXCEL Trial)" patients.

II. SCOPE

All CTL technologists may be involved in this protocol.

III. STATEMENTS/REQUIREMENTS

This procedure applies to the packaging, shipment, receipt and thawing of hematopoietic cell transplant products for patients enrolled on PTCTC Study Number: CEL2001. All Cellular Therapy Laboratory Technologists will follow this procedure. Any exceptions to this policy must be approved by the CTL (Cellular Therapy Lab) Processing Facility Director. Any exceptions that deviate from the study protocol must be approved by the Study PI.

- This procedure is used to support the PTCTC Study Number: CEL2001.
- All study forms are found in the corresponding confidential study binder.
- Always contact the study site manager for any questions or concerns.
- Any deviation that could impact the quality, purity, safety or testing of the study product must be reported to the study site manager.
- Deviations must be reported within 24 hours of discovery.

IV. DEFINITIONS

AABB: Association for the Advancement of Blood & Biotherapies

BMT: Bone Marrow Transplant

CBT: Cell based therapy

CHLA: Children's Hospital Los Angeles

CRF: Case Report Forms

CTL: Cellular Therapy Laboratory

FACT: Foundation for the Accreditation of Cellular Therapy

FDA: Food and Drug Administration

IRB: Institutional Review Board

ISBT: International information standard for coding and labeling of cell therapy products

NCH: Nationwide Children's Hospital

PI: Principal Investigator

RC: Research Coordinator

SOP: Standard Operating Procedure

V. EQUIPMENT/RESOURCES

Hematopoietic Cell Transplant Products

Credo Cube Transport Cooler Shipping Container

Shipping Address Label

Biohazard Bag

Absorbent Pads

'Do Not X-Ray' labels

Courier Shipping Documentation

6 Thermal Isolation Chamber (TIC) panels

1 Vacuum Insulation Panel (VIP) Lid

TempTale™ Ultra Temperature Monitoring device

Aqui-Pak™ Absorbent Pouches

6 bays (Therapak Cat#10316) or equivalent

Liquid-tight Zip-style or sealable specimen bag

Fisherbrand™ Universal All-Purpose Absorbent Pads (Fisher Cat# 19-40-910 or equivalent)

Sufficient Package cushioning (bubble wrap, air pillows, absorbent lab pads, egg crate or packing foam to fill CREDO Cube)

VI. PROCEDURE

A. Product Receipt and Documentation
   i. Whole blood will be collected by the clinical team and transported to CTL for shipment.
   ii. Log the product into the F-001 CTL Activity Log .

B. Packaging
   i. Credo Cube preparation MUST begin >24hrs BEFORE loading as described by EXCEL standards.
      1. Remove panels from the Credo Cube
         a. Place on a storage rack at **room temperature**.
         b. Place horizontally with coolant side down.
            i. Spread out from each other.
            ii. Do not stack more than 2 high as this may hinder temperature transfer.

iii. 

ii. Complete CBT-Form-170 Packing List for Transport of Whole Blood

iii. Check the expiration date on the side of the TempTale™ device and on the inside lP lid of the CREDO shipper.

1. DO NOT USE if it is past the expiration date. Record/confirm the serial number and expiration date on CBT-Form-170.

iv. Verify label on collection bag matches information on form CBT-Form-170.

1. Do not relabel or write on the attached label.

a. In the case of a discrepancy, notify the EXCEL trial coordinator.

i. Original labeler must correct the error.

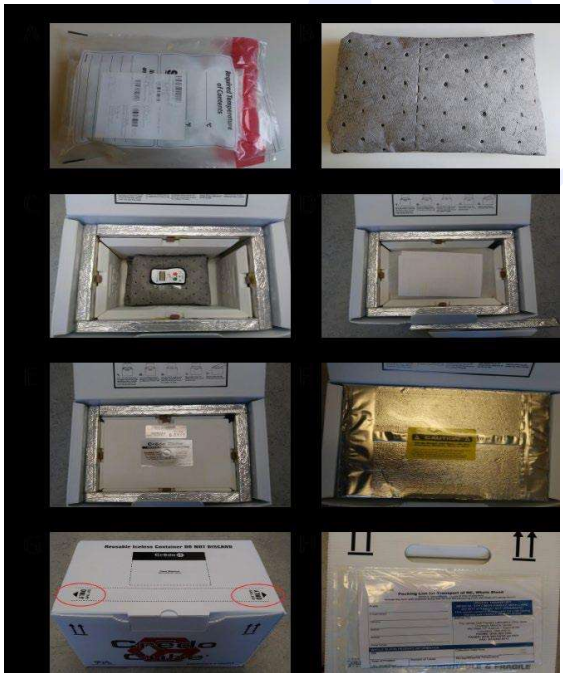
v. Verify that all seals are tight and Insert collection bag at ambient room temperature inside the liquid-tight secondary bag.

vi. Tightly wrap the bag in a universal absorbent material.

vii. Activate the TempTale™ device by pressing and holding the Start button (1- 3 seconds) until the "sunshine" icon appears in the upper left corner of the display.

1. Remove the adhesive strip from the back of the TempTale™ and affix the TempTale™ device face up on the universal absorbent material covering the blood bag.

viii. Place the bag in the CREDO Cube and ensure the bag is surrounded by package cushioning.

ix. 

x. Place CBT-Form-168 NK Cell Manufacturing Form, then the top TIC panel, and then the VIC lid on top of the packaging materials.

xi. Seal CREDO Cube with packing tape as indicated on the outside box. Affix CBT-Form-170 Packing List and CBT-Form-181 Chain of Custody to top of Credo Package.

xii. Log the product out of the F-001 CTL Activity Log

C. Shipping

i. Print and attach FedEx shipping label.

ii. Coordinate Shipment with FedEx as described in EXCEL manual of procedures.

D. Receipt

i. Upon receiving product back from Nationwide Children's Hospital (USC), follow receipt protocol as described in EXCEL manual of procedures. EXCEL Forms CBT-Form-185, CBT-Form-170, and CBT-Form-181 will have been completed by CBT Staff at Nationwide Children's Hospital.

ii. CTL will be notified in advance of delivery and will record the shipment date on the CTL calendar.

iii. CTL will follow all instructions for receipt as described in the most current version of the EXCEL manual of procedures. EXCEL Forms CBT-Form-169, CBT-Form-171, CBT-Form-182, CBT-158 should be included in the shipper received by CTL.

iv. Examine the attached data logger for any alarms or temperature excursions.

1. Any temperature excursions or product integrity deviations will be reported to the CTL Medical Director, CTL QA and to Nationwide Children's Hospital immediately.

a. In the case of a temperature deviation, complete transfer of the product to a functioning LN2 freezer prior to initiating any notifications.

b. The CTL Medical Director and The EXCEL Trial QA Team will decide if the product is suitable or needs to be replaced.

v. Place the IP into a prechilled canister (if necessary) and place into LN2 freezer #23.

1. IP must be stored at <-150 degrees C at all times.

2. Limit the time outside of the freezer during product inspection.

a. If the time will exceed 1 minute, hold IP at the vapor phase of Freezer #12 and verify IP there.

vi. F-004 Cryopreserved Product Receipt Checklist will be filled out at the time of unpacking of the LN2 dry shipper.

1. This form will be kept in the recipients CTL chart.

vii. Complete the EXCEL Forms CBT-Form-169, CBT-Form-171, and CBT-Form-182. Upon completion of these, email scanned copies of the completed forms to Shane.Wellman@nationwidechildrens.org

1. Keep originals in the patient's chart.

viii. Log the product into the F-001 CTL Activity Log

E. Thawing

i. The protocol states that IP infusions will take place on Day -1, Day +7, and Day +42.

1. Add this schedule to the CTL calendar.

a. Official dates and times for IP infusions will be set by the Riley coordinator or clinical team.

2. Bone marrow collection and infusion will be Day 0.

3. Written orders must be received for all infusions.

ii. CTL will only be responsible for thawing the received product as described in EXCEL manual of procedures.

1. Prepare a LN2 dry shipper and water bath as described in Procedure Infusion of Cryopreserved Products .
    a. IP will be thawed in saline at 37 degrees C.
2. Fill out the CH-2046 per Procedure Infusion of Cryopreserved Products .
    a. Not all fields will be applicable to this IP.
    b. Ensure that any study specific identifiers are included on the CH-2046.
    c. Have a second technologist verify the CH-2046 Infusion of Hematopoeitic Progenitor Cells before proceeding.
3. Order in Cerner per Procedure Infusion of Cryopreserved Products.
    a. Not all fields will be applicable to this IP.
    b. Ensure that any necessary study specific identifiers are included on in the order.
    c. Have a second technologist verify the Cerner order before proceeding.
4. IP should be stored in <-150 degrees C. When ready for thawing, IP will be thawed in saline at 37 degrees C.
5. The patient's armband will be compared to the CH-2046 by two qualified team members per Procedure Infusion of Cryopreserved Products .
6. The product label will be read against the CH-2046 at the bedside by two qualified team members.
    a. Any discrepancies between the patient armband and the IP label will be reported to the CTL Medical Director, CTL QA and the EXCEL Trial QA Team prior to thawing the product.
7. Prior to and during thawing inspect the IP bag for cracks and leaking.
    a. Product integrity deviations will be reported to the CTL Medical Director, CTL QA and to Nationwide Children's Hospital immediately.
    b. The CTL Medical Director and the EXCEL Trial QA Team will decide how to proceed.
8. Document the water bath temperature, thaw start, and thaw stop times on the F-045 LN2 Shipper and Water Bath QC.
9. Once the IP is thawed, hand it off to the infusion nurse.

F. Billing

i. Billing will be placed on the encounter corresponding with the patient's infusion day in Cerner.

1. Bill for SC Thaw only.

VII. CLINICAL SIGNIFICANCE/SPECIAL CONSIDERATIONS

The experimental product described in this protocol will be given to subjects with unmet medical needs for which there are no effective therapies known.

VIII. REFERENCES

AABB Standards for Cellular Therapy Product Services, current edition.

FDA CFR Title 21, Part 1271 Human Cells, Tissues and Cellular and Tissue Based Products FACT Standards, current edition.

A Phase II Pilot Study of Donor-Derived Ex-Vivo Expanded Natural Killer Cell Infusions in Children and Young Adults with High-Risk Acute Myeloid Leukemia Receiving Myeloablative HLA Haploidentical Hematopoietic Cell Transplant: A Multicenter Pediatric Transplantation and Cellular Therapy Consortium (PTCTC) Study (EXCEL Trial) PTCTC CT2001 - (EXCEL MOP, current edition)

IX. FORMS/APPENDICES

CBT-Form-168: NK Cell Manufacturing Form

CBT-Form-181: Whole Blood Product Chain of Custody

CBT-Form-170: Packing List for Whole Blood Products

CBT-Form-183: Credo Cube Conditioning, Assembly and Shipping Checklist

CBT-Form-169: Packing List for NK Cells

CBT-Form-171: Receipt of Final NK Cell Product Checklist

CBT-Form-182: NK Cell Product Chain of Custody

CBT-Form-158: Cryopreserved NK Cell Certificate of Analysis

CBT-Form-185: Receipt of Whole Blood Product Checklist

F-001 CTL Activity Log

F-004 Cryopreserved Product Receipt Checklist

F-045 LN2 Shipper and Water Bath QC

CH-2046 Infusion of Hematopoeitic Progenitor Cells

X. APPROVAL BODIES

None

Procedure#

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