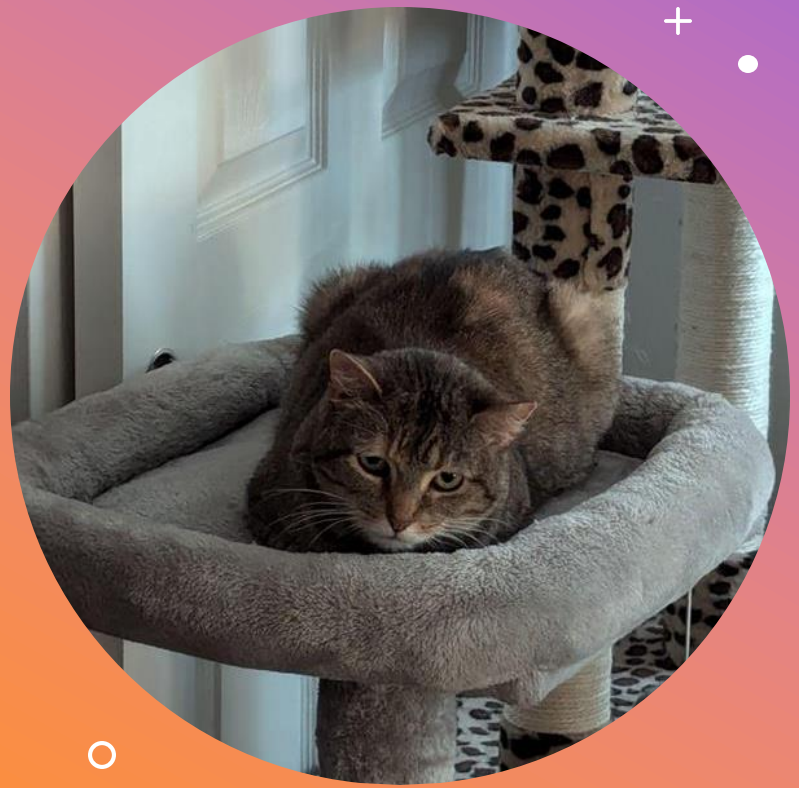
CBR-SCAR461-3001

A Phase 1, Dose-Escalation Study Evaluating Combo of CLBR001 + ABBV-461 in mBC

Dave



Fergie

AGENDA

Leukapheresis

CLBR001 Receipt + Storage

CLBR001 Thawing + Preparation

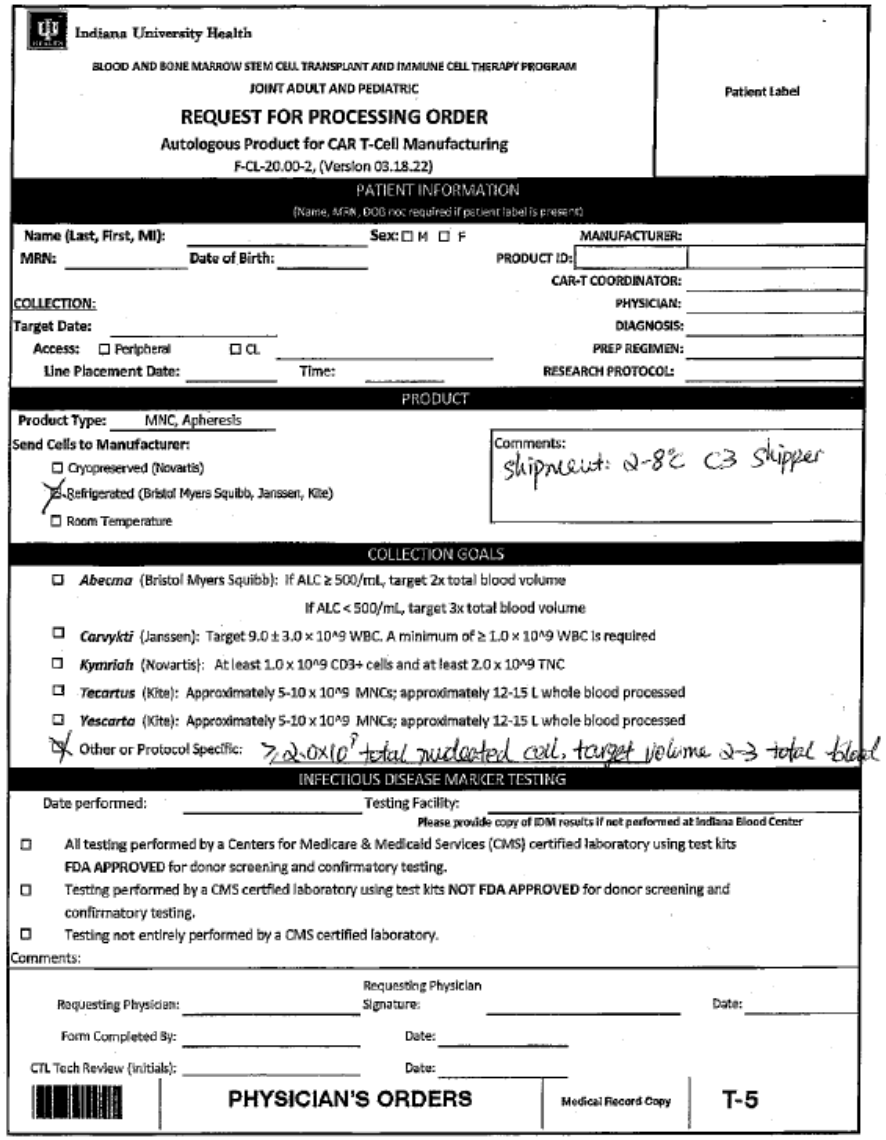
CLBR001 Accountability

LEUKAPHERESIS

- Study coordinator will contact Premier Research as soon as subject is identified/screened to secure a manufacturing and leukapheresis slot. CTL will also be notified.
- Manufacturing slots are available on set days and times, with no wiggle room.
  - Subject leukapheresis must align with a set manufacturing slot that is assigned.
  - We will work with CTL to schedule this around the manufacturing slot.

LEUKAPHERESIS

- Study staff will use form **F-CL-20.00-2** to request leukapheresis for patients.



Indiana University Health

BLOOD AND BONE MARROW STEM CELL TRANSPLANT AND IMMUNE CELL THERAPY PROGRAM
JOINT ADULT AND PEDIATRIC

REQUEST FOR PROCESSING ORDER

Autologous Product for CAR T-Cell Manufacturing
F-CL-20.00-2, (Version 03.18.22)

Patient Label

PATIENT INFORMATION
(Name, MRN, DOB not required if patient label is present)

Name (Last, First, MI): _____ Sex: ☐ M ☐ F
MRN: _____ Date of Birth: _____

MANUFACTURER:
PRODUCT ID:
CAR-T COORDINATOR:
PHYSICIAN:
DIAGNOSIS:
PREP REGIMEN:
RESEARCH PROTOCOL:

COLLECTION:
Target Date: _____
Access: ☐ Peripheral ☐ CL _____
Line Placement Date: _____ Time: _____

PRODUCT

Product Type: MNC, Apheresis

Send Cells to Manufacturer:
☐ Cryopreserved (Novartis)
☒ Refrigerated (Bristol Myers Squibb, Janssen, Kite)
☐ Room Temperature

Comments: shipment: 2-8°C C3 shipper

COLLECTION GOALS

☐ *Abecma* (Bristol Myers Squibb): If ALC ≥ 500/mL, target 2x total blood volume
If ALC < 500/mL, target 3x total blood volume
☐ *Carvykti* (Janssen): Target 9.0 ± 3.0 x 10^9 WBC. A minimum of ≥ 1.0 x 10^9 WBC is required
☐ *Kymriah* (Novartis): At least 1.0 x 10^9 CD3+ cells and at least 2.0 x 10^9 TNC
☐ *Tecartus* (Kite): Approximately 5-10 x 10^8 MNCs; approximately 12-15 L whole blood processed
☐ *Yescarta* (Kite): Approximately 5-10 x 10^8 MNCs; approximately 12-15 L whole blood processed
☒ Other or Protocol Specific: ≥ 2.0x10^7 total mobilized cell, target volume 2-3 total blood volume.

INFECTIOUS DISEASE MARKER TESTING

Date performed: _____ Testing Facility: _____
Please provide copy of IDM results if not performed at Indiana Blood Center

☐ All testing performed by a Centers for Medicare & Medicaid Services (CMS) certified laboratory using test kits **FDA APPROVED** for donor screening and confirmatory testing.
☐ Testing performed by a CMS certified laboratory using test kits **NOT FDA APPROVED** for donor screening and confirmatory testing.
☐ Testing not entirely performed by a CMS certified laboratory.

Comments: _____

Requesting Physician: _____ Requesting Physician Signature: _____ Date: _____
Form Completed By: _____ Date: _____
CTL Tech Review (initials): _____ Date: _____

PHYSICIAN'S ORDERS Medical Record Copy T-5

LEUKAPHERESIS

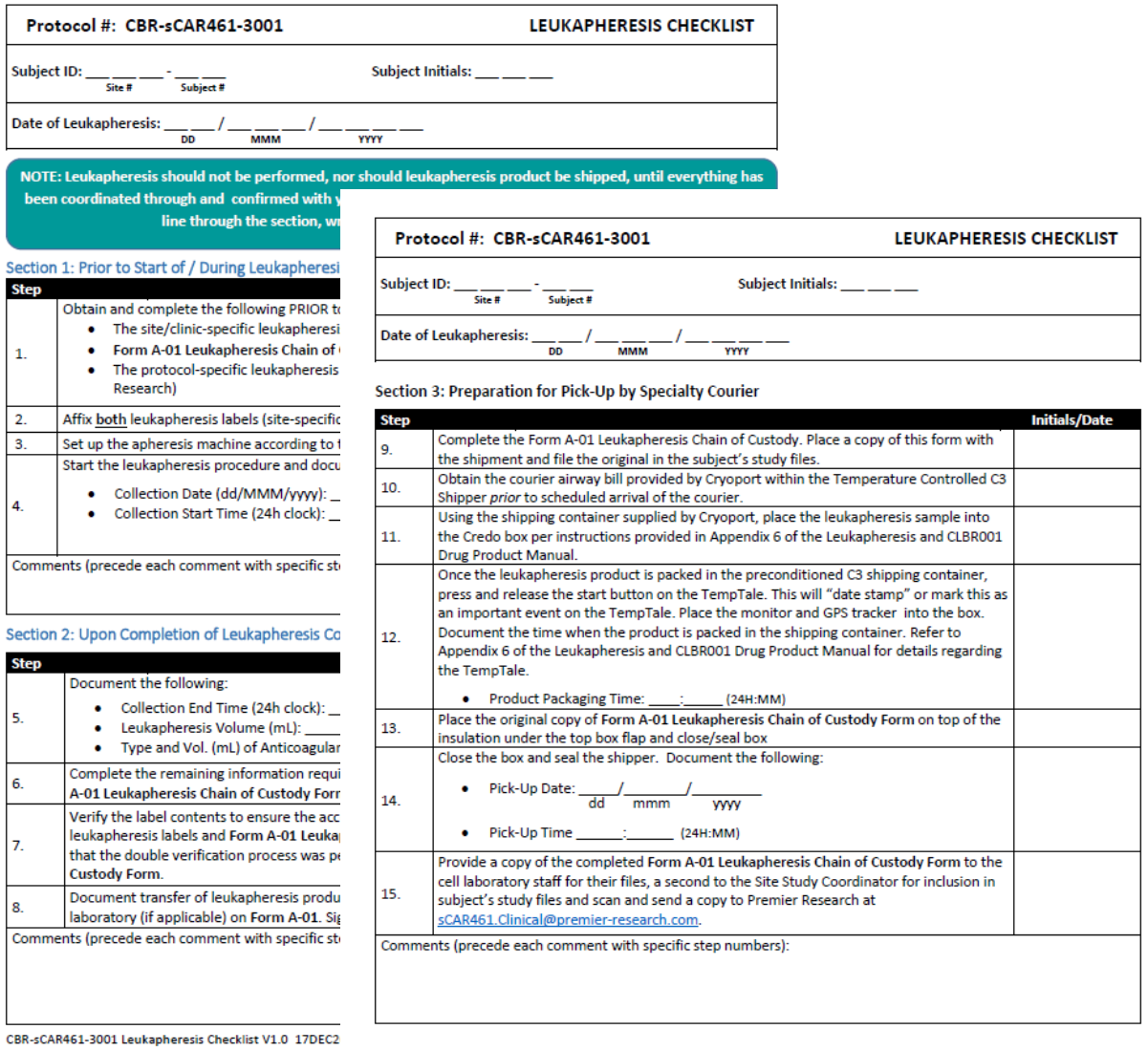
- Study specific labels will be provided to the site at time of activation.
- Will require the following information to be recorded by CTL.
  - Do **not** record PHI.

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)

LEUKAPHERESIS

- During leukapheresis, will also need to fill out the **Leukapheresis Checklist**.
- Provide original copy to study coordinator.



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 y… line through the section, wi…

Section 1: Prior to Start of / During Leukapheresi…

Step	
1.	Obtain and complete the following PRIOR t… • The site/clinic-specific leukapheresi… • **Form A-01 Leukapheresis Chain of …** • The protocol-specific leukapheresis … Research)
2.	Affix both leukapheresis labels (site-specific…
3.	Set up the apheresis machine according to t…
4.	Start the leukapheresis procedure and docu… • Collection Date (dd/MMM/yyyy): _ • Collection Start Time (24h clock): _

Comments (precede each comment with specific st…

Section 2: Upon Completion of Leukapheresis Co…

Step	
5.	Document the following: • Collection End Time (24h clock): _ • Leukapheresis Volume (mL): ___ • Type and Vol. (mL) of Anticoagular…
6.	Complete the remaining information requi… **A-01 Leukapheresis Chain of Custody Forr…**
7.	Verify the label contents to ensure the acc… leukapheresis labels and **Form A-01 Leuka…** that the double verification process was pe… **Custody Form**.
8.	Document transfer of leukapheresis produ… laboratory (if applicable) on **Form A-01**. Sig…

Comments (precede each comment with specific st…

CBR-sCAR461-3001 Leukapheresis Checklist V1.0 17DEC2…

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

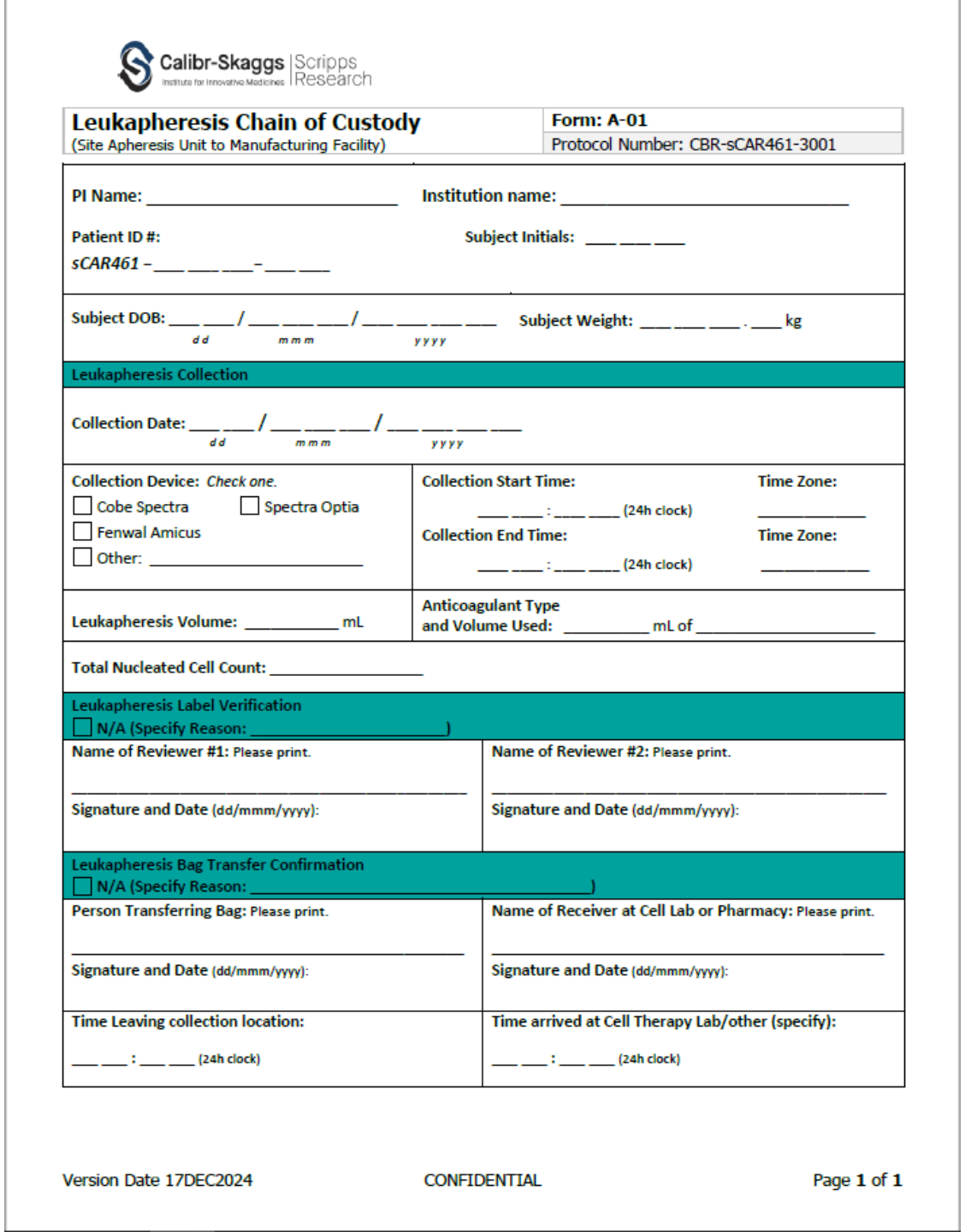
Step		Initials/Date
9.	Complete the Form A-01 Leukapheresis Chain of Custody. Place a copy of this form with the shipment and file the original in the subject's study files.	
10.	Obtain the courier airway bill provided by Cryoport within the Temperature Controlled C3 Shipper *prior* to scheduled arrival 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 C3 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):

CBR-sCAR461-3001 Leukapheresis Checklist V1.0 17DEC2024 Page 2 of 2

LEUKAPHERESIS

- Upon completion of leukapheresis, the **Form A-01 Leukapheresis Chain of Custody Form** must be completed by CTL.
- Email a completed copy to sCAR461.Clinical@premier-research.com
  - Provide original copy to study coordinator.



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 17DEC2024 CONFIDENTIAL Page 1 of 1

LEUKAPHERESIS

- After leukapheresis, product should be packaged and shipped immediately in the **Temperature Controlled C3 Shipper at 2-8C**.
  - Shipper may arrive the day before or day of leukapheresis.
  - Product should be shipped by 2pm on day of leukapheresis.
- Product can be held at room temp for up to 4 hours from end of collection in case of delay.
  - If delay occurs, please notify the Premier Research Logistics Manager.
  - **MUST** be picked up from the site by the courier on the same day it was collected.

LEUKAPHERESIS

- During screening, the Premier Research Logistics Manager will coordinate and schedule the pick-up of leukapheresis product by a specialty courier (Cryoport) for the same day as the procedure.
  - Should be arranged at least 5 business days in advance when feasible.
- Courier will arrive with **Temperature Controlled C3 shipper, Safepak XL, and a SmartPak II Condition Monitoring System** for temperature tracking in transit.
  - CTL staff will be asked to sign **TWO** copies of the airway bill for the delivery of the shipper to the site.
  - Email the Premier Research Logistics Manager to request a copy be provided via email if you wish.

CLBR001 RECEIPT + STORAGE

- First two cohorts have CLBR001 dose of 140x10⁶ CAR-T cells
  - Will be provided to the site in a single bag for IV infusion.
- Starting after second cohort, may decide to proceed with one or both of following CLBR001 doses: 140x10⁶ CAR-T cells, 420x10⁶ CAR-T cells.
  - 420x10⁶ CAR-T cells will be provided to the site in multiple bags (3 bags, each containing 140x10⁶ CAR-T cells) for IV infusion.
- Each infusion bag will be labeled with product & subject identifiers.
- Subjects will receive a **single dose of CLBR001 on D-1**.

CLBR001 RECEIPT + STORAGE

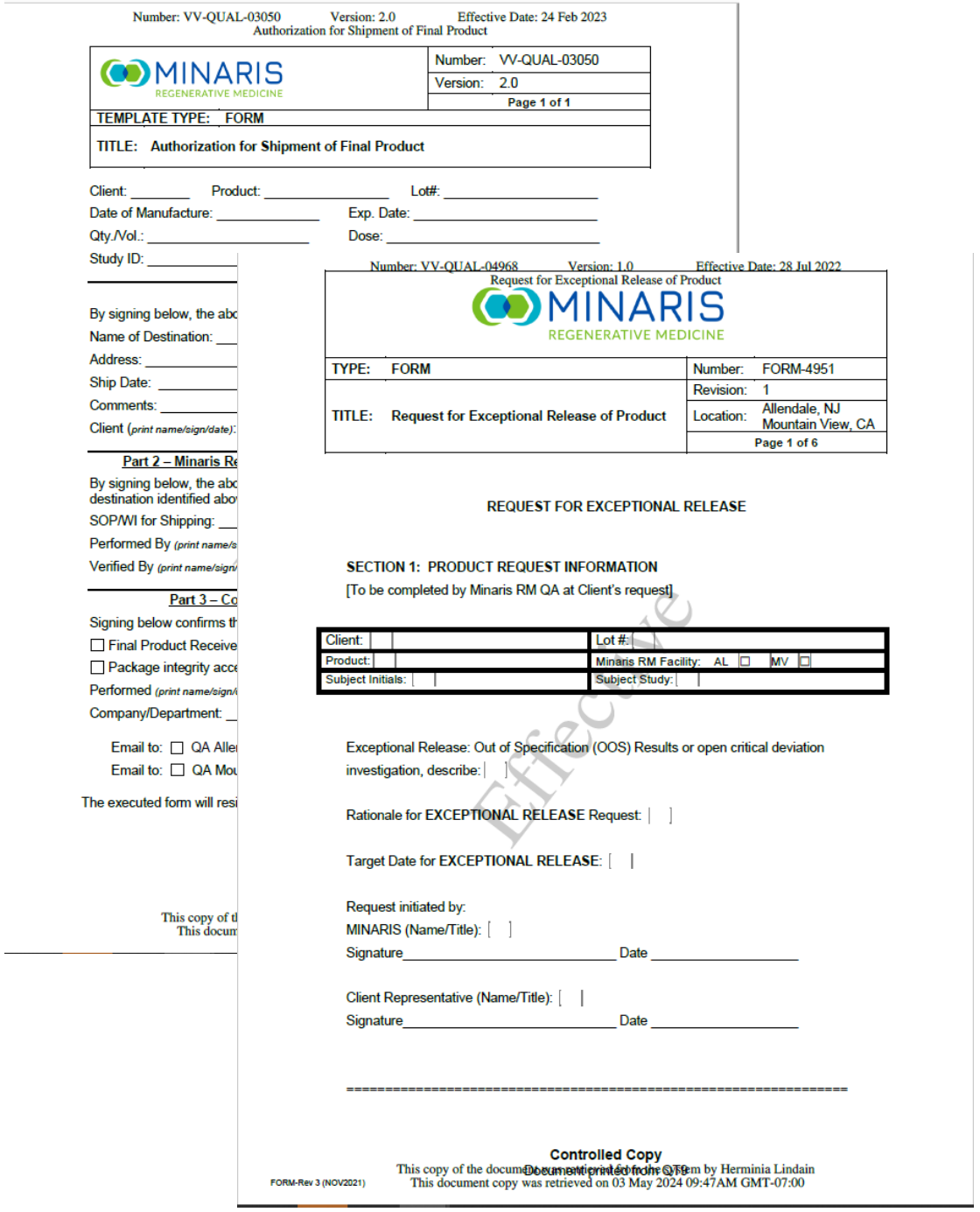
- CLBR001 product will be manufactured by Minaris.
- Following release testing and release authorization, the CLBR001 product is shipped in a LN2 Dry Shipper to the site.
  - Typically occurs within 21-28 days after leukapheresis product was received by Minaris.
- After receipt at site, store in vapor phase of LN2 cryotank in a secure, limited-access location.
- Each infusion bag will have a label containing the study number, as well as subject's study identification.

CLBR001 RECEIPT + STORAGE

- When frozen, the CLBR001 product is slightly opaque. When thawed, it is slightly turbid.
- Product must remain frozen until subject is ready for treatment.
- If, for any reason, the subject will not be given their CLBR001 product, do not discard or thaw.
  - The sponsor will contact the site to initiate the return process for any unused CLBR001 product.
- Anything thawed + infused should be discarded per site SOP.
- Anything thawed + partially infused (stopped or interrupted for any reason): please contact sponsor immediately. Testing or collection of the bag may be needed.

CLBR001 RECEIPT + STORAGE

- CLBR001 product will arrive with <u>completed</u> **Form VV-QUAL-03050 Authorization for Shipment of Final Product** and **Form VV-QUAL-02814 QA Release for Final Product to Client**.
  - Provide these forms to the study coordinator.
  - Form VV-QUAL-02814 requires treating investigator signature.



Number: VV-QUAL-03050 Version: 2.0 Effective Date: 24 Feb 2023
Authorization for Shipment of Final Product

MINARIS REGENERATIVE MEDICINE

Number:	VV-QUAL-03050
Version:	2.0
	Page 1 of 1

TEMPLATE TYPE: FORM

TITLE: Authorization for Shipment of Final Product

Client: _____ Product: _____ Lot#: _____
Date of Manufacture: _____ Exp. Date: _____
Qty./Vol.: _____ Dose: _____
Study ID: _____

By signing below, the abc
Name of Destination: ___
Address: _____
Ship Date: _____
Comments: _____
Client (*print name/sign/date*):

Part 2 – Minaris Re
By signing below, the abc
destination identified abo
SOP/WI for Shipping: ___
Performed By (*print name/s*
Verified By (*print name/sign/*

Part 3 – Co
Signing below confirms th
☐ Final Product Receive
☐ Package integrity acce
Performed (*print name/sign/*
Company/Department: _

Email to: ☐ QA Alle
Email to: ☐ QA Mou

The executed form will resi

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Number: VV-QUAL-04968 Version: 1.0 Effective Date: 28 Jul 2022
Request for Exceptional Release of Product

MINARIS REGENERATIVE MEDICINE

TYPE:	FORM	Number:	FORM-4951
		Revision:	1
TITLE:	Request for Exceptional Release of Product	Location:	Allendale, NJ Mountain View, CA
			Page 1 of 6

REQUEST FOR EXCEPTIONAL RELEASE

SECTION 1: PRODUCT REQUEST INFORMATION
[To be completed by Minaris RM QA at Client's request]

Client:	Lot #:
Product:	Minaris RM Facility: AL ☐ MV ☐
Subject Initials:	Subject Study:

Exceptional Release: Out of Specification (OOS) Results or open critical deviation investigation, describe: [ ]

Rationale for EXCEPTIONAL RELEASE Request: [ ]

Target Date for EXCEPTIONAL RELEASE: [ ]

Request initiated by:
MINARIS (Name/Title): [ ]
Signature_____ Date _____

Client Representative (Name/Title): [ ]
Signature_____ Date _____

==========

Effective

Controlled Copy
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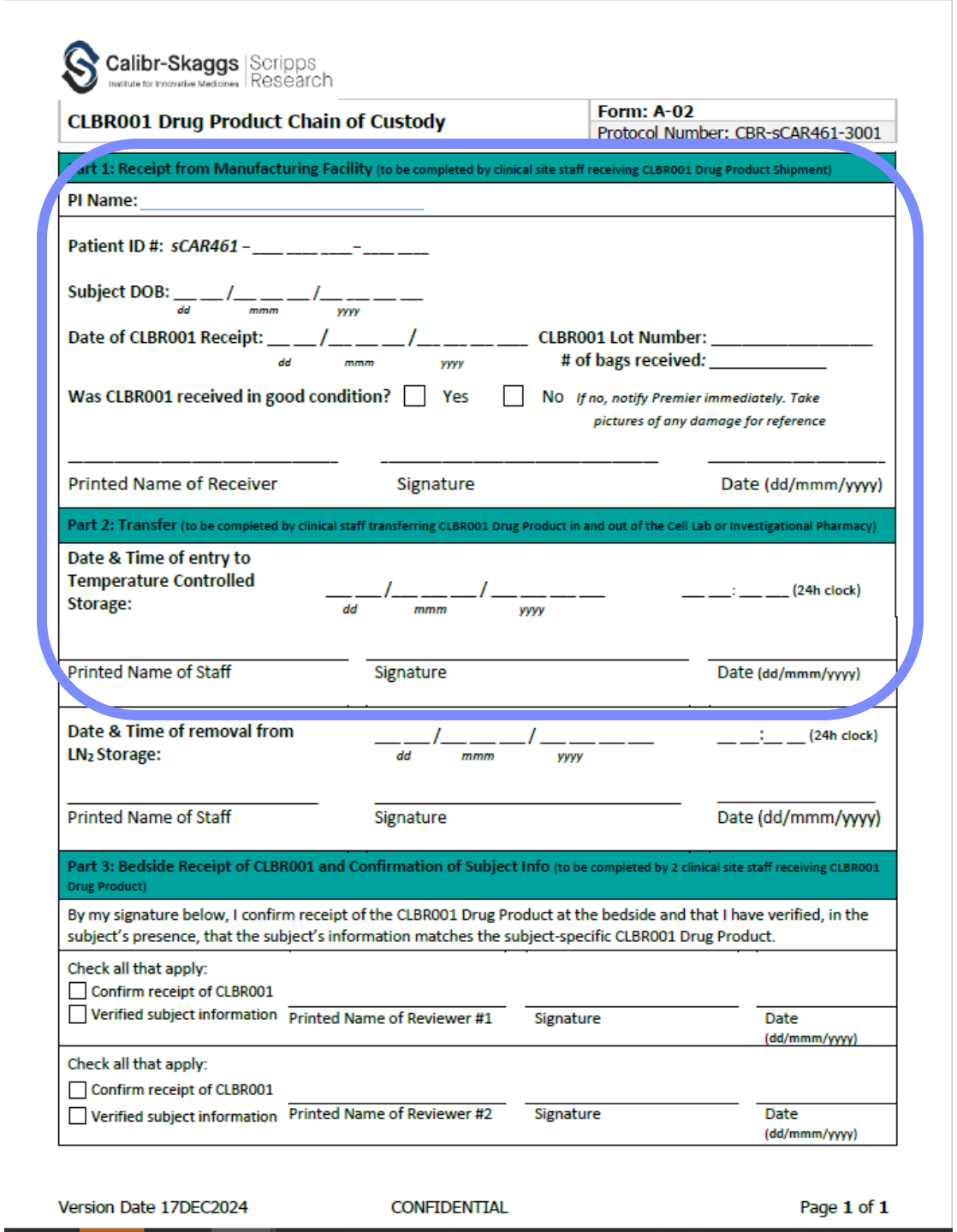
This document copy was retrieved on 03 May 2024 09:47AM GMT-07:00
FORM-Rev 3 (NOV2021)

CLBR001 RECEIPT + STORAGE

- Upon receipt of the CLBR001 product, CTL will inspect the shipper to ensure no visible damage.
- Document receipt of product by completing Parts 1 & 2 of **Form A-02: CLBR001 Drug Product Chain of Custody Form**.
  - Email copy to sCAR461.Clinical@premier-research.com after Parts 1 & 2 completed.
  - Part 3 will be filled out later, before dosing.



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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: ___ ___ / ___ ___ ___ / ___ ___ ___ ___ (dd / mmm / yyyy) CLBR001 Lot Number: _____

# 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 Temperature Controlled Storage: ___ ___ / ___ ___ ___ / ___ ___ ___ ___ (dd / mmm / yyyy) ___ ___ : ___ ___ (24h clock)

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

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

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 17DEC2024 CONFIDENTIAL Page 1 of 1

CLBR001 RECEIPT + STORAGE

- Transfer the CLBR001 product from the LN2 Dry Shipper within 1 business day of CLBR001 product arrival at site.
  - Two independent reviewers must verify the information between **Form A-02: CLBR001 Drug Product Chain of Custody Form** and **Form VV-QUAL-02814 QA Release for Final Product to Client**.
  - Confirm the information on the label on the cassette matches the **Form VV-QUAL-02814 QA Release for Final Product to Client**.
    - Do not open the cassette or thaw until ready to infuse.
- Store the CLBR001 product in the vapor phase of LN2 according to standard site practice.
- Complete steps 1-4 on page 1 of the **CLBR001 Checklist**.

CLBR001 RECEIPT + STORAGE

- If not provided via email from Cryoport at time of delivery, please ensure a copy of the **temperature summary** during transport is obtained from Premier Research.
  - Forward the summary or provide a copy to the study coordinator.
- Within 1-2 business days after transferring CLBR001 product from LN2 Dry Shipper to LN2 vapor phase, prepare the LN2 Dry Shipper for return to vendor.
  - See Appendix 8 in the **Leukapheresis + CLBR001 Manual** for instructions.

CLBR001 THAWING + PREPARATION

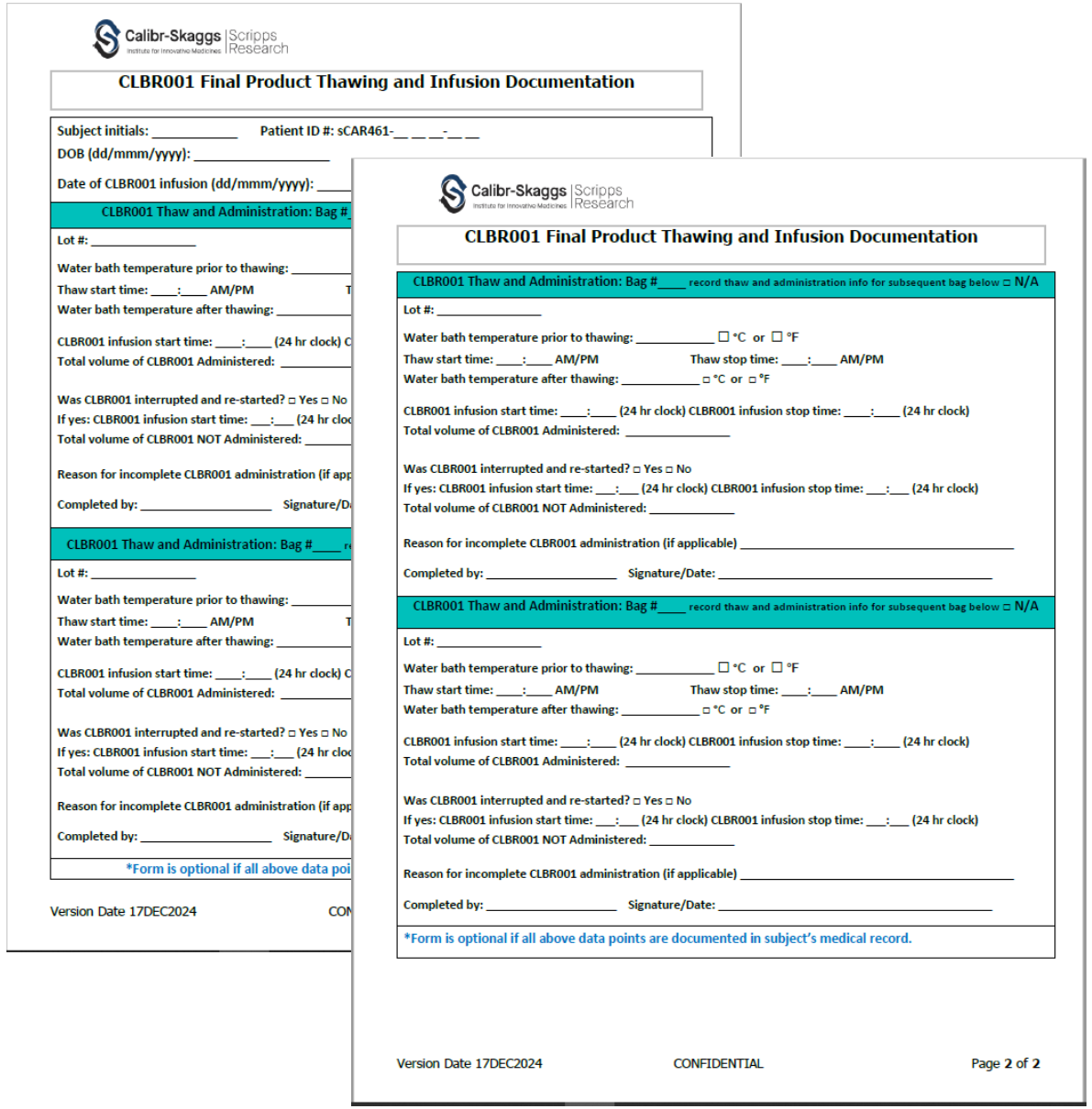
- Thawing will occur immediately prior to scheduled infusion.
  - Time between product thawing and COMPLETION of infusion should not exceed 2 hours.
- Follow site processes to authorize transfer of CLBR001 product to hospital unit.
  - Complete Part 3 of **Form A-02: CLBR001 Drug Product Chain of Custody Form** after confirming study subject's information matches the form.
    - Please note that Part 3 must be done in the presence of the subject, with 2 independent reviewers.
    - Email a copy to sCAR461.Clinical@premier-research.com and provide original to study coordinator.
  - Complete steps 5-11 on page 2 of the **CLBR001 Checklist**. Give the CLBR001 Checklist to the nursing staff with CLBR001 product.

CLBR001 THAWING + PREPARATION

- Thaw the CLBR001 product, with extreme care, in a 37.1C water bath near patient's bedside.
  - Thawing takes 2-5 minutes depending on bag size.
  - Massage to increase thaw rate if necessary.
  - After thawed, remove the bag from the water bath and invert 5 times to gently mix.
  - If multiple bags are involved, remove, thaw, and infuse **one bag at a time**.

CLBR001 THAWING + PREPARATION

- Document the process on **Appendix 11: CLBR001 Final Product Thawing and Infusion Documentation**.
  - Provide copy to study coordinator.



Calibr-Skaggs | Scripps Research

CLBR001 Final Product Thawing and Infusion Documentation

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

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 ☐ 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.

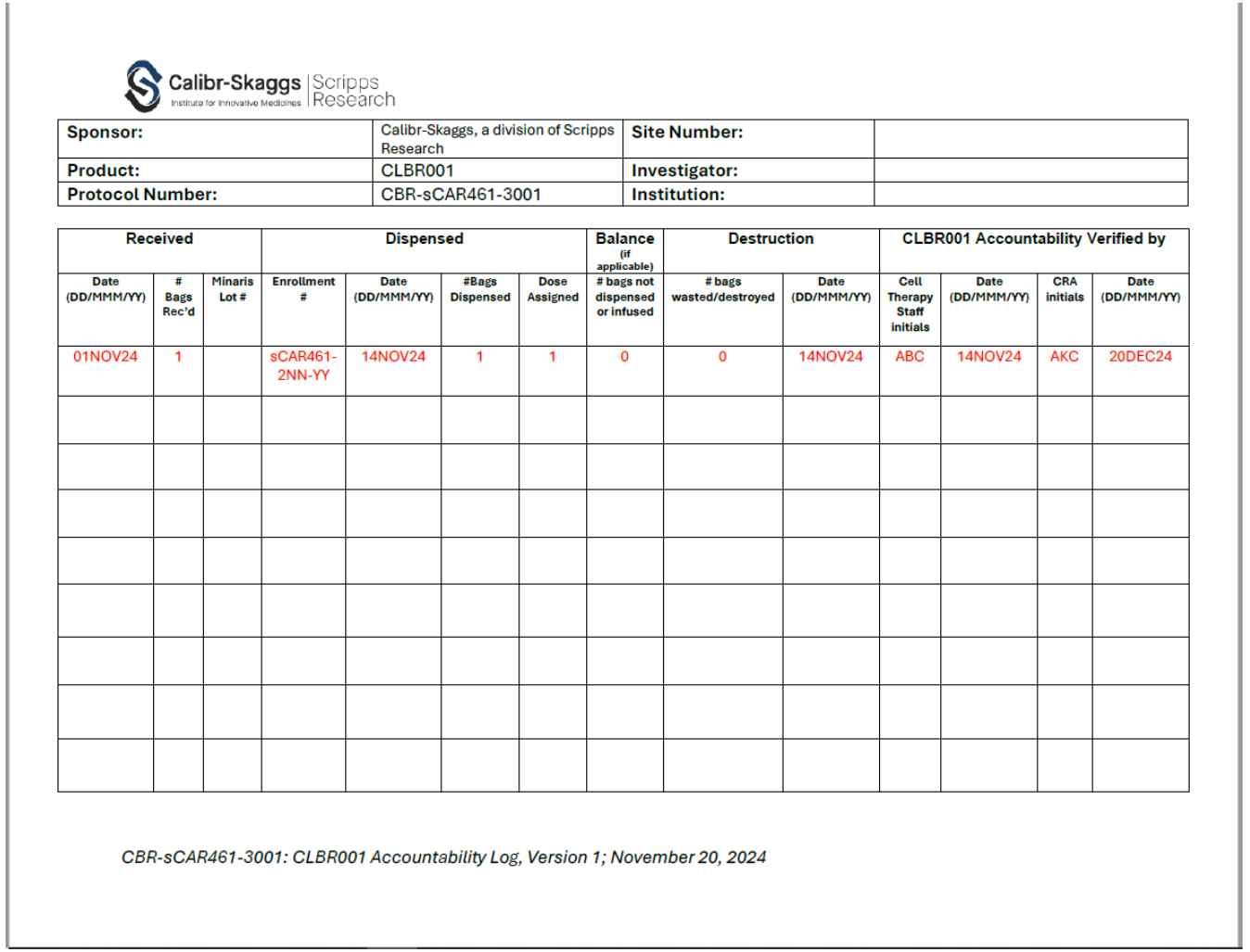
Version Date 17DEC2024 CONFIDENTIAL Page 2 of 2

CLBR001 THAWING + PREPARATION

- Post-thaw, remove the CLBR001 drug product bag from steriZip overpouch.
- If any tears or holes, document observations, take pictures of damage, and report immediately to Premier Research via sCAR461.Clinical@premier-research.com and the study coordinator at IU.
  - Study coordinator at IU will complete a CLBR001 Incident Report Form.
- Do NOT administer the drug product until clearance is received from the sponsor/Premier Research.

CLBR001 ACCOUNTABILITY

- Maintain **CLBR001 Accountability Log** for entire trial.
  - Ensure it is readily available for monitoring.
  - Scan via email to study coordinator when requested.



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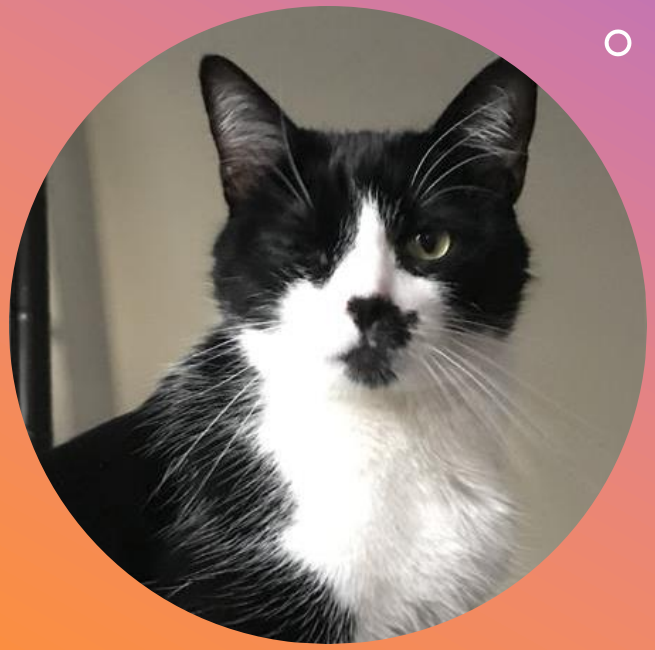
Sponsor:	Calibr-Skaggs, a division of Scripps Research	**Site Number:**	
Product:	CLBR001	**Investigator:**	
Protocol Number:	CBR-sCAR461-3001	**Institution:**	

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 20, 2024



Dave

QUESTIONS?