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

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Sponsor: Calibr-Skaggs Institute for Innovative Medicines

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Leukapheresis and CLBR001 Drug Product Manual Approval

Calibr-Skaggs Approval:

Name and Title	Signature	Date Signed
Jessica Greene, Senior Clinical Trial Manager	Jessica Greene	26-FEB-2025

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Version 2.0	07-FEB-2025	Updated Minaris Forms
Version 3.0	26-FEB-2025	Updated Appendix Images

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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.

2. DRUG PRODUCT ACCOUNTABILITY AND INVENTORY

Traceability is defined as the documentation and management of activities to support the collective tracking and control of a subject's autologous cells "needle-to-needle". Our obligation, as per regulations, is to ensure an adequate chain of custody from procurement of the cells, through manufacturing, testing and storage, to infusion or disposal.

Traceability ensures that cells taken from a subject are returned to that subject. A study-specific process has been developed with defined steps to be followed in conjunction with existing site-specific or institutional procedures. Training on this process and associated checklists and forms will occur at the Site Initiation Visit (SIV), and further as needed. Each center already has some level of traceability as standard practice. However, traceability is a critical component for a clinical trial using autologous cells, so it is imperative that appropriate staff sign-off occurs at each step in the process according to the prepared checklists that are specific to this study protocol. These checklists were developed to ensure that relevant traceability details from cell procurement through infusion are documented accurately. It is also critical that these checklists are completed in "real time", not after activities have been completed. Premier Research will be responsible for archiving all traceability documentation in the TMF per regulations.

All checklists used in this process for each subject must be maintained with the subject study record and a copy provided to Premier Research (sCAR461.Clinical@premier-research.com). Additionally, there are 2 mandatory forms that are required to be completed to document traceability:

- **Form A-01 Leukapheresis Chain of Custody Form**
- **Form A-02 CLBR001 Drug Product Chain of Custody Form**

All checklists and forms will be supplied to the site by the Sponsor/Premier Research at the time of SIV, with updated forms supplied in real time.

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 said task.

Detailed records will be maintained to allow for accurate accountability of the drug product in accordance with applicable Sponsor and clinical site procedures.

These records will include details of storage of the CLBR001 drug product, transfer of the CLBR001 drug product from the manufacturing facility, transfer of the CLBR001 drug

product within the clinical site, administration to subject, and disposal of remaining materials.

The accountability logs (or equivalent) must be used to document all drug product received, dispensed, and destroyed or returned. Logs must be legible, kept current, and made available for all monitoring visits and when close-out activities occur. A final review and verification of accountability logs by the site monitor will be performed after data has been locked at the site.

3. STUDY-RELATED CONTACTS

The leukapheresis procedures and the procedures related to the handling of the CLBR001 drug product will require the coordination of efforts and resources at the clinical site and across multiple parties. It is important to understand the groups involved and their respective roles in order to successfully prepare and safely administer the study product.

Premier Research is the Sponsor-designated contract research organization (CRO) for this study and the primary contact for the site. They will be responsible for communicating with all involved groups, specifically to confirm availability of slots at the drug product manufacturing facility and to coordinate the scheduling of the study subject's leukapheresis procedure with the same-day pick-up of the leukapheresis product via specialty courier or equivalent shipping and logistics vendor. Premier Research will also coordinate the timing of subsequent CLBR001 delivery from the manufacturing facility to the site in advance of the Lymphodepleting Chemotherapy (LD Chemo) and the scheduling of the subject's CLBR001 administration.

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 a specialty courier and, upon completion of manufacture and approval for release, ship the CLBR001 drug product back to the site.

Cryoport is designated to manage the transport of the **leukapheresis product to the GMP manufacturing facility (Minaris).** This includes delivery of preconditioned Temperature Controlled certified 2-8°C C3 Shipper to the site prior to the day of the Leukapheresis procedure and the same-day pick-up of the leukapheresis product from the site for overnight delivery to the manufacturing facility. 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 Logistics Manager as to which courier will be performing each delivery and pick up.

Cryoport is designated to organize the transport of the **cryopreserved CLBR001 drug product from Minaris to the site** using 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 Logistics Manager as to which courier will be performing each delivery and pick up.

4. LEUKAPHERESIS

4.1. Preparing for Leukapheresis

In general, preparation for leukapheresis and handling of the leukapheresis product will follow institutional policies and procedures at the site's apheresis center. However, please ensure that all protocol-specific procedures are performed according to the study schedule.

Upon identification of a potential candidate for screening, the site will remain in close communication with Premier Research in order to coordinate the scheduling for the leukapheresis procedure. Leukapheresis procedure must align with available manufacturing slots at the manufacturing facility (Minaris) and subjects may not proceed with leukapheresis until site is granted a slot and subject is approved for study enrollment.

The leukapheresis product will be picked up on the day of collection by Cryoport. Premier Research will coordinate this with the site and will need to communicate the pick-up time to Cryoport at least five (5) business days prior to the leukapheresis procedure.

4.2. Labeling the Leukapheresis Collection Bag

A study-specific leukapheresis label is required on each leukapheresis product and can be used in conjunction with labeling used at the site as part of standard process. Study Specific labels will be provided to the sites at time of site activation. This study specific label will require the following information to be handwritten at the appropriate point during leukapheresis procedure:

Prior to Start of Leukapheresis	• Local Leukapheresis Collection Number (site assigned) • Subject ID in the format of: sCAR461 - 2 # # - # # **Study ID - Site ID - Subject ID** • Subject initials (XXX) • Subject DOB (dd/mmm/yyyy; e.g., 06DEC2015) • 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). Please mark "N/A" checkbox and strike through name fields on all associated documents and labels where applicable.	

Upon completion of leukapheresis, the site must confirm that the subject information on the leukapheresis label(s) and **Form A-01 Leukapheresis Chain of Custody Form**, including all identifiers, is consistent, accurate, and complete.

4.3. Leukapheresis Product Storage, Handling, and Shipping

4.3.1 Product Storage

After leukapheresis, the leukapheresis product should immediately be packaged for shipping in the **Temperature Controlled C3 Shipper at 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 should a delay occur.

It is important to note that the cell manufacturing process is scheduled to start on the day following leukapheresis collection. Therefore, leukapheresis product must be picked up from the site by the courier **on the same that it was collected**.

4.3.2 Product Handling and Shipping

During screening of potential subjects, and as eligibility is confirmed, 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 should be arranged at least five (5) business days in advance when feasible.

It is preferred that the Temperature Controlled C3 shipper (2-8°C) arrives at least 1 day prior to Leukapheresis, however in certain situation the Temperature Controlled C3 shipper (2-8°C) may arrive the morning of leukapheresis. A designated courier will arrive at your site's pre-determined location with a Temperature Controlled C3 shipper (2-8°C), a Safepak XL, and a SmartPak II Condition Monitoring System to track temperature and location of the leukapheresis product during shipment from the site to the manufacturing facility. Sites will be asked to sign two copies of the airway bill for the delivery of the shipper to the site. If electronically managed, the site will need to print out a physical copy and copy should be kept by the site in its records. If changes need to be made to the airway bill or if the site contact is unable to locate the airway bill within the shipper, please contact the Logistics Manager to request that Cryoport provide an emailed copy to the site.

4.4. Scheduling, Preparation and Conducting Leukapheresis Procedure

Once a potential subject is identified for study participation:

1. Contact Premier Research (sCAR461.Clinical@premier-research.com) to determine the availability of slots at the manufacturing facility.
2. Schedule leukapheresis. This must be in coordination with Premier Research and available manufacturing slots. Premier will arrange for same-day pick-up of the leukapheresis product by Specialty Courier.
    - Manufacturing slot are available on set days and times. Subject leukapheresis must be scheduled to align with a set manufacturing slot that the Sponsor and Premier has confirmed has been assigned to that subject.
    - Contact Premier Research as soon as possible (sCAR461.Clinical@premier-research.com) if there is a change in the subject's eligibility or a need to change the date of leukapheresis. It may not be feasible to change the date of leukapheresis.
    - Please relay to Premier Research the time for the courier to arrive at least 5 business days prior to leukapheresis.
    - Premier Research will provide the site with email confirmation for the pick-up by the specialty courier. They will also ensure that the return shipment Airwaybill is available from the specialty courier and provided to the site via e-mail. The site will have to ensure Airwaybill is printed and in-hand at the time of pick-up. Contact Premier Research (sCAR461.Clinical@premier-research.com) if support is needed.

NOTE: Leukapheresis should not be performed, nor should leukapheresis product be shipped to Minaris, until subject eligibility has been confirmed and a manufacturing slot has been assigned. Processing of leukapheresis product MUST begin within 24 hrs of collection. Additionally, the Temperature Controlled C3 shipper must be on site prior to the leukapheresis.

3. Temperature Controlled C3 Shipper:
    - When Temperature Controlled C3 Shipper (2-8°C) is received, keep shipper box lid closed to maintain temperature until ready to load leukapheresis product.
    - Temperature Controlled C3 Shipper will arrive on site at least one (1) day prior to Leukapheresis procedure. The shipper is pre-conditioned prior to arrival and validated to hold temperature (2-8°C) for 96 hours from the time shipper left Cryoport. In the event the Temperature Controlled C3 Shipper arrives more than 2 days prior to leukapheresis, contact Logistics Manager for further guidance to ensure Temperature Controlled C3 Shipper will not be used beyond the 96 hour pre-conditioned limit.
    - For sites that require same day delivery of the Temperature Controlled C3 Shipper, please confirm with Premier Research as availability varies.

- Shipment of leukapheresis in the Temperature Controlled C3 Shipper should be between 2-8°C from the site to Minaris.

4. Obtain and complete (A) the site-specific leukapheresis label, (B) **Form A-01 Leukapheresis Chain of Custody Form** and (C) the protocol-specific leukapheresis label before initiation of the procedure:

5. Affix **both** leukapheresis labels (site-specific and study-specific) to the collection bag.

NOTE: Labels should be affixed prior to start of collection. Additional site-specific information may be added to the collection bag 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.

6. Set up the apheresis machine according to the clinical site's SOPs.

   Start the leukapheresis procedure and document the collection date and the collection start time in subject source, leukapheresis checklist, and the A-01 form. **NOTE: Collect enough volume to ensure a minimum total nucleated cell count of 2.0 x 10^9 from a single leukapheresis session prior to shipment to Minaris. Autologus plasma is added back (approximately 150mL) to the leukapheresis cells. Leukapheresis target collection volume is 2.0-3.0 Total Blood Volume.**

   The blood sample that is taken from the leukapheresis product may be collected before or after the plasma is added, as long as the total cell count represents the post plasma addition.

After leukapheresis collection has been completed:

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. If applicable, document transfer of leukapheresis product from the apheresis unit to the site stem cell laboratory on **Form A-01 Leukapheresis Chain of Custody Form**. Sign any site-specific log books. If leukapheresis product is not transferred to the stem cell 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.

NOTE: Unless otherwise noted in the delegation of authority/responsibility log, the stem cell laboratory personnel is responsible for the shipment of cells to the manufacturing facility.

In preparation for the pre-arranged pick-up by the courier:

11. 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.
    - If available, attach a copy of the de-identified WBC and differential results to **Form A-01 Leukapheresis Chain of Custody Form**. Otherwise, email the results to Premier Research (sCAR461.Clinical@premier-research.com) as soon as they are available.
12. Obtain the airway bill prior to scheduled arrival of specialty courier, who will supply the following:
    - Temperature Controlled C3 Shipping container (2-8°C)
    - SmartPak II: Temperature and location tracker
    - SafePakXL (or similar): packing container
13. Place the leukapheresis product into the Temperature Controlled C3 Shipper (2-8°C) container per instructions provided in Appendix 6.
14. Document the time when the product is packed in the shipping container on the Leukapheresis Checklist. Please refer to Appendix 6a and 6b for further details regarding the Cryoports SmartPak II condition monitoring system.
15. 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.
16. Close the box and seal the shipper. Document date and time of pick-up by specialty courier.
17. Provide a copy of the completed **Form A-01 Leukapheresis Chain of Custody Form** to the stem cell laboratory staff for local files, to the Site Study Coordinator for inclusion in subject's study files and to your CRA and Premier Research at sCAR461.Clinical@premier-research.com

5. CLBR001 DRUG PRODUCT

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).

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. 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"**. In addition, the label will contain the clinical study protocol number (CBR-sCAR461-3001) and the subject's study number, initials, and birth date.

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 an outline of the CLBR001 handling, administration and management.

NOTE: If, for any reason, the subject will not be administered his or her CLBR001 drug product, maintain in frozen storage. Do not discard and do not thaw. The Sponsor or Premier Research will contact the site to coordinate the return 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 Sponsor and Premier Research immediately. Additional sampling of drug product or collection of the bag may be required for investigation. Any CLBR001 drug product that has been thawed and not infused as well as infusion bags from completed infusions should be discarded according to clinical site SOPs. Final disposition of the CLBR001 drug product will be documented in the CLBR001 Drug Product Accountability Log.

5.1. Receipt and Storage of CLBR001 Drug Product at Site Storage Location

The CLBR001 drug product is shipped in a cryogenic shipping container to the predetermined contact at the site's stem cell laboratory. The drug product will arrive in a large dry liquid nitrogen LN_2 vapor shipper **FORM VV-QUAL -03050 - Authorization for Shipment of Final Product** and **FORM VV-QUAL-02814 - QA Release for Final Product to the Client**, which will include quality assessment information of the product. The CLBR001 drug product will be located inside an aluminum cassette held within a transport tray in the LN_2 Dry Shipper, see Appendix 7 The full CLBR001 drug product label is attached/located on the outside of the metal cassette as well as the product infusion bag.

PLEASE NOTE:

- USE APPROPRIATE PERSONAL PROTECTIVE EQUIPMENT WHEN HANDLING THE CLBR001 DRUG PRODUCT. CASSETTE WILL BE COLD.
- EXERCISE CAUTION TO PREVENT/MINIMIZE THAWING OF THE CLBR001 DRUG PRODUCT DURING HANDLING.

- DO NOT REMOVE THE CLBR001 DRUG PRODUCT FROM THE SHIPPER UNTIL THE INSTRUCTIONS BELOW HAVE BEEN READ COMPLETELY.
- OPEN THE SHIPPER ONLY WHEN READY TO CONFIRM CLBR001 DRUG PRODUCT LABEL INFORMATION **AND** TRANSFER THE DRUG PRODUCT TO THE STEM CELL LABORATORY'S CRYOSTORAGE TANKS.
- WORK QUICKLY AND CAREFULLY DURING THE REMOVAL AND INSPECTION OF DRUG PRODUCT.

Upon receipt of cryoshipper from Cryoport:

1. Receive and inspect the cryogenic shipper to ensure no visible damage. Document receipt of product and package integrity by completing Part 2 of **Form A-02: CLBR001 Drug Product Chain of Custody Form** (Appendix 2: CLBR001 Drug Product Chain of Custody Form). Email a copy of the completed form to Premier Research at sCAR461.Clinical@premier-research.com. Additionally, if ANY visible damage to the outer shipping container is present, please take pictures of all damaged areas for reference and submit to Premier Research along with the completed form.
2. If not provided via a notification email from Cryoport at time of delivery, ensure a copy of the temperature summary during transport is obtained from Premier Research. The temperature summary report must be maintained with all paperwork associated with the shipment of CLBR001 drug product specific to the subject (i.e. Completed Form VV-QUAL -03050 (Authorization for Shipment of Final Product) and Form VV-QUAL-02814 (QA Release for Final Product to the Client).
3. Transfer the CLBR001 drug product from the LN_2 Dry Shipper as follows:
   - Open the shipper only when ready to transfer the product to the stem cell laboratory's cryostorage tanks. This should occur within 1 business day of product arrival at site.
   - Using two independent reviewers, verify information between **Form A-02 CLBR001 Drug Product Chain of Custody** and **Form VV-QUAL-02814 QA Release for Final Product to the Client.**
   - Locate and remove the transport sleeve to extract the aluminum cassette containing the product. Do not open the cassette until ready to thaw. Do not thaw until ready to infuse.
   - Confirm that information on the label on the cassette matches the **Form VV-QUAL-02814 QA Release for Final Product to the Client.**

4. 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. Complete the Part 2 of **Form A-02 CLBR001 Drug Product Chain of Custody.**

5.2. Return the Cryoshipper/ Dry Shipper

Within 1-2 business days after transferring the CLBR001 Drug Product from the LN_2 Dry Shipper into stem cell laboratory cryostorage tanks, prepare the LN_2 Dry Shipper for return to the vendor. See Appendix 8 (Appendix 8 Instructions for Return of the Cryoshipper/ Dry Shipper) for instructions on attaching the pre-printed airway bill to return the shipper. Place the shipper in the FedEx pick-up area for pick-up.

5.3. Transfer and 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**.

Prior to subject's scheduled date of CLBR001 drug product infusion:

1. Follow site processes to authorize transfer of CLBR001 drug product from stem cell laboratory to hospital unit where infusion will occur. Document name of person giving authorization (e.g., the PI or Sub-I) and the date authorization given.

On the subject's scheduled date of CLBR001 drug product infusion:

2. Prepare CLBR001 drug product for transport. Confirm the Study Subject's information on the CLBR001 drug product matches **Form A-02 CLBR001 Drug Product Chain of Custody Form.**

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

3. Follow site SOPs for transferring the frozen CLBR001 drug product from LN_2 storage at the stem cell laboratory to the subject's bedside (or to a location in close proximity). Do not remove outer cassette until ready to thaw. Document the time of removal from LN_2 storage and complete, sign, and date the appropriate fields in Part 2 of **Form A-02 CLBR001 Drug Product Chain of Custody**. Retain a copy of this **Form A-02 CLBR001 Drug Product Chain of Custody**, as necessary.
4. Upon receiving the CLBR001 drug product at the subject's bedside (or to the designated area for cellular administration), verify that the subject's information matches the information on documents from the subject-specific CLBR001 drug product. This must be done by 2 independent reviewers in the presence of the subject and documented as such.
5. 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 Premier Research (sCAR461.Clinical@premier-research.com). File in the subject's study files.

6. In general, the thawing of the CLBR001 drug product will follow guidelines and/or procedures at the site. Once the water bath is in close proximity to the subject's bedside and the temperature is at 37.1°C:

   Document the following throughout the thawing process **(on Appendix 11: CLBR001 Final Product Thawing and Infusion Documentation):**
   - Water bath temperature prior to thawing
   - Thaw start time
   - Water bath temperature after thawing
   - Thaw stop time

   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 Premier Research 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, order number; SZ1823 or equivalent) and seal prior to water bath thaw to prevent water contacting bag. ***Note: SteriZip overpouch (or equivalent) is not provided. Please contact Premier Research if your site is having difficulty procuring this item.**
7. 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.
8. 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.
9. 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.

Proceed to **Section 5.4 Administration of CLBR001 Drug product**

5.4. Administration of CLBR001 Drug product

Upon completion of thawing of the CLBR001 drug product:

1. Remove inner 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 Premier Research (sCAR461.Clinical@premier-research.com), and do not administer the drug product until clearance to proceed is provided by Sponsor / Premier Research
3. Twist off (1) spike port cover to expose the female spike port.

4. 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.
5. 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.

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's SOP. The duration of the infusion will be based on the total volume to be infused but will generally not exceed 10-15 minutes (not inclusive of the 5-10 minute pause required, see below) if there are no complications. 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. The infusion line should be flushed to ensure complete administration of CLBR001.

Document the following during the administration process as indicated below (**Appendix 11: CLBR001 Final Product Thawing and Infusion Documentation**):

- Infusion start times
- Start time of required pause
- End time of required pause
- Infusion stop times
- Total volume of CLBR001 drug product infused
- Volume of CLBR001 drug product not infused and reason for not infusing (if applicable)
- If CLBR001 was interrupted and re-started for a reason other than required pause, infusion start and stop times.

The entire contents of each bag should be infused.

NOTES:

- **Refer to CBR-sCAR461-3001 Protocol, which contains additional details, including infusion reactions and premedication (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.**

6. Administer approximately 5mL of CLBR001 initially, followed by a pause of 5-10 minutes. If no severe reaction occurs, CLBR001 administration may resume at a flow rate of approximately 5 to 6 mL per minute, until complete. The central line should not be flushed during the 5-10 min pause. **Note: The 5-10 minute pause is NOT considered an interruption of the cell dose and does not need to be recorded in the source documentation or the EDC as an interruption.**

7. After the infusion is complete, flush the infusion line with normal saline per clinical site SOPs 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 SOPs and after documenting accountability in the CLBR001 Accountability Log, see Appendix 5. Redact or black-out information on the CLBR001 drug product label on the metal cassette before discarding cassette, according to clinical site SOPs.

NOTE: 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 Sponsor or Premier Research will contact the site to coordinate the return 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 Sponsor and Premier Research immediately. Additional sampling of drug product or collection of the bag may be required for investigation. Any CLBR001 drug product that has been thawed and not infused (e.g. if dose has been modified at the site), please document approximate volume not infused, according to site SOPs. This bag as well as infusion bags from completed infusions should be discarded according to clinical site SOPs. Final disposition of the CLBR001 drug product will be documented in the CLBR001 Accountability Log.

6. TEMPERATURE LOGS

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 7 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 Premier Research (sCAR461.Clinical@premier-research.com). 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**.
- 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.

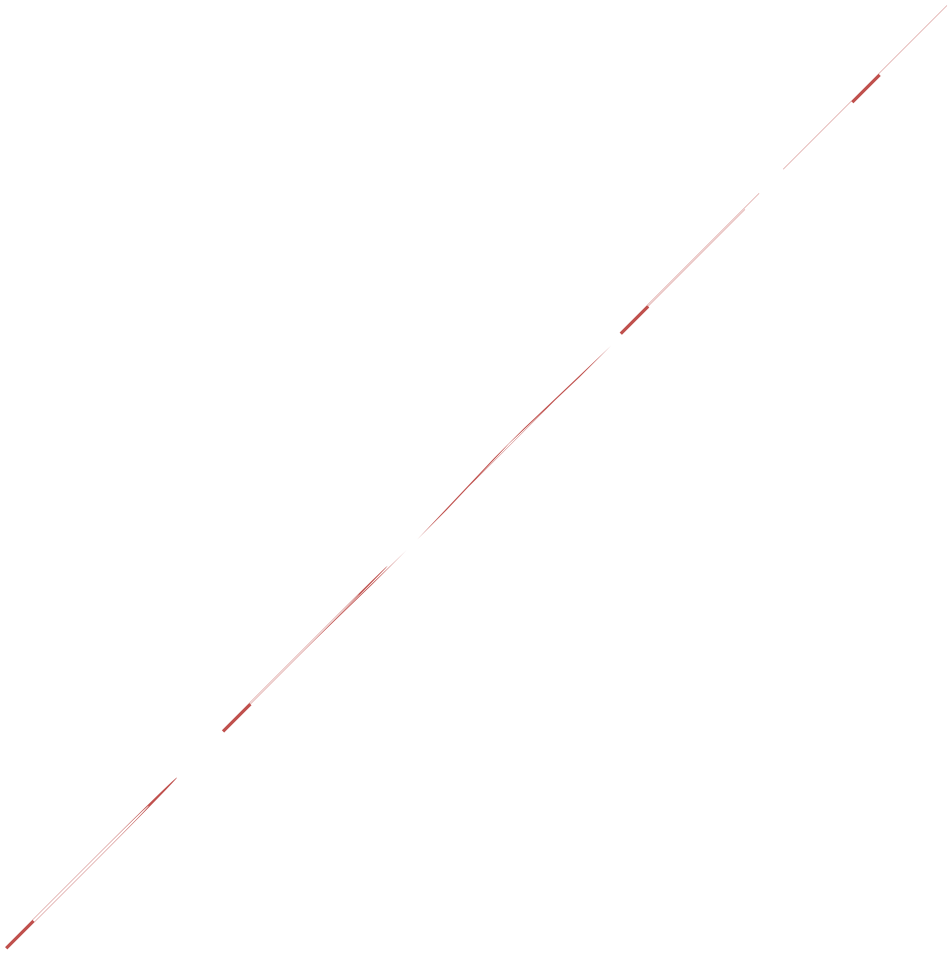
9. ADDITIONAL RESOURCES

The following documents are included as additional resources:

- Investigator's Brochure for CBR-sCAR461-3001
- Checklist templates for leukapheresis collection procedures and CLBR001 drug product-related procedures outlined in the manual
- Subject Traceability Registration Procedure

10. APPENDICES

Please note that the forms and checklists within the appendix are intended for reference only. The forms and checklists to be completed will be located within the Study Operations Manual.



Appendix 1 Form A-01 Leukapheresis Chain of Custody Form
FOR REFERENCE ONLY, USE CURRENT FORM PROVIDED SEPARATELY

Calibr-Skaggs Institute for Innovative Medicines | Scripps Research

Leukapheresis Chain of Custody (Site Apheresis Unit to Manufacturing Facility)	Form: A-01 Protocol Number: CBR-sCAR461-3001

PI Name: _____ **Institution name:** _____

Patient ID #: **Subject Initials:** ___ ___ ___

sCAR461 – ___ ___ ___ – ___ ___

Subject DOB: ___ ___ / ___ ___ ___ / ___ ___ ___ ___ (dd / mmm / yyyy) **Subject Weight:** ___ ___ ___ . ___ kg

Leukapheresis Collection

Collection Date: ___ ___ / ___ ___ ___ / ___ ___ ___ ___ (dd / mmm / yyyy)

Collection Device: *Check one.* ☐ Cobe Spectra ☐ Spectra Optia ☐ Fenwal Amicus ☐ Other: _____	**Collection Start Time:** ___ ___ : ___ ___ (24h clock) **Time Zone:** _____ **Collection End Time:** ___ ___ : ___ ___ (24h clock) **Time Zone:** _____
Leukapheresis Volume: _____ mL	**Anticoagulant Type and Volume Used:** _____ mL of _____

Total Nucleated Cell Count: _____

Leukapheresis Label Verification

☐ N/A (Specify Reason: _____)

Name of Reviewer #1: Please print. _____ **Signature and Date** (dd/mmm/yyyy):	**Name of Reviewer #2:** Please print. _____ **Signature and Date** (dd/mmm/yyyy):

Leukapheresis Bag Transfer Confirmation

☐ N/A (Specify Reason: _____)

Person Transferring Bag: Please print. _____ **Signature and Date** (dd/mmm/yyyy):	**Name of Receiver at Cell Lab or Pharmacy:** Please print. _____ **Signature and Date** (dd/mmm/yyyy):
Time Leaving collection location: ___ ___ : ___ ___ (24h clock)	**Time arrived at Cell Therapy Lab/other (specify):** ___ ___ : ___ ___ (24h clock)

Version Date (05OCT2024) CONFIDENTIAL Page 1 of 1

Appendix 2 Form A-02 CLBR001 Drug Product Chain of Custody Form
FOR REFERENCE ONLY, USE CURRENT FORM PROVIDED SEPARATELY

Calibr-Skaggs Institute for Innovative Medicines | Scripps Research

CLBR001 Drug Product Chain of Custody | **Form: A-02** | Protocol Number: CBR-sCAR461-3001

Part 1: Receipt from Manufacturing Facility (to be completed by clinical site staff receiving CLBR001 Drug Product Shipment)

PI Name: _____

Patient ID #: *sCAR461* –___ ___ ___–___ ___ ___

Subject DOB: ___ ___/___ ___ ___/___ ___ ___ ___
dd mmm yyyy

Date of CLBR001 Receipt: ___ ___/___ ___ ___/___ ___ ___ ___ **CLBR001 Lot Number:** _____
dd mmm yyyy
# of bags received: _____

Was CLBR001 received in good condition? ☐ Yes ☐ No *If no, notify Premier immediately. Take pictures of any damage for reference*

Printed Name of Receiver	Signature	Date (dd/mmm/yyyy)

Part 2: Transfer (to be completed by clinical staff transferring CLBR001 Drug Product in and out of the Cell Lab or Investigational Pharmacy)

Date & Time of entry to LN_2 Storage: ___ ___/___ ___ ___/ ___ ___ ___ ___ ___ ___: ___ ___ (24h clock)
dd mmm yyyy

Printed Name of Staff	Signature	Date (dd/mmm/yyyy)

Date & Time of removal from LN_2 Storage: ___ ___/___ ___ ___/ ___ ___ ___ ___ ___ ___:___ ___ (24h clock)
dd mmm yyyy

Printed Name of Staff	Signature	Date (dd/mmm/yyyy)

Part 3: Bedside Receipt of CLBR001 and Confirmation of Subject Info (to be completed by 2 clinical site staff receiving CLBR001 Drug Product)

By my signature below, I confirm receipt of the CLBR001 Drug Product at the bedside and that I have verified, in the subject's presence, that the subject's information matches the subject-specific CLBR001 Drug Product.

Check all that apply:
☐ Confirm receipt of CLBR001
☐ Verified subject information

Printed Name of Reviewer #1	Signature	Date (dd/mmm/yyyy)

Check all that apply:
☐ Confirm receipt of CLBR001
☐ Verified subject information

Printed Name of Reviewer #2	Signature	Date (dd/mmm/yyyy)

Version Date (15NOV2024) CONFIDENTIAL Page 1 of 1

Appendix 3 Leukapheresis Checklist (Collection to Shipment)

FOR REFERENCE ONLY, USE CURRENT FORM PROVIDED SEPARATELY

Protocol #: CBR-sCAR461-3001	LEUKAPHERESIS CHECKLIST
Subject ID: ___ ___ ___ - ___ ___ (Site # / Subject #)	Subject Initials: ___ ___ ___
Date of Leukapheresis: ___ ___ / ___ ___ ___ / ___ ___ ___ ___ (DD / MMM / YYYY)	

NOTE: Leukapheresis should not be performed, nor should leukapheresis product be shipped, until everything has been coordinated through and confirmed with your Premier Research Clinical Lead (CL). If a step is not required, line through the section, write "NA" and include your initials and date.

Section 1: Prior to Start of / During Leukapheresis

Step		Initials/Date
1.	Obtain and complete the following PRIOR to initiation of leukapheresis: • The site/clinic-specific leukapheresis label • **Form A-01 Leukapheresis Chain of Custody Form** • The protocol-specific leukapheresis label (to be provided to site by Premier Research)	
2.	Affix both leukapheresis labels (site-specific and protocol-specific) to the bag.	
3.	Set up the apheresis machine according to the clinical site's SOPs.	
4.	Start the leukapheresis procedure and document the following: • Collection Date (dd/MMM/yyyy): _____/_____/_____ • Collection Start Time (24h clock): _____:_____ (24H:MM)	
Comments (precede each comment with specific step numbers):		

Section 2: Upon Completion of Leukapheresis Collection

Step		Initials/Date
5.	Document the following: • Collection End Time (24h clock): _____:_____ (24H:MM) • Leukapheresis Volume (mL): _____ • Type and Vol. (mL) of Anticoagulant Used: _____	
6.	Complete the remaining information required on the leukapheresis label(s) and on **Form A-01 Leukapheresis Chain of Custody Form**.	
7.	Verify the label contents to ensure the accuracy of the recorded information on the leukapheresis labels and **Form A-01 Leukapheresis Chain of Custody Form**. Document that the double verification process was performed on **Form A-01 Leukapheresis Chain of Custody Form**.	
8.	Document transfer of leukapheresis product from the apheresis unit to the site stem cell laboratory (if applicable) on **Form A-01**. Sign any site-specific log books.	
Comments (precede each comment with specific step numbers):		

FOR REFERENCE ONLY, USE CURRENT FORM PROVIDED SEPARATELY

Protocol #: CBR-sCAR461-3001	**LEUKAPHERESIS CHECKLIST**
Subject ID: ___ ___ ___ - ___ ___ (Site # / Subject #)	Subject Initials: ___ ___ ___
Date of Leukapheresis: ___ ___ / ___ ___ ___ / ___ ___ ___ ___ (DD / MMM / YYYY)	

Section 3: Preparation for Pick-Up by Specialty Courier

Step		Initials/Date
9.	Complete the Form A-01 Leukapheresis Chain of Custody. Place a copy of this form with the shipment and file the original in the subject's study files.	
10.	Obtain the courier airway bill provided by Cryoport within the Temperature Controlled Shipper *prior* to scheduled arrival of the courier.	
11.	Using the shipping container supplied by Cryoport, place the leukapheresis sample into the Credo box per instructions provided in Appendix 6 of the Leukapheresis and CLBR001 Drug Product Manual.	
12.	Once the leukapheresis product is packed in the preconditioned shipping container, press and release the start button on the TempTale. This will "date stamp" or mark this as an important event on the TempTale. Place the monitor and GPS tracker into the box. Document the time when the product is packed in the shipping container. Refer to Appendix 6 of the Leukapheresis and CLBR001 Drug Product Manual for details regarding the TempTale. • Product Packaging Time: ____:_____ (24H:MM)	
13.	Place the original copy of **Form A-01 Leukapheresis Chain of Custody Form** on top of the insulation under the top box flap and close/seal box	
14.	Close the box and seal the shipper. Document the following: • Pick-Up Date: _____/_____/_____ (dd / mmm / yyyy) • Pick-Up Time _____:_____ (24H:MM)	
15.	Provide a copy of the completed **Form A-01 Leukapheresis Chain of Custody Form** to the cell laboratory staff for their files, a second to the Site Study Coordinator for inclusion in subject's study files and scan and send a copy to Premier Research at sCAR461.Clinical@premier-research.com.	
Comments (precede each comment with specific step numbers):		

Appendix 4 CLBR001 Drug Product Checklist (Receipt to Infusion)

FOR REFERENCE ONLY, USE CURRENT FORM PROVIDED SEPARATELY

Calibr-Skaggs Institute for Innovative Medicines | Scripps Research

Patient ID #: sCAR461-2__ __-__ __

This procedure serves to ensure accurate management and administration of CLBR001 Drug Product. This Checklist is to accompany the CLBR001 Drug Product from receipt at the clinical site through its infusion.

Section 1: Receipt of Cryo-shipper		
Step #	**Steps**	**Initials/Date**
1	Receive and inspect the cryo-shipper to ensure there is no visible damage. Document receipt of product and package integrity by completing **Section 3 of Form 3391 - Authorization for Shipment** and email a copy as instructed on the form. ➢ If there is ANY visible damage to the outer shipping container, take pictures of all damaged areas for reference and submit to Premier along with Minaris Form 3391 to sCAR461.Clinical@premier-research.com	
2	Transfer the CLBR001 Drug Product from the Temperature Controlled shipper as described in Appendix 7 of the **Leukapheresis and CLBR001 Drug Product Manual.** ☐ Open the shipper only when ready to transfer the product to the cell lab's cryostorage tanks. This should occur within 1 business day of receipt (See Appendix 7). ☐ **Using two independent reviewers**, verify information between **Form A-01 Leukapheresis Chain of Custody** and **Forms 3391** (**Authorization for Shipment**) and **4674** (**Release for infusion**). ☐ Email completed 3391 (Authorization for Shipment) to the email indicated at the bottom of form, cc: sCAR461.Clinical@premier-research.com ☐ Locate and remove the aluminum cassette(s) containing the product from the transport sleeve. Do NOT open the cassette(s) until ready to thaw. Do NOT thaw until ready to infuse. ☐ File the completed Form 3391 and 4674 in the subject's study files.	1st Reviewer: 2nd Reviewer:
3	Store the CLBR001 Drug Product, in the aluminum cassette(s), in the vapor phase of liquid nitrogen according to standard site practice. Document the: • Storage location: _____ • Storage date (dd/mmm/yyyy): _____/_____/_____ • Storage time (24h clock): _____:_____ (HH:MM)	
4	Complete **Part 1** of **Form A-02 CLBR001 Drug Product Chain of Custody.**	
Section 1 Comments (precede each comment with specific step number):		

FOR REFERENCE ONLY, USE CURRENT FORM PROVIDED SEPARATELY

Calibr-Skaggs Institute for Innovative Medicines | Scripps Research

Patient ID #: sCAR461-2__ __-__ __

Section 2: Transfer and Thawing of CLBR001 Drug Product		
Step #	**Steps**	**Initials/Date**
5	Follow site processes to authorize the transfer of CLBR001 Drug Product from cell lab to the unit where infusion will occur. Document name of person giving authorization (eg, the PI or Sub-I) and the date authorization given.	
6	Prepare the CLBR001 for transport. Confirm the Subject info on the CLBR001 Drug Product Label(s) matches **Form A-02 CLBR001 Drug Product Chain of Custody**	
7	Transfer the frozen CLBR001 Drug Product from Temperature Controlled storage at the cell lab to the Subject's bedside (or to a location in close proximity). Document the time of removal from Temperature Controlled 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.	
8	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.	1st Reviewer: 2nd Reviewer:
9	Open the aluminum cassette and remove double bagged drug product. Check that the outer bag remains sealed and that there are no holes or tears. Do not remove outer bag *until after thawing*. If the integrity of the outer bag has been compromised, document the observations, take a picture of the issue, and notify Premier at sCAR461.Clinical@premier-research.com. Inspect the inner bag for damage as well and then you may proceed **with extreme care** to thaw the CLBR001 drug product. ➢ Note: This process should be repeated for each bag of CLBR001 drug product; do not thaw a subsequent bag of CLBR001 until prior bag is fully infused.	
10	Submerge the CLBR001 Drug Product bag in its outer bag in the water bath to initiate thawing. Document the following in subject's medical records ***or*** in the CLBR001 Final Product Thawing and Infusion Documentation form: • Water Bath Temperature Prior to Thawing • Thaw Start Time Thawing of CLBR001 will only take about 5 minutes. Monitor the thawing of the Drug Product and massage gently to increase thaw rate. ➢ Note: This process should be repeated for each bag of CLBR001 drug product; do not thaw a subsequent bag of CLBR001 until prior bag is fully infused.	
11	Remove the bag from the water bath when a small amount of unthawed Drug Product remains and gently mix by inverting the bag 5 times. Document the following in subject's medical records ***or*** in the CLBR001 Final Product Thawing and Infusion Documentation form: • Water Bath Temperature After Thawing • Thaw Stop Time Proceed to Section 3 when ready. ➢ Note: This process should be repeated for each bag of CLBR001 drug product; do not thaw a subsequent bag of CLBR001 until prior bag is fully infused.	
Section 2 Comments (precede each comment with specific step number):		

FOR REFERENCE ONLY, USE CURRENT FORM PROVIDED SEPARATELY

Calibr-Skaggs Institute for Innovative Medicines | Scripps Research

Patient ID #: sCAR461-2__ __-__ __

Section 3: Administration of CLBR001 Drug Product **Note:** 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.		
Step #	**Steps**	**Initials/Date**
12	Inspect the inner bag for tears or holes. If any damage is seen on the outer or inner bag, document observations, take pictures of damage, and report to Premier (sCAR461.Clinical@premier-research.com) immediately to obtain approval to proceed. If there is damage, DO NOT administer the CLBR001 unless clearance to proceed is provided by Sponsor/Premier. ➢ Note: This process should be repeated for each bag of CLBR001 drug product. **NOTE:** A leukoreduction filter must NOT be used for the infusion of the CLBR001 T -cell product.	
13	Cut off the covering on one of the unused spike port covers to expose the female spike port.	
14	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 of not more than 6.5mm. While inserting the spike, do not twist or fold the other ports. Twist the spike only into the port, taking care to not also twist the port while inserting the spike.	
15	Oversee the infusion, documenting the start and stop times of the infusion. Refer to Protocol sections regarding Study Treatment, which contains additional details, including premedication, infusion reactions, and availability of emergency medical equipment. **NOTE:** 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 guidelines listed in the study Protocol.	
16	Initially, administer 5mL of CLBR001, followed by a pause of 5-10 minutes. If no severe reaction occurs, CLBR001 administration may resume at a flow rate of approximately 5 to 6 mL per minute, until complete.	
17	After the infusion is complete, rinse the infusion line per clinical site SOPs to ensure all CLBR001 Drug Product has been administered.	
18	Record total volume of CLBR001 Drug Product infused and, if applicable, the volume of Drug Product that was not infused and the cause for not infusing all of the Drug Product. The volume of un-administered CLBR001 Drug Product may be measured by drawing into a syringe.	
19	Destroy any excess CLBR001 Drug Product and dispose of the CLBR001 Drug Product bag(s) according to the clinical site SOPs and after documenting accountability in the **Accountability Log.** Make sure to redact or black out information on the CLBR001 Drug Product label on the metal cassette before discarding cassette, according to clinical site SOPs.	
Section 3 Comments (precede each comment with specific step number):		

Appendix 5 Drug Product Accountability Log Templates
FOR REFERENCE ONLY, USE CURRENT FORM PROVIDED SEPARATELY

Calibr-Skaggs Institute for Innovative Medicines | Scripps Research

Sponsor:	Calibr-Skaggs, a division of Scripps Research	**Site Number:**	
Product:	CLBR001	**Investigator:**	
Protocol Number:	CBR-sCAR461-3001	**Institution:**	

Received			Dispensed				Balance (If applicable)	Destruction		CLBR001 Accountability Verified by			
Date (DD/MMM/YY)	# Bags Rec'd	Minaris Lot #	Enrollment #	Date (DD/MMM/YY)	#Bags Dispensed	Dose Assigned	# bags not dispensed or infused	# bags wasted/destroyed	Date (DD/MMM/YY)	Cell Therapy Staff initials	Date (DD/MMM/YY)	CRA initials	Date (DD/MMM/YY)
01NOV24	1		sCAR461-2NN-YY	14NOV24	1	1	0	0	14NOV24	ABC	14NOV24	AKC	20DEC24

CBR-sCAR461-3001: CLBR001 Accountability Log, Version 1; November 15, 2024

Appendix 6 Instructions for Preparing a Shipment of the Leukapheresis Product to the Manufacturer (Minaris) with Cryoport

1. When the leukapheresis visit is scheduled you should coordinate leukapheresis product pick-up with Premier Research. Upon doing so, you will receive a confirmation email that contains 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 your CRA or Premier Research directly.

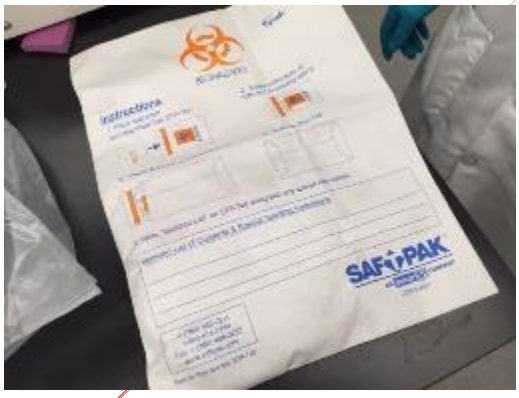
2. Cryoport Courier will arrive with the following items:
   - GTC 4L insulated box with 6 pre-conditioned cold packs lining the inside (Credo Cube):

   - IATA approved bags and absorbent sheet:

- Temperature monitor and GPS tracking device (SmartPak II)

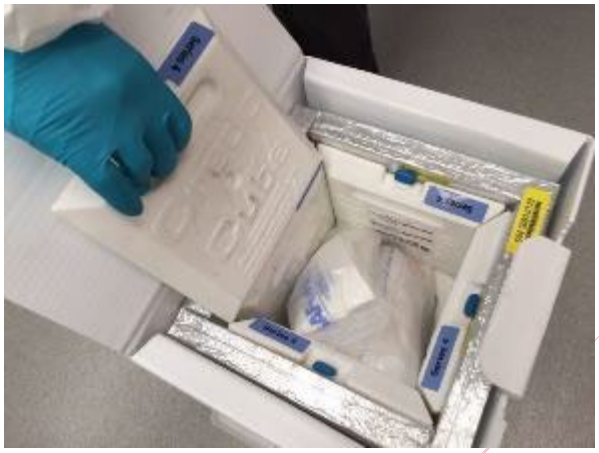
3. Packaging the leukapheresis collection bag:

- Wrap the absorbent sheet around leukapheresis bag and place into plastic bag the specimen bag as shown:



- An additional wrap may be applied as shown but not required or supplied:

- Confirm that the SmartPakII has been started by pushing the 'Touch Sensitive Button' on the SmartPak II device. The sensor data may take up to 3 minutes to display in Live View (please see appendix 6b).
- Place active SmartPak II into the bottom of the box (see Appendix 6A for device picture and instructions)
- Place the packaged leukapheresis bag into the box:



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

Appendix 6A Instructions for Use of SmartPak II Monitor

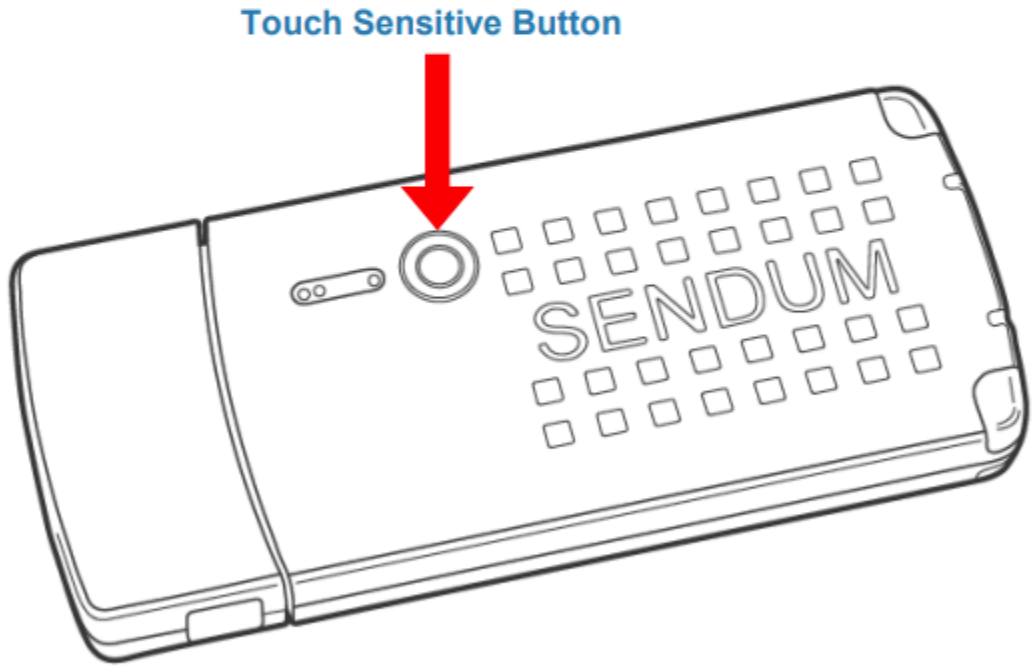
cryoport
SCIENCE. LOGISTICS. CERTAINTY.

SmartPak II™ Push Button Activation Instructions

Standard operation of the SmartPak II™ is to record every 5 minutes and to transmit all of the data at hourly intervals. The SmartPak II™ device must be in communication with a local cell tower in order to transmit data every hour.

To retrieve the most updated sensor data information, push the "Touch Sensitive Button" on the SmartPak II™ device. The most updated sensor data may take up to 3 minutes to display in Live View.

Please refer to Form 9215 v1 for instructions on how to access Live View.



24-HOUR HELP LINE
(949) 470-2305

Cryoport, Inc. • 17305 Daimler St. • Irvine, CA 92614
Phone: 1-949-470-2300 Fax: 1-949-470-2306
www.cryoport.com • E-mail Contact: cs@cryoport.com

Appendix 6B Instructions for Use of SmartPak II Monitor

cryoport
SCIENCE. LOGISTICS. CERTAINTY.

NOT FOR IVF SHIPMENTS

SmartpakII™

Pickup/Delivery Temperature Data

1. Email Data

Internal Temperature with Standard Deviation may be obtained directly from the email that was provided during Pickup/Delivery in the Details Section or by selection any Live View Link.

Pick Up/Delivery DetailsLeg X (Company to Company) on order XXXXX has been picked up or delivered and is now en route.

Time of Pickup: XX/XX/XX; X:XX AM/PM -XXXX

Temperature statistics while waiting pickup on leg X, from 11/29/2016 08:48 AM(UTC -0600) to 11/29/2016 03:06 PM(UTC -0600).

Package	Data Logger	Metric	Min	Max	Average	Standard Deviation	Last Reading	Last Reading At	Live View
1	99000512004539	Internal Temperature	-194.75 °C	194.05°C	-194.38°C	0.18°C	-194.45°C	11/29/2016 1:05 PM (UTC -0600)	Live View

The "Live View" feature may be viewed by clicking on the link provided.
Link will only be viewable if "SRV-LIV" was purchased!

2. Live View

ONLY AVAILABLE IF THE LIVE VIEW SRV-LIV WAS PURCHASED

Important Live View Indicators

Internal Temperature Orientation Battery Level Location

24-HOUR HELP LINE
(949) 470-2305

Instructions Continued on Back of Sheet.

Form 9215 v1 Effective 3/6/17

cryoport
SCIENCE. LOGISTICS. CERTAINTY.

NOT FOR IVF SHIPMENTS

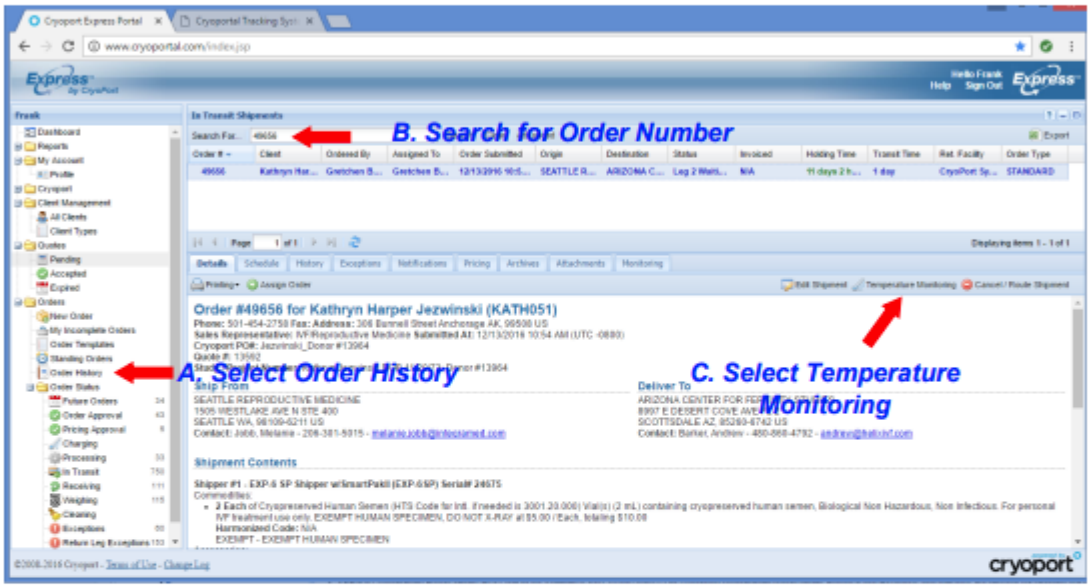
SmartpakII™

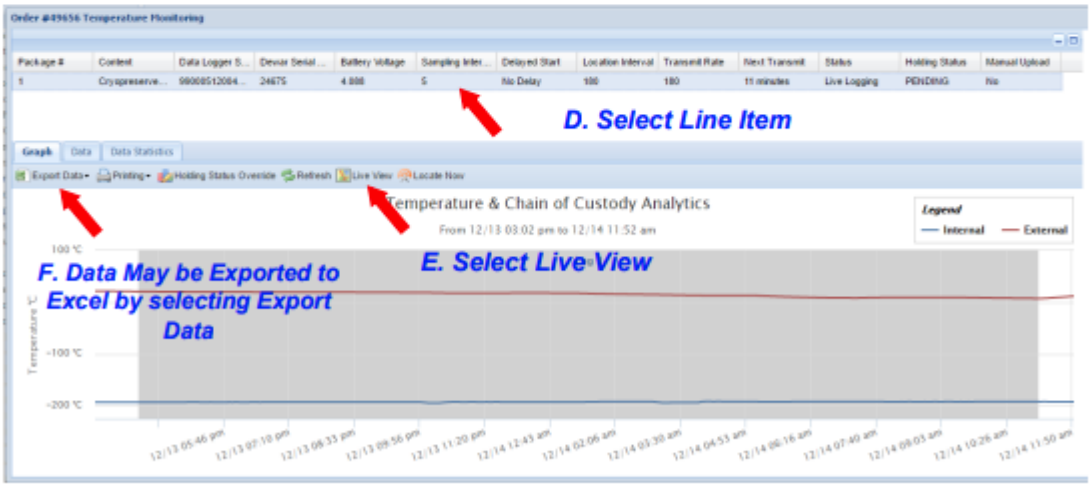
Pickup/Delivery Temperature Data

3. Portal

Link will only be viewable if "SRV-LIV" was purchased!

The "Live View" feature may be viewed from the portal by searching for the Order Number. Follow these instructions!





G. Live View will be displayed, see section 2 on Page 1

24-HOUR HELP LINE
(949) 470-2305

Cryoport, Inc. • 17305 Daimler St. • Irvine, CA 92614
Phone: 1-949-470-2300 Fax: 1-949-470-2306
www.cryoport.com • E-mail: cs@cryoport.com

Form 9215 v1 Effective 3-6-17

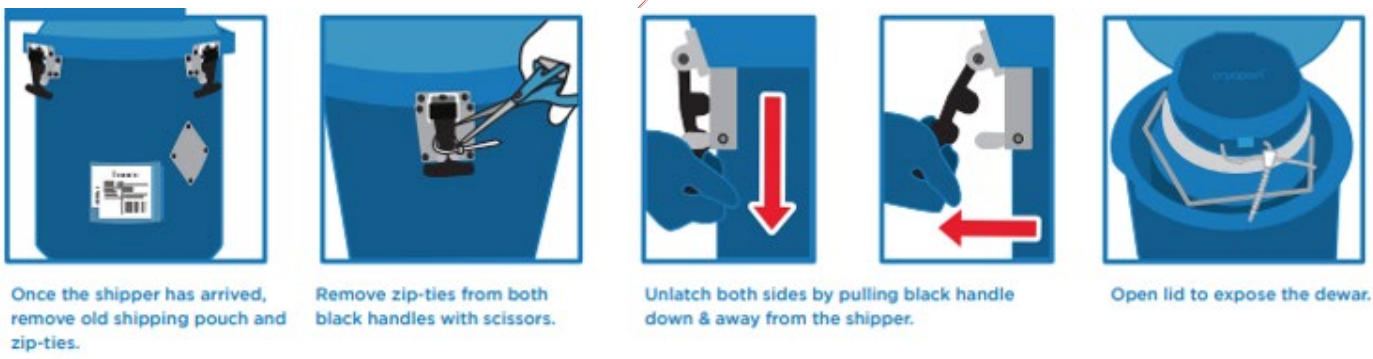
Appendix 7 Instructions for Receipt of CLBR001 Drug Product and Removal from Cryoshipper/Dry Shipper

1. Courier will deliver CLBR001 drug product frozen within a LN_2 dry shipper contained within an outer packaging shell on a rolling pallet.

2. Upon receipt, inspect the shipper itself for damage. Document inspection on Part 2 of the accompanying "CLBR001 Drug Product Chain of Custody Form" and submit to Premier Research (sCAR461.Clinical@premier-research.com) . Reference Appendix 2 for information on completing and submitting CLBR001 Drug Product Chain of Custody Form.

3. Transfer the material from the LN_2 Dry shipper to cryostorage within 1 business day of receipt

4. Open the outer packaging shell and remove the CoT for the CLBR001 drug product, which will be at the top of the shipper, once it's opened.



5. Confirm that the CoT information matches the study subject information from Form A-01

6. The LN_2 dry shipper will have a SmartPak II (temperature monitor and GPS system) on the top of the tank. Follow instructions below for ensuring data is properly queued-up with the tracking network:

STEP 1

Tap and release the touch sensitive button. The Network LED light will turn on (red or green light) within approximately 5 seconds. If a Network LED light does not turn on after 5 seconds, tap and release the touch sensitive button again. Repeat until a Network LED light turns on.

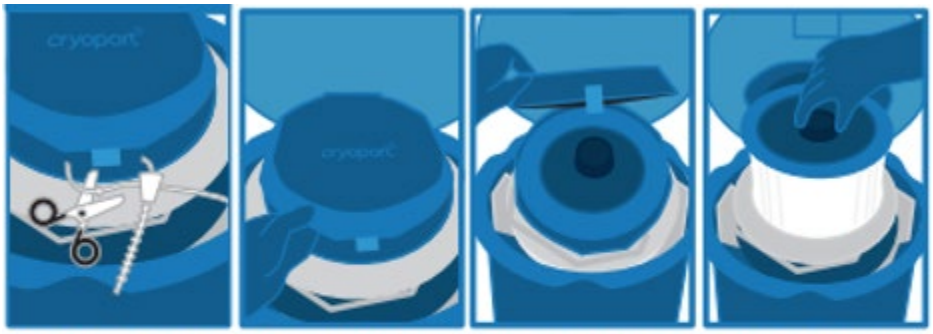
STEP 2

Wait to see a solid Green LED light. After 5 minutes, refresh your Live View™ link. The queued-up data should fully be displayed up to the timestamp you executed in Step 1.

PLEASE NOTE: The Network LED light may be "blinking" RED. The blinking could last up to one minute (depending on the cellular coverage condition) before it changes to a solid Green.

IF THE DRY SHIPPER DOES NOT EMIT VAPOR WHEN PLUG IS REMOVED
PLEASE CONTACT CUSTOMER SERVICE IMMEDIATELY, BY CALLING (949) 470-2305 OR EMAIL CS@CRYOPORT.COM

7. Cut the Zip tie on the hinged cap with scissors. Open the hinged cap by pulling up on one of the two lift handles on the lid. With gloved hands, pull up on the circular handle in the center of the vapor plug to remove the vapor plug. Set the vapor plug aside.



Cut off the zip tie on the hinged cap with scissors.

Open the hinged cap by pulling up on one of the two lift handles on the lid. With gloved hands, pull up on the circular handle in the center of the vapor plug to remove the vapor plug. Set the vapor plug aside.

8. Remove the loaded cassette holder by pulling upwards.

9. Confirm label on cassette matches CoT and place cassette in cryostorage tank in the stem cell laboratory.

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)

Appendix 8 Instructions for Return of the Cryoshipper/Dry Shipper

1. Return the cassette holder to the dry shipper

Place any returnable accessories back into the 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 puch and place on the metal diamond (see step 5 below)

Replace the vapor plug.

Close the hinged cap by pulling down on the lid.

Secure the hinged cap with a zip tie.

Remove the Leg 3 shipping pouch from the document protector attached to the dewar handle inside of the container.

Remove the EMPTY label from the shipping pouch and place on the metal diamond.

7. Place in Fed-Ex pick-up location
8. Questions contact Premier Research at sCAR461.Clinical@premier-research.com.

Appendix 9 Guidelines for Apheresis Collection

Summary:
Proper collection bag sampling technique is essential to obtaining a well-mixed, representative sample for complete blood counts and cell enumeration. The following procedure outlines the recommended steps for collection bag sampling. NOTE: Collect enough volume to ensure a target (i.e., minimum) total nucleated cell count of 2.0 x 10^9 from a single leukapheresis session. A white blood cell (WBC) count and differential must be run from the collected product after leukapheresis.

Procedure:

1. Ensure cells are well mixed by gently agitating the apheresis product bag back and forth. Hold the container in the palm of the hands and use a circular motion to ensure that the product flows from one end of the container to the other.
2. Position apheresis product bag sample side down. Open the slide clamp(s) to one of the sample bulbs.
3. Squeeze the sample bulb several times to ensure the sample is representative of the apheresis product.
4. Note the volume of the sample required and confirm you have the appropriate amount and are minimizing product loss.
5. Close the slide clamp as close to the product bag as possible.
6. Make a hermetic seal on the sample bulb tubing below the slide clamp.
7. A minimum of 3 hermetic seals are required prior to removing the bag from the instrument, leaving at least two seals on the product tubing. More seals may be used without adversely impacting the operation.
8. Cut the seal farthest from the apheresis product bag leaving at least two hermetic seal with the apheresis product.
9. Transfer the sample to the appropriate labeled test tube for requested testing and send sample to appropriate lab.

Figure: Collection bag sampling bulbs (Arrow)

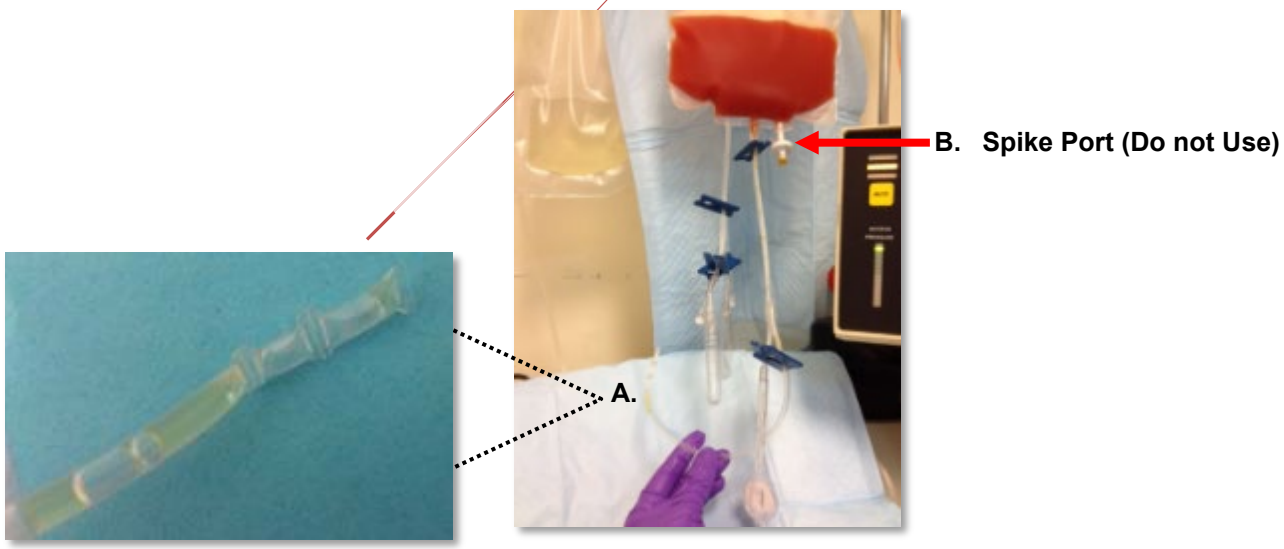
Appendix 10 Guidelines for Hermetically Sealing the Apheresis Collection Bag

Summary:
Proper hermetic sealing of the collection bag is essential to maintain product integrity. The following procedure outlines the recommended steps for hermetically sealing of the collection bag.

Procedure:

1. Once apheresis product has been collected per apheresis collection requirements, the product can be removed from the apheresis kit.
2. Using heat sealer or grommets and crimper, make a hermetic seal on the apheresis tubing as far from the apheresis product bag as possible, leaving as much tubing as possible on the product line. To prevent pressure build-up within the tubing, seal from the bag to the instrument. Do not strip the tubing.
3. A minimum of 3 hermetic seals are required prior to removing the bag from the instrument, leaving at least two seals on the product tubing. More seals may be used without adversely impacting the operation.
4. Cut the seal farthest from the apheresis product bag leaving at least two hermetic seal with the apheresis product.

Figure: Hermetically Sealing of Collection Bag



Appendix 11: Documentation of CLBR001 thaw and infusion times

FOR REFERENCE ONLY, USE CURRENT FORM PROVIDED SEPARATELY

Calibr-Skaggs Institute for Innovative Medicines | Scripps Research

CLBR001 Final Product Thawing and Infusion Documentation

Subject initials: _____ Patient ID #: sCAR461-2__ __ __-__ __

DOB (dd/mmm/yyyy): _____

Date of CLBR001 infusion (dd/mmm/yyyy): _____

CLBR001 Thaw and Administration: Bag #____ record thaw and administration info for subsequent bag below

Lot #: _____

Water bath temperature prior to thawing: _____ ☐ °C or ☐ °F

Thaw start time: ____:____ AM/PM Thaw stop time: ____:____ AM/PM

Water bath temperature after thawing: _____ ☐ °C or ☐ °F

CLBR001 infusion start time: ____:____ (24 hr clock) CLBR001 infusion stop time: ____:____ (24 hr clock)

Total volume of CLBR001 Administered: _____

Was CLBR001 interrupted and re-started? ☐ Yes ☐ No

If yes: CLBR001 infusion start time: ___:___ (24 hr clock) CLBR001 infusion stop time: ___:___ (24 hr clock)

Total volume of CLBR001 NOT-Administered: _____

Reason for incomplete CLBR001 administration (if applicable) _____

Completed by: _____ Signature/Date: _____

CLBR001 Thaw and Administration: Bag #____ record thaw and administration info for subsequent bag below ☐ N/A

Lot #: _____

Water bath temperature prior to thawing: _____ ☐ °C or ☐ °F

Thaw start time: ____:____ AM/PM Thaw stop time: ____:____ AM/PM

Water bath temperature after thawing: _____ ☐ °C or ☐ °F

CLBR001 infusion start time: ____:____ (24 hr clock) CLBR001 infusion stop time: ____:____ (24 hr clock)

Total volume of CLBR001 Administered: _____

Was CLBR001 interrupted and re-started? ☐ Yes ☐ No

If yes: CLBR001 infusion start time: ___:___ (24 hr clock) CLBR001 infusion stop time: ___:___ (24 hr clock)

Total volume of CLBR001 NOT-Administered: _____

Reason for incomplete CLBR001 administration (if applicable) _____

Completed by: _____ Signature/Date: _____

*Form is optional if all above data points are documented in subject's medical record.