LEUKAPHERESIS AND CLBR001 DRUG PRODUCT MANUAL

Protocol: CBR-sCAR461-3001

A Phase 1, Open-Label, Dose-Escalation Study Evaluating the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of the Combination of CLBR001, an Engineered Autologous T Cell Product, and ABBV-461, an Antibody-Based Biologic, in Subjects with Locally Advanced or Metastatic Breast Cancer

Investigational Product: CLBR001

Version 5.0

Date: 28-OCT-2025

Sponsor: Calibr-Skaggs Institute for Innovative Medicines
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Leukapheresis and CLBR001 Drug Product Manual Approval

Print Name	Title	Signature	Date
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Version 1.0	17-DEC-2024	Original
Version 2.0	07-FEB-2025	Updated Minaris Forms
Version 3.0	26-FEB-2025	Updated Appendix Images
Version 4.0	06-AUG-2025	Added Language about Flush after CLBR001 administration; removed protocol required pause during CLBR001 administration; updated leukapheresis label information; added language regarding WBC on leukapheresis product; removed appendices and incorporated info into manual; general updates throughout manual
Version 5.0	28-OCT-2025	Updated Sponsor Contact email address; added Nanocool guidance

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1. INTRODUCTION

The purpose of this manual is to provide supportive information on the leukapheresis procedure and the handling and traceability of the CLBR001 drug product. This manual is a working document that should serve as a reference over the course of the study; updates will be generated in the event procedures are modified.

Unless specifically noted in this manual for study specific processes and the protocol, site should follow institutional standard operating procedures. In the event site process does not align with study-specific processes in this manual, please contact Sponsor.

2. DRUG PRODUCT TRACEABILITY

Traceability is defined as the documentation and management of activities to support the collective tracking, and control of a subject's autologous cells and CLBR001 product. Per regulations, adequate chain of custody will be ensured from procurement of the cells, through manufacturing, testing and storage, to infusion and/or disposal.

Study- specific traceability processes have been developed with defined steps to be followed in conjunction with existing site-specific or institutional procedures.

All study developed checklists, tools and forms used in these processes must be maintained with the subject study record. Copies should be provided to Calibr-Skaggs team as they are completed by using the Clinical Shared Inbox: sCAR461Clinical@scripps.edu. Copies should be provided to Calibr-Skaggs team as they are completed. **Mandatory** forms that are required to be completed to document traceability and process are listed:

- ☐ **A-01 Leukapheresis Chain of Custody Form:** to be printed by site staff for each subject apheresis; copy to be sent with apheresis shipment, copy emailed to Calibr-Skaggs team at email address above, and original with Subject source; will be used to verify CLBR001 Drug Product receipt, so ensure team receiving CLBR001 also receives a copy.
- ☐ **A-02 CLBR001 Drug Product Chain of Custody Form:** to be printed by site staff for each CLBR001 delivery. Copy to be emailed to Calibr-Skaggs team at email address above after Part 1 is completed, and then again after Parts 2 and 3 are completed; original to stay with subject source.
- ☐ **Leukapheresis Checklist**: Not required to be sent to Calibr-Skaggs team but should be made available in subject source for CRA review.
- ☐ **CLBR001 Drug Product Checklist:** Not required to be sent to Calibr-Skaggs team but should be made available in subject source for CRA review.
- ☐ **Minaris Form: Authorization for Shipment of Final Product:** will be sent to site with each CLBR001 shipment; site must complete section 3 of form and send to Minaris at email address on form, as well as Calibr-Skaggs team at email address above.
- ☐ **Minaris Form: QA Release of Final Product:** will be sent to site with each CLBR001 shipment; Must be maintained with subject's CLBR001 records.
- ☐ **Subject Traceability Procedure Form:** to be used by site staff as a guide through vein to vein process; not required to be sent to Calibr-Skaggs team.
- ☐ **CLBR001 Accountability Log:** mandatory to be completed upon receipt and to document final disposition of CLBR001; form should be placed in subject source for CRA review and verification.
- ☐ **CLBR001 Final Product Thawing and Infusion Documentation:** optional if all data points are documented elsewhere in subject source.
- ☐ **Cohort and Dose Assignment Form:** site will receive this form prior to administration of CLBR001. Form will detail subject Cohort Assignment, the CLBR001 Lot number, CLBR001 dose the subject will receive as well as the Priming and Full dose of ABBV-461.

Form should be shared with all relevant site staff (Pharmacy, Cellular Therapy, Nursing) for verification purposes and filed in subject source.

Drug product accountability and traceability is ultimately the responsibility of the Investigator. However, individual tasks may be delegated to a suitably qualified individual who has had appropriate study-specific training and whose name has been appropriately listed on a delegation of responsibility log for such tasks.

3. STUDY-RELATED CONTACTS

Leukapheresis and procedures related to the handling of the CLBR001 drug product will require coordination of efforts and resources between the site and multiple other parties. The non-site groups involved are defined:

Calibr-Skaggs is the Sponsor of the trial and will also manage all clinical aspects of the patient journey while on trial. The Calibr-Skaggs Clinical Trial Manager (CTM) will communicate with the site team each step of trial processes with all involved groups, including confirming availability of slots at the drug product manufacturing facility. The Calibr-Skaggs CTM will work closely with the Premier Research Logistics Manager (LM) to coordinate the vein-to-vein process.

Premier Research is the Sponsor-designated contract research organization (CRO) for Logistics Management of all CLBR001 Logistics. The Premier Research Logistics Manager (LM) will work with the Calibr-Skaggs CTM to communicate each step of the processes with all involved groups, including to coordinate the scheduling of study subject leukapheresis procedure including the same-day pick-up of the leukapheresis product via specialty courier or equivalent shipping and logistics vendor. Premier Research LM will also coordinate the timing of subsequent CLBR001 delivery from the manufacturing facility to the site and the subsequent initiation of study treatment. Given the time-sensitive and critical nature of the collection of leukapheresis cells, shipment of leukapheresis cells to Minaris, development of CLBR001 cell product, shipment of CLBR001 cell product to the site, and ultimately the administration of CLBR001 cell product to the subject, the Premier Research Logistics Manager will work with sites on a regular/ daily basis to track successful completion of all steps of the process.

IMPORTANT: All correspondence to Calibr-Skaggs team, including the Premier Research Logistics Manager should include the clinical inbox: sCAR461Clinical@scripps.edu. Sites should cc their CRA on all correspondence as well.

Minaris is the designated GMP cell manufacturing facility – also known as a contract manufacturing organization (CMO) - for the CLBR001 drug product. They will receive the leukapheresis product from the site via arranged courier, manufacture and complete release testing of CLBR001 drug product, and upon approval for release, prepare the CLBR001 drug product for shipment to the site. All Minaris communications are done through the Premier Logistics Manager.

Cryoport is designated to manage the transport of the **leukapheresis product from the clinical site to the GMP manufacturing facility (Minaris).** This includes delivery of a Temperature Controlled 2-8°C Shipper to the site and pick-up of the leukapheresis product from the site for delivery to the manufacturing facility. Depending on the specific logistics of your site and location, the courier may be FedEx, Cryoport, or another specialty courier. Your site will be notified by the Premier Logistics Manager as to which courier will be performing each delivery and pick up. Generally, the shipper will be a C3 shipper and will be delivered pre-conditioned to the site the day prior to leukapheresis. The leukapheresis product generally must be packed and available

for same day pick up by the courier and will be delivered the morning following leukapheresis to Minaris. All Cryoport communications are done through the Premier Logistics Manager.

Cryoport is also designated to organize the transport of the **cryopreserved CLBR001 drug product from Minaris to the site** using a cryogenic shipping container (such as a Dry LN_2 shipper) supplied by Cryoport. This drug product manual includes instructions on returning the cryogenic shipping container to Cryoport after the site has retrieved the drug product and placed it into local LN_2 storage. A courier will be contracted to perform the delivery and pick up of the LN_2 Dry Shipper. Depending on the specific logistics of your site and location, the courier may be FedEx, Cryoport, World Courier or another specialty courier. Your site will be notified by the Premier Logistics Manager as to which courier will be performing each delivery and pick up. All Cryoport communications are done through the Premier Logistics Manager.

4. LEUKAPHERESIS

Once a potential subject is identified for study participation, site should follow the process outlined in the Subject Traceability Procedure document to secure a slot and move through screening and eligibility (**Subject Traceability Procedure Timepoints #1-3**). When in doubt, site should contact the Calibr-Skaggs team at sCAR461Clinical@scripps.edu with any questions or concerns about slots or subject eligibility.

Leukapheresis may not be initiated until subject eligibility approval has been provided to the site in writing (**Subject Traceability Procedure Timepoint #5).**

Leukapheresis should be scheduled at the site once a patient has been granted a specific manufacturing slot; manufacturing slot dates are typically not flexible. Manufacturing initiation at Minaris will generally occur on Thursdays (the morning following leukapheresis procedure), meaning that Leukapheresis will typically be required to be scheduled on a Wednesday morning, with pick up by the courier for same day shipping at 2pm. There may be instances of a different schedule; in this instance, the CTM and Logistics Manager will work with the site on ensuring a smooth process. Site should remain in close communication with the Calibr-Skaggs team regarding scheduling and patient enrollment leading up to a subject's scheduled leukapheresis.

Premier Research Logistics Manager will coordinate this with the site and Cryoport (typically at least five (5) business days prior to scheduled leukapheresis).

4.1 C3 Shipper Receipt at Site

Also referred to as Subject Traceability Procedure Timepoint #6

It is preferred that the Temperature Controlled shipper (C3 shipper or similar; 2-8°C) arrives the day prior to Leukapheresis. On rare occasions, the Temperature Controlled shipper (C3 shipper or similar; 2-8°C) may be scheduled to arrive the morning of leukapheresis or earlier than the day prior to leukapheresis. If either of these exceptions must occur, the Sponsor/CRO team will provide the site with instructions to ensure appropriate shipper temperature management.

When the Temperature Controlled Shipper (C3 shipper or similar; 2-8°C) is received by the site, keep shipper box lid closed to maintain temperature until ready to load leukapheresis product.

The site must email Calibr-Skaggs team at sCAR461Clinical@scripps.edu to confirm receipt of the shipper. Leukapheresis should not begin until site has confirmed shipper is on site.

The Temperature Controlled Shipper (C3 shipper or similar), will come to site with the following items:

- An absorbent sock
- Temperature and GPS tracker, SmartPak II- no action needed from site staff as tracker is already on and collecting data

Image 1. SmartPakII; device will vary in color and is embedded in lining of shipper

Image 2. C3 shipper; GTC 4L insulated box with 6 pre-conditioned cold packs lining the walls

4.1.1 NanoCool

Sites will be shipped a study specific NanoCool shipper upon activation. NanoCool is a contingency plan in the event there is an issue with the C3 shipper. No action is necessary upon receipt of NanoCool, except to store. If a NanoCool needs to be utilized, the Calibr-Skaggs team will provide specific guidance to sites. There is also a NanoCool guidance document at the end of this manual.

4.2 Leukapheresis Procedure

Also referred to as Subject Traceability Procedure Timepoint #7.

Forms for this timepoint:

- ☐ (1) CBR-sCAR461-3001 Leukapheresis Study Specific Product Labels
- ☐ (2) CBR-sCAR461-3001 Leukapheresis Checklist

- ☐ (3) Leukapheresis Chain of Custody Form A-01 *(copy of form to be included with leukapheresis product shipped to Minaris)*
- ☐ (4) Subject Traceability Procedure Form
- ☐ (5) Shipping Airway Bills

Leukapheresis must be performed per this manual and site leukapheresis standard procedures. If site-specific processes for leukapheresis differ from guidance provided in this manual then a discussion with the Sponsor is required prior to proceeding. Early morning Leukapheresis required to meet same day 2:00 pm product pick up time.

Site staff should confirm temperature-controlled shipper is on site PRIOR to the start of Leukapheresis. Leukapheresis should not begin without shipper on site. Please contact the Calibr-Skaggs team at sCAR461Clinical@scripps.edu if there are concerns over the shipper.

1. Set up the apheresis machine according to the clinical site's SOPs
2. Label the leukapheresis collection bag (see **Section 4.3** for details)
3. Start the leukapheresis procedure and document the collection date and the collection start time in subject source, **Leukapheresis Checklist**, and the **A-01 Leukapheresis Chain of Custody Form**.
4. Collect enough volume to ensure a minimum total nucleated cell count of 2.0×10^9 from a single leukapheresis session. Leukapheresis target collection volume is 2.0-3.0 Total Blood Volume.
5. Autologous plasma is added back (approximately 150mL) to the leukapheresis cells.
6. A blood sample must be collected from the leukapheresis product. This may be done before or after the plasma is added, as long as the total cell count represents the post plasma addition.
7. Document the collection end time and the leukapheresis volume (mL), verify autologous plasma was added (approximately 150mL) and the type and volume (mL) of the anticoagulant used.
8. Complete the remaining information required on the Leukapheresis label(s) and on **Form A-01 Leukapheresis Chain of Custody Form**.
9. Verify the label contents to ensure the accuracy of the recorded information on **Leukapheresis Labels**, **Leukapheresis Checklist** and **Form A-01 Leukapheresis Chain of Custody Form**. Document that the verification process was performed on **Form A-01 Leukapheresis Chain of Custody Form**.
10. A white blood cell count with differential should be drawn on the final product and a copy of DE-IDENTIFIED results must be sent to the Calibr-Skaggs team with the **A-01 Form** at sCAR461Clinical@scripps.edu (or as soon as resulted).
11. If applicable, document transfer of leukapheresis product from the apheresis unit to the site cellular therapy laboratory on **Form A-01 Leukapheresis Chain of Custody Form**. Sign any site-specific logbooks. If leukapheresis product is not transferred to the cellular therapy laboratory prior to shipment to the manufacturing facility, please indicate 'N/A' in the final section of Form A-01. Failure to complete this step can result in a delay in processing receipt of the apheresis product at the manufacturing facility.
12. Complete the **Form A-01 Leukapheresis Chain of Custody Form.** Place a copy of this form with the shipment and place the original in the subject's study files.
13. Attach a copy of the de-identified WBC and differential results to **Form A-01 Leukapheresis Chain of Custody Form**. Email the results and the A-01 Form to the Calibr-Skaggs team at sCAR461Clinical@scripps.edu and file in site files.
14. Have airway bill (previously provided by Logistics Manager) ready prior to scheduled arrival of specialty courier.

15. Place the leukapheresis product into the Temperature Controlled Shipper (2-8°C). See additional packing instructions in **Section 4.4.1** of this Manual.
16. Document the time when the product is packed in the shipping container on the Leukapheresis Checklist.
17. Place a copy of **Form A-01 Leukapheresis Chain of Custody Form** on top of the insulation under the top box flap and close/seal box. Additional packing instructions can be found in **Section 4.4.1** of this Manual.
18. Close the box and seal the shipper. Document date and time of pick-up by specialty courier.
19. Original **Form A-01 Leukapheresis Chain of Custody Form** to be kept with subject's source records at site; A copy should be made for the cell therapy lab staff for their files, and a second to the Site Study Coordinator for inclusion in subject's study files. Please also scan and send a copy to the Calibr-Skaggs team at sCAR461Clinical@scripps.edu. This form will be used by site staff to verify CLBR001 shipment upon site delivery, so please also ensure the CLBR001 receiving team receives a copy if different from above.

4.3 Labeling the Leukapheresis Collection Bag

A study-specific leukapheresis label is required on the leukapheresis product and will be provided to the sites by the Sponsor. This study-specific label should be affixed to the collection bag prior to the start of collection and will require the following information to be placed on the label at the appropriate point during leukapheresis procedure:

Prior to Start of Leukapheresis	• Subject ID in the format of: sCAR461 - 2 # # - # # **Study ID - Site ID - Subject ID** • Subject initials (NNN) • Subject weight (##.# kg; e.g., 74.6 kg) • Collection Date (dd/mmm/yyyy)
After Completion of Leukapheresis Procedure	• Collection End Time (24h format) • Leukapheresis Volume (mL)
* Do not include protected health information such as subject's full name or hospital number on the apheresis product sent to the manufacturing facility (Minaris). Additional site-specific information may be added to the collection bag (same or opposite side as study label) as necessary but must not obscure any information on the label(s) and no PHI other than subject DOB and initials may be on the label when product is shipped to Minaris.	

4.4 Leukapheresis Product Packaging, Handling, and Shipping

Premier Research Logistics Manager will be in close contact with site team regarding shipping logistics and will ensure copies of airway bills are available to site staff prior to shipping.

Beginning in January 2026, Cryoport will send instructions for shipments which will be accessible via QR codes placed on the enclosure placard and shipment envelopes in each shipment. The QR codes will link directly to product-specific landing pages, where site staff can download the most current instruction PDFs and view step by step instructional videos.

4.4.1 Packing and Shipping Leukapheresis Collection Bag

When the leukapheresis visit is scheduled, Premier Research Logistics Manager will reach out to arrange shipment of Temperature Controlled Shipper (C3 shipper or similar) to site. Once orders are submitted, Premier Research Logistics Manager will send site the airway bill for the outgoing shipment. Please print this as it will need to be provided to the courier with the outbound leukapheresis product shipment. If there are any questions or you need a new airway bill, please contact the Calibr-Skaggs team directly sCAR461Clinical@scripps.edu.

The Premier Research Logistics Manager will coordinate and schedule the pick-up of leukapheresis product by a specialty courier for the same day as the leukapheresis procedure. This pick-up will be arranged at least five (5) business days in advance when feasible.

Upon completion of leukapheresis process, collected product must immediately be packaged for shipping in the Temperature Controlled Shipper (C3 or similar; 2-8°C). In the event there is a delay in packaging, the leukapheresis product can be held at room temperature (10-25°C) up to a maximum of 4 hours from the end of collection. Please notify the Premier Research Logistics Manager at (sCAR461Clinical@scripps.edu) as soon as possible should a delay occur.

CLBR001 manufacturing process is initiated the morning following leukapheresis using fresh (not frozen) apheresis product. Therefore, leukapheresis product must be picked up from the site by the courier **on the same day that it was collected, as scheduled and communicated to the site** (typically at 2pm).

1. Place leukapheresis bag inside of the absorbent sock. An additional wrap or bag, such a biohazard bag may be used but not required or supplied

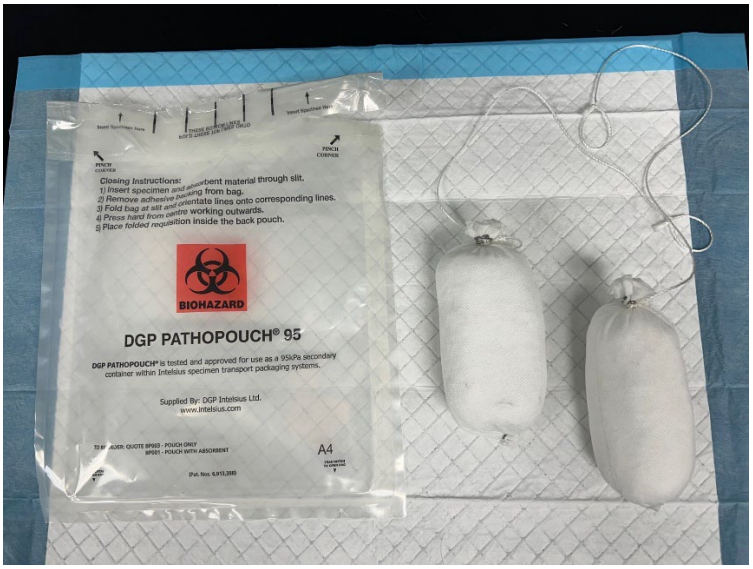

Image 3. Packing supplies for the Leukapheresis Collection Bag

2. Place the packaged leukapheresis bag into the box:

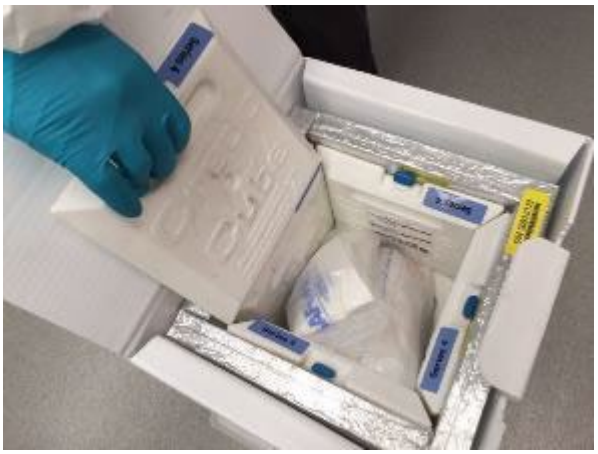

Image 4. Inside of the C3 shipper once leukapheresis bag has been placed in box

3. Place Form A-01 on top of insulation under top lid of box.
4. Close box and seal outer box.
5. Hand airway bill to courier who will attach to box

Image 5. C3 shipper packed up

5. CLBR001 DRUG PRODUCT INFORMATION

The CLBR001 drug product is an engineered autologous CAR-T cell product.

The process to produce the drug product begins with leukapheresis of the enrolled subject and ends with a final product that comprises the subject's T cells transduced with a "switchable" chimeric antigen receptor (CLBR001 cell product).

Following release testing and release authorization, the CLBR001 drug product is shipped frozen in a liquid nitrogen LN2 dry shipper from the manufacturing facility to the study site.

The CLBR001 drug product is subject-specific and supplied cryopreserved in cryostorage infusion bags. The final product bag will be frozen inside a protective aluminum cassette. Following release testing and release authorization, the CLBR001 drug product is shipped frozen in a liquid nitrogen LN_2 Dry shipper from the manufacturing facility to the study site. The CLBR001 drug product is typically shipped back to site approximately 21-28 days after leukapheresis product was received by Minaris.

Site will receive the **Cohort and Dose Assignment Form**, which will detail the cohort the subject is assigned, the Lot number of CLBR001, as well as the dose of CLBR001 to be given to subject. Usually, site staff will receive this form prior to CLBR001 delivery, however in some cases (i.e. awaiting Cohort Review Committee outcomes, etc.) it may come after the delivery of CLBR001.

Upon receipt at the site, the subject-specific CLBR001 must be stored in vapor phase of liquid nitrogen cryotank in a secure, limited-access location. Each infusion bag will have affixed to it a label containing the following: **"FOR AUTOLOGOUS USE ONLY. NOT EVALUATED FOR INFECTIOUS SUBSTANCES"**. CLBR001 Labels will include study number (CBR-sCAR461-3001), subject initials, subject ID and Lot number.

When frozen, CLBR001 drug product will appear slightly opaque. After thawing, the product will be a slightly turbid suspension.

The product must remain frozen until the subject is ready for treatment to assure viable live autologous cells are administered to the subject.

Please refer to the **Investigator's Brochure** and to the Study Protocol **CBR-sCAR461-3001** for additional details on CLBR001 handling, administration and management.

5.1 CLBR001 Site Receipt, Storage and Accountability

Forms for this section:

- ☐ **(1) Drug Product Chain of Custody Form A-02, Part 1**
- ☐ **(2) CLBR001 Drug Product Checklist, Section 1**
- ☐ **(3) CLBR001 Accountability Log**
- ☐ **(4) Minaris Form: Authorization for Shipment of Final Product, Part 3**
- ☐ **(5) Certificate of Analysis**
- ☐ **(6) Subject's Leukapheresis Chain of Custody Form A-01** (for verification)
- ☐ **(7) Minaris Form: QA Release of Final Product**

The CLBR001 drug product is shipped in a cryogenic shipping container to the predetermined contact at the site's cellular therapy laboratory. The drug product will arrive in a large dry liquid nitrogen LN_2 vapor shipper with an **Authorization for Shipment of Final Product Form, QA Release of Final Product Form and Certificate of Analysis**. The CLBR001 drug product will be located inside an aluminum cassette held within a cassette rack in the LN_2 Dry Shipper. The full CLBR001 drug product label is attached/located on the outside of the metal cassette as well as the product infusion bag.

If site-specific processes for Cellular Therapy processes differ from guidance provided in this manual discussion with the Sponsor is required.

5.1.1 Receipt of CLBR001 in Cryoshipper from Cryoport

Also referred to as Subject Traceability Procedure Timepoint #13

Do not remove CLBR001 from shipper until the instructions below have been read in their entirety. Extreme caution to prevent and minimize thawing of CLBR001 during handling.

1. Receive and inspect the cryogenic shipper to ensure no visible damage. Document receipt of product and package integrity by completing Section 3 **of Authorization for Shipment of Final Product Form** which came in shipment as well as Part 1 of **Form A-02: CLBR001 Drug Product Chain of Custody Form**. Email a copy of the completed forms to the Calibr-Skaggs team at sCAR461Clinical@scripps.edu.

   If ANY visible damage to the outer shipping container is present, please take pictures of all damaged areas for reference and submit to the Calibr-Skaggs team along with the completed **A-02 Form** at sCAR461Clinical@scripps.edu.

2. If not provided via a notification via Cryoport at time of delivery, ensure a copy of the temperature summary report is obtained from Premier Research Logistics Manager. The temperature summary report must be maintained with all paperwork associated with the shipment of CLBR001 drug product specific to each subject.

5.1.2 Transfer and Storage of CLBR001 Drug Product

The transfer of CLBR001 drug product from Dry shipper to Cellular Therapy Lab Cryostorage should occur within 1 business day of receipt. Transfer the CLBR001 drug product from the LN_2 Dry Shipper as follows:

1. Open the shipper only when ready to transfer the product to the cell therapy lab's cryostorage tanks. This should occur within 1 business day of receipt.
2. Open the outer packaging shell by cutting zip ties and unlatching both sides by pulling black handles down and away from shipper (see image 6 below). Open lid to expose the dewar. With gloved hands, pull up on the circular handle in the center of the vapor plug and remove the vapor plug. Set vapor plug aside (see image 7 below).
3. Locate and remove the transport sleeve to extract the aluminum cassette containing the product. Do not thaw until ready to infuse. Per Internal Site Policy, site may gently open the cassette to verify bag integrity and label information upon receipt, but bag should not be removed from cassette until ready to thaw.

4. Using two independent reviewers, verify information between **Form A-01 Leukapheresis Chain of Custody** *(at site)* and **Authorization for Shipment of Final Product Form** *(received with shipment)*
5. Confirm that information on the label on the cassette matches the **Authorization for Shipment Form.**
6. Email completed **Authorization for Shipment of Final Product** to the Minaris email indicated at the bottom of form and cc: sCAR461Clinical@scripps.edu
7. Store the CLBR001 drug product bag in the vapor phase of liquid nitrogen according to standard practice at the clinical site. The drug product bag should remain within the provided aluminum cassette or other protective container. Document the storage location and date/time.
8. Complete the Part 1 of **Form A-02 CLBR001 Drug Product Chain of Custody.** Email a copy of the form to the Calibr-Skaggs team at **sCAR461Clinical@scripps.edu**
9. File the completed **Authorization for Shipment of Final Product Form** and **Form A-02 Drug Product Chain of Custody** in the subject's study files.

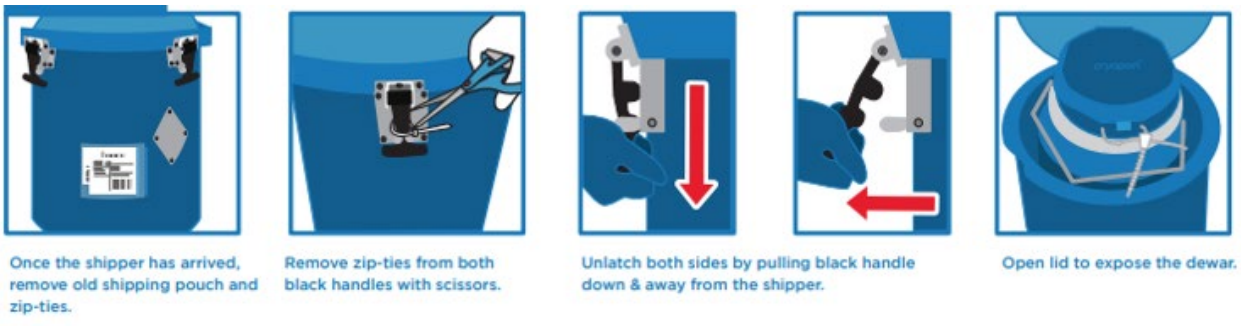

Image 6. Instructions on how to open Dry Shipper

Image 7. Vapor Plug instructions

Image 8 series. Remove cassette holder

Cassette dimensions and specifications

Dimensions
Width: 3.5 INCHES (50mL bag) / 6 INCHES (250mL bag)
Height: 6 INCHES (50mL bag) / 7.5 inches (250mL bag)
thickness: 0.44 INCHES (50mL & 250mL bags)

CANISTER, ALUMINUM, FOR CRYOMACS 200-074-400 (50mL bag), & CHARTERMED CF-250 (250ML bag)

Image 9. Cassette dimensions

5.2 Return of the Cryoshipper/ Dry Shipper

Within 1-2 business days after transferring the CLBR001 Drug Product from the LN_2 Dry Shipper into cellular therapy laboratory cryostorage tanks, prepare the LN_2 Dry Shipper for return to the vendor. See below for details on packing up shipper for return:

1. Return the cassette holder to the dry shipper

Image 10. Return cassette rack into dry shipper

2. Replace the vapor plug (see step 1 below)
3. Close the hinged cap by pulling down on the lid (see step 2 below)
4. Secure the hinged cap with a zip tie (see step 3 below)
5. Remove the Leg 3 shipping pouch from the document protector attached to the dewar handle inside of the container (see step 4 below)
6. Remove the EMPTY label from the shipping pouch and place on the metal diamond (see step 5 below)

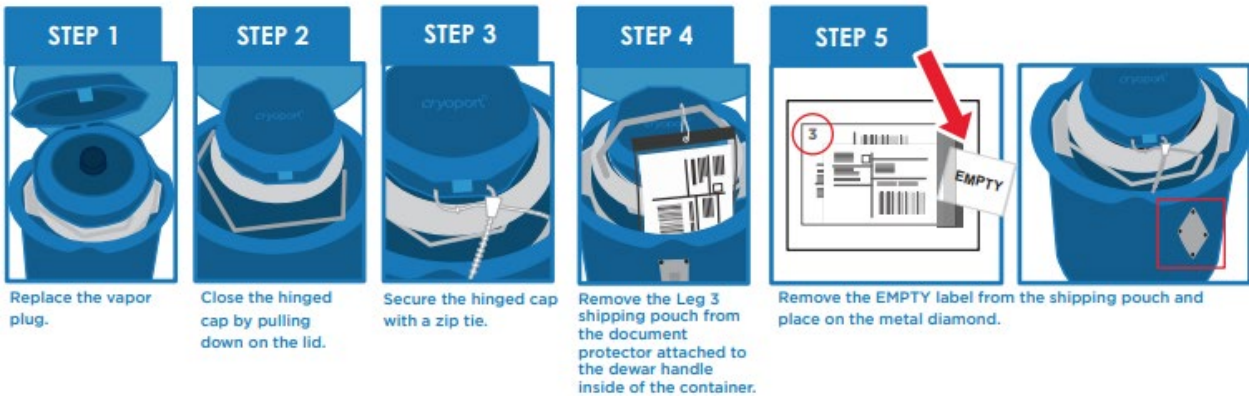

Image 11. Steps to packing up Dry Shipper

7. Place in Fed-Ex pick-up location
8. Questions contact the Calibr-Skaggs team at sCAR461Clinical@scripps.edu.

5.3 CLBR001 Transfer and Thawing of CLBR001 Drug Product

Also known as Subject Traceability Procedure Timepoint #15.

Forms for this section:

- ☐ **(1) Drug Product Chain of Custody Form A-02, Parts 2 and 3**
- ☐ **(2) CLBR001 Drug Product Checklist, Section 2**
- ☐ **(3) CLBR001 Final Product Thawing and Infusion Documentation** *(Optional if documented in subject medical records)*
- ☐ **(4) CLBR001 Accountability Log**

Prior to CLBR001 dosing, Investigator/site should complete protocol-required procedures, review subject and confirm the subject meets CLBR001 administration eligibility criteria. Completion of **CBR-sCAR461-3001 Checklist-CLBR001** is required to be completed and filed in site source. This checklist does NOT need to be sent to the Calibr-Skaggs team for review as long as subject meets eligibility per checklist.

5.3.1 Transfer to Patient bedside

1. Document name of person giving authorization (e.g., the PI or Sub-I) and the date authorization given.

2. Prepare CLBR001 drug product for transport. **Do not remove outer cassette until ready to thaw.** Confirm the Study Subject's information on the CLBR001 drug product matches Form A-02 CLBR001 Drug Product Chain of Custody Form.

3. Document the time of removal from LN2 storage and complete, sign, and date the appropriate fields under the **Part 2** of **Form A-02 CLBR001 Drug Product Chain of Custody.** Retain a copy of the **Form A-02**, as necessary.

4. Ensure that the CLBR001 drug product is maintained under frozen conditions during this transport, taking precautions to prevent premature or inadvertent thawing.

5.3.2 Thawing of CLBR001 Drug Product

The thawing of the CLBR001 drug product will occur immediately prior to the scheduled infusion. Time between drug product thawing and the COMPLETION of infusion should be as expeditious as possible (not to exceed 2 hours) in order to maintain maximum product viability.

1. Upon receiving the CLBR001 Drug Product at the subject's bedside, or a location in close proximity, verify that the subject's information matches the information on documents from the subject specific CLBR001 Drug Product and the label(s) on the cassette(s). This must be done by 2 independent reviewers in the presence of the subject and documented as such. Complete **Part 3** of **Form A-02 CLBR001 Drug Product Chain of Custody Form.** File in the subject's study files.
   In general, the thawing of the CLBR001 drug product will follow site SOP. Once the water bath is in close proximity to the subject's bedside and the temperature is at 37.1°C.

2. Open the aluminum cassette and remove the CLBR001 drug product. Check that the bag remains sealed and that there are no holes and tears. If the integrity of the bag has been compromised, document the observations, take a picture of the issue, and notify the Calibr-Skaggs team and your CRA. If there are no issues with the product you may proceed **with extreme care** to thaw the CLBR001 drug product; place in clean steriZip overpouch (OriGEN Biomedical, or equivalent per site SOP) and seal prior to water bath thaw to prevent water contacting bag. **Note:** SteriZip overpouch (or equivalent) is not provided. If site SOP does not use an overpouch, sponsor approval required.

3. Submerge the CLBR001 drug product bag in the water bath to initiate thawing. Thawing of the CLBR001 drug product will only take about 2-5 minutes depending on bag size. Monitor the thawing of the CLBR001 drug product and massage gently to increase the thaw rate.

4. Remove the bag from the water bath when a small amount of unthawed CLBR001 drug product remains and gently mix by inverting the bag 5 times.

5. High dose preparations may require multiple bags to achieve the full dose. If multiple bags of CLBR001 drug product are provided, remove, thaw, and begin infusion as described in Section 5.4 for only **ONE BAG** AT A TIME. Only remove and initiate thawing of another bag when it is ready to be infused. Document water bath temperatures and start/stop time for thawing of additional bags as above.

6. Complete **Part 3** of **Form A-02 CLBR001 Drug Product Chain of Custody**. Please email a copy of Form A-02 at this point to the Calibr-Skaggs team at sCAR461Clinical@scripps.edu. File original in subject source.

5.4 Administration of CLBR001 Drug Product

Also referred to as Subject Traceability Procedure Timepoint #16.

Administer CLBR001 per site SOP for CAR-T cell administration and this manual. Contact Sponsor if there are discrepancies between site and study processes.

Forms for this section:

- ☐ **(1) CLBR001 Drug Product Checklist, Section 3**
- ☐ **(2) CLBR001 Final Product Thawing and Infusion Documentation** *(Optional if documented in subject source)*
- ☐ **(3) CLBR001 Accountability Log**

1. Upon completion of CLBR001 thawing, remove CLBR001 drug product bag from steriZip overpouch (post thaw).

2. Inspect the bag for tears or holes. If any damage is seen on the outer and/or inner bag(s) document observations, take pictures of damage, and report to the Calibr-Skaggs team (sCAR461Clinical@scripps.edu), and do not administer the drug product until clearance to proceed is provided by Sponsor / Premier Research Logistics Manager.

3. Twist off (1) spike port cover to expose the female spike port. Firmly grasp the middle of the exposed port and insert a standard (ISO) male spike that is approximately 2.5 cm in length and with an outer diameter (OD) of not more than 6.5mm. Twist the spike into the port, taking care to not also twist the port while inserting the spike.

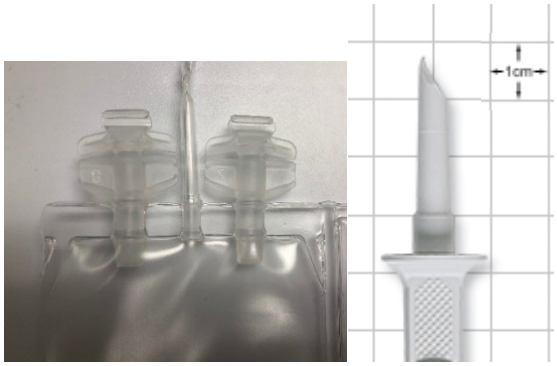

Image 12. Bag ports and male spike

4. Oversee the infusion, documenting the start and stop times of the infusion. See the protocol for details regarding pre-infusion assessments and premedication as well as post-infusion evaluations and medications for mild infusion reactions. Please make sure that all protocol-specific procedures are performed according to the study schedule.

5. The CLBR001 drug product will be administered by intravenous infusion via gravity or infusion pump at a flow rate of approximately 5 to 6 mL per minute through an 18-gauge latex free Y-type blood set or per site SOP. The duration of the infusion will be based on the total volume to be infused but will generally not exceed 10-15 minutes. The time between drug product thawing and the completion of infusion should be as expeditious as possible, preferably not to exceed 2 hours (maximum allowable time is 4 hours) in order to maintain maximum product viability.

6. The entire contents of each bag should be infused. Document the following during the administration process as indicated below (**CLBR001 Final Product Thawing and Infusion Documentation** or patient Medical Records):
    - ☐ Infusion start times
    - ☐ Infusion stop times
    - ☐ Total volume of CLBR001 drug product infused
    - ☐ If CLBR001 was interrupted and re-started, infusion start and stop times.
    - ☐ Volume of CLBR001 drug product not infused and reason for not infusing (if applicable)

    If a severe reaction occurs at any time, stop the infusion of CLBR001 immediately and continue with patient care per site SOPs, Investigator's clinical judgement and Infusion Related Reactions guidelines listed in the CBR-sCAR461-3001 Protocol.

7. After the infusion is complete, flush the infusion line with normal saline per clinical site SOP to ensure all CLBR001 drug product has been administered. Record the stop time after the end of flush.

8. Destroy and dispose of the CLBR001 drug product bag(s) according to clinical site SOP after documenting accountability in the **CLBR001 Accountability Log**. Redact or black-out information on the CLBR001 drug product label on the metal cassette before discarding cassette, according to clinical site SOPs. Final disposition of the CLBR001 drug product will be documented in the **CLBR001 Accountability Log**.

5.5 Instances of CLBR001 Not Given or Partial Dose Given

If, for any reason, the subject will not have CLBR001 drug product administered, maintain in frozen storage. Do not discard and do not thaw. The Calibr-Skaggs team will contact the site to coordinate the final disposition (return or destruction) of the unused CLBR001 drug product.

In the event that drug product has been thawed and administration has been interrupted or stopped for any reason, please contact the Calibr-Skaggs team immediately.
Additional sampling of drug product or collection of the bag may be requested by the Calibr-Skaggs team for investigation.

Any CLBR001 drug product that has been thawed and not infused (e.g. if interruption occurred), please document approximate volume not infused, according to site SOP. The partially administered infusion bag should be discarded according to clinical site SOPs.

6. Temperature Reporting

If not provided by the Cryoport automatic notification of delivery, the Premier Research Logistics Manager will provide the site with the temperature monitoring report of the CLBR001 drug product downloaded from the SmartPak II temperature monitoring device. Please contact the

Premier Research Logistics Manager to request a copy of the temperature monitoring report if not received automatically through Cryoport. This report should be filed in the subjects study records.

The temperature for storage locations of the leukapheresis product prior to shipment and the CLBR001 drug product received from the manufacturing facility must be recorded throughout the study. Please refer to **Section 0 Reporting Quality issues or Temperature Excursions**, if the storage temperature is out of range at any time during the study. Sites should provide the completed/up-to-date temperature log using either the provided study template or approved site template to the monitor.

7. Reporting Quality issues or Temperature Excursions

Any quality issues or temperature excursions that occur during shipment or while on site must be reported within 24 hours of becoming aware of the issue or event. The drug product in question should be placed under quarantine at appropriate storage temperature and not dispensed to any subjects until further instructions are provided based on Sponsor review of the issue or event. Please send all temperature excursion or quality issues notifications to the Calibr-Skaggs team (sCAR461Clinical@scripps.edu). Please be sure to provide all relevant details and documentation, including, if applicable, temperature monitor read-outs, pictures, etc.

8. Communications

It is expected that any formal communications are printed out if necessary and filed in the site files or pharmacy files. This includes, but is not limited to:

- Forms associated/referenced in this manual, such as **Form A-01 Leukapheresis Chain of Custody Form** and **Form A-02 CLBR001 Drug Product Chain of Custody Form** and corresponding checklists.
- Drug product issues and resolutions (i.e., temperature excursions)
- Formal communications from the Sponsor, CRO, and other study vendors
- Emails where a decision was made regarding study conduct or subject treatment

Printing any study-related document should be done in a secure, limited-access location and must be kept confidential at all times.

9. Additional Resources

The following documents are included as additional resources:

- Investigator's Brochure for CBR-sCAR461-3001
- Form A-01 Leukapheresis Chain of Custody Form
- Form A-02 CLBR001 Drug Product Chain of Custody Form
- Leukapheresis Checklist
- CLBR001 Drug Product Checklist
- Minaris Form: Authorization for Shipment of Final Product
- Minaris Form: QA Release of Final Product
- Subject Traceability Procedure Form
- CLBR001 Accountability Log
- CLBR001 Final Product Thawing and Infusion Documentation
- Cohort and Dose Assignment Form
- CBR-sCAR461-3001 Screening Eligibility Checklist
- CBR-sCAR461-3001 Lymphodepletion Eligibility Checklist

- CBR-sCAR461-3001 CLBR001 Eligibility Checklist
- CBR-sCAR461-3001 ABBV-461 Eligibility Checklist
- NanoCool Contingency Plan

CBR-sCAR461-3001 NanoCool Logistics Contingency Plan

The purpose of the NanoCool Shipper is to ensure there is a contingency plan for adequate temperature controlled (2-6°C) shipping materials in the event of any issues with the C3 shipper for apheresis shipping. Each site activated on CBR-sCAR461-3001 will receive a study specific NanoCool Shipper from Cryoport prior to first subject apheresed.

No action is needed from the site, other than to store the study specified NanoCool Shipper until deemed appropriate for use by Calibr-Skaggs team.

If the NanoCool Shipper is needed, please follow the below instructions:

1. Open box, remove cooling engine and place silver foil side down on a flat surface. Plush straight down on the activation button.

2. Notice the NanoCool logo turning blue between 30 seconds and 3 minutes, indicating cooling has begun. Confirm by touching the surface of the cooling engine near the activation button.

3. Load Product into the payload compartment, replace cooling engine, close the box and tape shut prior to shipping.

4. Hand airway bill to specialty courier who will attach to box.

5. Document time of pick up by specialty courier.

Questions? Reach out to Calibr-Skaggs team at sCAR461Clinical@scripps.edu