INVESTIGATIONAL PRODUCT MANUAL (IPM)

Investigational Product Name:
cemacabtagene ansegedleucel (cema-cel)

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1. IPM GLOSSARY

ABBREVIATION	DEFINITION OF TERM
CAR T	Chimeric Antigen Receptor T-Cell
cema-cel	cemacabtagene ansegedleucel
CoA	Certificate of Analysis
CoC	Chain of Custody
CoI	Chain of Identity
CRA	Clinical Research Associate
CSTD	Closed System Transfer Device
ICF	Informed Consent Form
IP	Investigational Product
IPM	Investigational Product Manual
IRT	Interactive Response Technology
ISF	Investigator Site File
LD	Lymphodepletion
LN_2	Liquid Nitrogen
SID	Subject ID

2. INTRODUCTION

This Investigational Product Manual (IPM) provides guidance for Investigational Product (IP) ordering, receipt, storage, management, preparation, administration, and accountability.

The IPM should be utilized in conjunction with the associated study protocol.

3. INVESTIGATIONAL PRODUCT

In this IPM, IP refers to cemacabtagene ansegedleucel (also known as ALLO-501A) and hereafter referred to as cema-cel).

3.1. DESCRIPTION OF CEMA-CEL

Cema-cel is a pre-manufactured, TCRαβ depleted T-cell suspension designed to become active, proliferate, secrete cytokines, and kill CD19+ B cells following administration to lymphodepleted participants with B-cell malignancies. Further details on cema-cel may be found in the cema-cel Investigator's Brochure.

3.2. CEMA-CEL PRESENTATION

Cema-cel is supplied as a frozen cell suspension, packaged in a clear plastic 2 mL vial with an elastomeric stopper, and plastic snap-fit cap. Each vial of cema-cel contains an **extractable volume of 1 mL at a concentration of 20 x 10^6 CAR+ cells/mL** and are for single use only.

The cema-cel dosage form is composed of CAR+_TCRαβ−_CD52+/− CAR T cells formulated at 20 × 10^6 viable CAR+ T cells/mL. The cells are formulated in a 1:1 mixture of CryoStor® Basal solution and CryoStor CS10 solution resulting in a final concentration of 5% dimethyl sulfoxide (DMSO).

The cema-cel packaging configuration is 6 vials, packaged in an outer carton that measures approximately 7.1 x 4.7 x 4.1 cm.

3.3. CEMA-CEL LABELING

Cema-cel is labeled in accordance with the International Conference on Harmonization/ Guideline for Good Clinical Practice and applicable regulatory requirements.

Cema-cel kits have product labels affixed to them including kit numbers and lot numbers. The lot numbers should match the lot number listed on the cema-cel vials.

Cema-cel vials have product labels directly affixed to them, with lot numbers that must be correctly matched to the intended subject ID (SID) prior to administration.

Label examples are provided in **APPENDIX 1.** CEMA-CEL LABELS

4. ALLO PARTICIPANT PATHWAY

The ALLO Participant Pathway encompasses a participant's time on an Allogene study, beginning when they are identified as a potential participant through infusion (or randomization into an observation arm, as applicable per study design).

ALLO Participant Pathway milestones will be documented on respective study forms or within an Interactive Response Technology (IRT) system, to capture enrollment progress and/or IP traceability as a participant proceeds through the study.

Prior to site activation, clinical site staff should designate a responsible party (or parties) to manage the identification, screening, and enrollment of study participants. This responsibility may include participant registration, completion of study forms, treatment scheduling and communication to sponsor, randomization, IP receipt and reconciliation.

The following ALLO Participant Pathway milestone activities may impact IP shipment planning and ordering as detailed in the following sub-sections.

4.1. SCREENING

During screening, it is crucial that a tentative participant treatment schedule is considered and communicated to Allogene. Tentative treatment scheduling communication will ensure IP shipments are planned in advance to support treatment schedule and institutional requirements for IP shipment deliveries. It is the responsibility of the institutional Principal Investigator to assess and confirm participant eligibility per protocol requirements during screening.

4.2. ENROLLMENT

Allogene Medical Monitor acknowledgment is required to formally initiate a participant's cema-cel shipment to the clinical site. Formal participant enrollment is required to initiate a participant's IP shipment to the clinical site.

4.3. RANDOMIZATION, IF APPLICABLE

For studies where randomization occurs per protocol, randomization must be completed after Allogene Medical Monitor acknowledgement to confirm if a cema-cel shipment is required to support participant treatment.

4.4. LYMPHODEPLETION, IF APPLICABLE

For studies where lymphodepletion is required per protocol, or when a participant is randomized to receive lymphodepletion (e.g. ALPHA3), IP will be scheduled for delivery to the clinical site **after** lymphodepletion begins and will arrive prior to scheduled infusion date.

Note: If institutional procedure requires IP to be onsite prior to lymphodepletion, notify Allogene via study-distribution list.

Reference the following documents for more details:

- Study-specific protocol for more information regarding lymphodepletion regimen and requirements.
- ALLO-647 IPM for more information specific to ALLO-647 investigational product that will be provided by Allogene.

5. CEMA-CEL ORDERS AND INVENTORY MANAGEMENT

Cema-cel is sent as a single, participant-specific treatment shipment and **will not be resupplied for an individual participant**, unless damaged or not used within the allotted timeframe.

Clinical sites **will not** have cema-cel inventory to manage onsite.

Allogene or designee (hereafter referred to as Allogene) will place the cema-cel order based on the participant treatment timeline and confirm shipment details upon enrollment.

6. CEMA-CEL SHIPMENTS

Transportation of cema-cel, including courier scheduling, import and/or export, will be managed by Allogene as appropriate to support participant activity for the study.

Prior to delivery at the clinical site, staff must ensure:

- Correct delivery location and details have been provided to Allogene.
- Confirmation of IP storage option selected for site, e.g. storage in liquid nitrogen (LN_2) shipper, or transfer to onsite LN_2 vapor phase freezer.
- Appropriate staff are available to confirm receipt of shipment.

6.1. IP SHIPPER

Cema-cel shipments will be cryopreserved and shipped in an LN_2 shipper to the clinical site.

The LN_2 shipper is a liquid nitrogen dry vapor shipper, containing an inner dewar housed by an outer box. The inner dewar is surrounded by fleece lining with insulating properties and uses LN_2 as a coolant in the specimen chamber to maintain internal temperatures below -150 °C.

The dewar dimensions measure approximately 14.75” x 14.75” x 26.75” (37.5 cm x 37.5 cm x 67.9 cm) and weighs approximately 25 lbs / 12 kg.

Figure 1. cema-cel dewar reference

6.2. IP SHIPMENT AND TEMPERATURE MONITORING

A Smartpak II monitoring system is integrated with the LN_2 shipper to provide near real time tracking. Tracking features include the monitoring of location, and measurement of temperature, pressure, humidity, orientation, shock, light, and shipper battery life. The Smartpak II monitor will record the internal temperature of the dewar for the duration of the product transport and until the IP is removed from the shipper. Once IP is removed from the shipper, the clinical site is responsible for temperature monitoring oversight.

When IP shipments are initiated, clinical sites will receive an email with a link for online access to the Smartpak II Live View features. Instructions on how to review and download the temperature report are provided in the Unpacking and Return Instructions document included within the outer shipment box of the LN_2 shipper.

6.3. IP SHIPMENT DOCUMENTS

The following documents will accompany the cema-cel shipment:

- cema-cel packing slip
- Courier Airway Bill
- Unpacking and Return Instructions
- Inclusion of batch documents, including CAR T Drug Product Certificate of Compliance, Leukapheresate Certificate of Analysis (CoA), and for donor material sourced from Charles River Lab Cell Solutions, Donor Eligibility Determination Form
- Courier return label (for shipper return)

The following documents may also be included for some studies:

- Commercial invoice (international shipments only)
- FRM-0088, Clinical Product Chain of Custody | vLN_2 Shipments (when product receipt is not managed via IRT)

Document examples may be referenced in **APPENDICES APPENDIX** 2. CEMA-CEL PACKING SLIP**APPENDIX 5.** COMMERCIAL INVOICE (INTERNATIONAL SHIPMENTS ONLY).

6.4. LOST OR DELAYED SHIPMENTS

Allogene will monitor the progress of IP shipments and will inform the clinical site if the shipment is delayed in transit or lost.

Clinical sites should also monitor the progress of IP shipments via Smartpak II Live View and notify Allogene via the study distribution list if a shipment does not arrive.

Allogene will initiate a replacement shipment to the site for lost or delayed shipments as needed.

7. CEMA-CEL RECEIPT AT CLINICAL SITE

Upon receipt of the cema-cel LN_2 shipper, **two** designated staff are required to confirm and verify receipt of shipment. Clinical site staff must complete chain of custody documentation upon receipt and removal of IP from shipper.

Designated staff should perform the following unless otherwise guided by institutional procedures:

- Carefully transport the shipper to a storage or unpacking location, utilizing a dolly (or alternative) as needed to move the shipper to an area free from other samples or participant materials as best as possible.
- The shipper should be tilted as minimally as possible during transport to location to avoid initiating a temperature excursion.
- Check the outer shipper for any obvious or visible damage, i.e. broken shipper. If damage is identified, notify Allogene via the study distribution list as soon as possible.
- Log into Smartpak II Live View and confirm whether the IP was maintained at the required temperature while in transit.

IP vial inspection should **only take place at the time that the product is removed from the LN_2 shipper.**

Note: If any expected documents or the courier return label are not included in the shipper, contact Allogene via the study distribution list to obtain the missing item(s).

Copies of all packing and shipping documents, including shipment temperature records must be filed within the Investigator Site File (ISF) or Pharmacy Binder.

7.1. IP REMOVAL FROM LN_2 SHIPPER

Utilize the Unpacking and Return Instructions provided for detailed guidance for unpacking the IP vials. IP receipt documentation will require **two** different signatures to complete and verify the receipt.

The responsible clinical site staff must inspect and inventory the shipment to ensure contents match the accompanying shipping manifest, the IP was maintained at the required temperature while in transit (and/or shipper storage as applicable), and the IP carton(s) and/or vials are neither damaged nor have visual anomalies and are acceptable for dispensing.

Upon completion of IP inspection, clinical site staff must submit completed chain of custody documentation and temperature report to Allogene.

Copies of all packing and shipping documents, including shipment temperature records must be filed within the Investigator Site File (ISF) or Pharmacy Binder.

7.2. DAMAGED OR INCOMPLETE IP SHIPMENTS

If upon inspection, it is noted that the shipper and/or IP appear damaged or missing, immediately quarantine the supply and notify Allogene. Allogene will evaluate the notification and may require additional information from the clinical site. Disposition instructions will be provided to the clinical site.

Clinical sites must **not use the quarantined product** until disposition instructions are received from Allogene.

Allogene will initiate a replacement shipment to the site for lost, damaged or misplaced shipments, as necessary.

7.3. IP SHIPPER RETURN

The LN_2 shipper and the Smartpak II monitoring device should be returned to the depot within 2 business days of removing IP from the shipper.

To return the empty LN_2 shipper, use the pre-printed courier label provided and follow the Unpacking and Return Instructions provided with the shipment for return to courier.

Note: If a return label is not provided, please contact Allogene via the study distribution list to request.

8. CEMA- CEL STORAGE AND HANDLING

8.1. PRODUCT STORAGE

Cema-cel must be stored at a temperature ≤ -135 °C. Avoid cema-cel vial exposure to direct sunlight and ultraviolet light.

Clinical sites are provided two storage options for cema-cel storage:

1. IP may be stored in the LN_2 shipper until ready to prepare for participant dose.
2. IP may be transferred to an onsite LN_2 vapor phase freezer.
    a. **Note**: Onsite freezer must be approved by Allogene, or designee, prior to use for storage.

8.1.1. IP STORAGE: LN_2 SHIPPER

When storing IP in the LN_2 shipper until dose preparation, the clinical site is responsible for ensuring that the storage location can accommodate the shipper (see **Section 6.1** for shipper dimensions).

The LN_2 shipper should be stored in a secure location that adheres to institutional and local requirements for IP storage.

Notes:

- To preserve the integrity and temperature of the IP vials, the tamper evident seal on the shipper should not be broken until the time of thaw for dose preparation.
- Allogene will schedule IP delivery and monitor LN_2 shipper validation in accordance with participant treatment timeline to ensure IP and shipper remain within acceptable temperature range.
    - If there are any delays in treatment, contact Allogene via the study distribution list for further guidance.

8.1.1.1. TEMPERATURE MONITORING AT CLINICAL SITE FOR LN_2 SHIPPER STORAGE

The Smartpak II will continuously monitor, log, and display the near real time temperature in the shipper. At a minimum of once a day, clinical site staff are required to review the Smartpak II temperature data for any temperature excursions and verify temperature remains in range, per institutional guidance.

In the event a temperature excursion is detected by the Smartpak II, Allogene will receive an email notification and will also notify the clinical site. Please refer to Section 16 for more information on temperature excursions.

When reviewing the Smartpak II dashboard via the Live View service, it is important to note the material dispatch and receipt date/time to verify any temperature excursions.

Note: Any visible excursions outside of these times will be due to the opening of the unit prior to the material being packed. Any temperature excursions within the material dispatch and receipt date/time should be investigated.

8.1.2. IP STORAGE: ONSITE LN_2 VAPOR PHASE FREEZER

If IP will be stored in the clinical site's LN_2 vapor phase freezer until dose preparation, the use of the clinical site's LN_2 vapor phase freezer must be approved by Allogene prior to use, e.g., during the site qualification or initiation process (PSSV & SIV).

The clinical site is expected to provide the following information at a minimum:

- Location of the LN_2 vapor phase freezer
- Most recent LN_2 calibration certificate
- Temperature Monitoring/Excursion SOP
- IP Storage/Transport SOP
- IP Destruction SOP (if applicable)

IP must be stored in a monitored and calibrated LN_2 vapor phase freezer that is maintained at a temperature of ≤ -135°C.

IP must be transferred to the clinical site's LN_2 vapor phase freezer immediately to ensure product temperature is maintained.

8.1.2.1. TEMPERATURE MONITORING AT CLINICAL SITE FOR ONSITE LN_2 VAPOR PHASE FREEZER

The clinical site is responsible for documenting applicable information associated with the transfer of IP from the LN_2 shipper to the LN_2 vapor phase freezer, as applicable for study, i.e. within IRT or via documentation.

8.2. IP HANDLING

8.2.1. PRODUCT TRANSPORT

Transportation of cema-cel within an institution should be minimized to the extent possible and should adhere to institutional guidelines.

For clinical sites that have an off-site location or separate buildings for storage, preparation and/or administration of IP, an IP transport procedure must be provided to Allogene for review.

At minimum, the procedure should identify:

- Transportation steps
- Method of transport

- Description of the transport container
- Process to maintain/record temperature during the transit time.
- Method to log departure and arrival times.

For cema-cel, transport procedures should take into consideration the requirement for the product to be infused within 2 hours from the thaw start time.

Note: Thaw start time begins upon removal from LN2 storage/shipper, **not** thaw in water/dry bead bath.

8.2.2. SPECIAL HANDLING AND SPILL MANAGEMENT

Only qualified personnel who are familiar with procedures that minimize undue exposure to themselves and to the environment should undertake the preparation, handling, and safe disposal of cema-cel.

Cema-cel contains live human cells and is considered a biohazardous agent. Avoid splashes or aerosols. Avoid contact with eyes, skin, and clothing. When handling, use appropriate personal protective equipment and follow local site procedures. Ensure hands are washed thoroughly after handling.

Cema-cel is classified as Risk Group 1. To ensure adequate sterility and safety of the final product administered to the study participant, all handling and preparations of products are, although not required, but recommended to be carried out in a ClassIIA1 or higher-level Biological Safety Cabinet (BSC).

Note: If ClassIIA1 or higher-level BSC is not available at the clinical site, laminar air flow hoods are allowed only after being endorsed by Allogene.

If a spill occurs at any point during the handling of IP, the area should immediately be quarantined to prevent inadvertent exposure or tracking of product to other areas and local/institutional procedures should be followed. Local/institutional procedures and documentation of staff training must be available for review by the study monitor/Clinical Research Associate (CRA).

Spill kits that contain decontamination solution as well as appropriate disposable PPE and spill cleaning materials **MUST** be available at all times when handling IP. After containment of the spill, decontaminate the area according to your standard local procedures.

8.2.3. ENVIRONMENTAL EXPOSURE

The effect of cema-cel on a fetus is unknown. If a pregnant health care worker is exposed to cema-cel (e.g., by inhalation or spillage), the investigator must submit information regarding the exposure to Allogene within 24 hours of awareness.

If a male healthcare worker is exposed to cema-cel (e.g., by inhalation or spillage) prior to or around the time of conception and/or is exposed during his partner's pregnancy the investigator must submit information regarding the exposure to Allogene within 24 hours of awareness.

In all cases, the information submitted should include the anticipated date of delivery.

Refer to local and institutional guidelines and policies for injuries, including needle sticks, related to the handling and preparation of cema-cel.

9. CEMA-CEL PREPARATION

Only delegated clinical site personnel who are appropriately trained on the procedures detailed in this document may perform the preparation and administration steps specified in this IPM. Clinical site personnel involved in these steps must comply with all applicable regional and institutional regulations and standards.

A supplemental 'Dose Preparation Instructions' video which includes a visual representation of vial thawing, and preparation guidelines for cema-cel is available for reference. Please reach out to Allogene via the study distribution list to receive access.

IMPORTANT: If during IP preparation, the cema-cel vials are noted to be in any way damaged, notify Allogene via study distribution list.

Reference **Section 11. CEMA-CEL DOSE PREPARATION** for detailed instructions.

9.1. EQUIPMENT AND SUPPLIES

The following equipment and supplies will be needed for IP preparation and administration.

Clinical sites are responsible for ensuring that these supplies, or equivalent, are available prior to product preparation.

Equipment/Item	Description
Luer lock latex-free polypropylene syringes	To be used for the preparation and infusion of cema-cel. Use a 10 mL Luer lock latex-free polypropylene syringe with volume gradation of 0.1 mL or 0.2 mL. Larger syringes with volume gradations greater than 0.2mL are not recommended.
IV catheter, central or peripheral	Use a 20 or wider Gauge (G) IV catheter. 18 G is preferable. **Use of a needleless connector is preferred and primarily used for luer lock syringe infusion of cema-cel**.

Equipment/Item	Description

Dispensing needles with luer lock connection	• **Cema-cel Withdrawal**: To be used for the withdrawal of cema-cel product into the luer lock latex-free polypropylene syringes. Stainless steel needles with a bore size 18 Gauge (G) x 1 ½ inch for withdrawal of the product from the vial into syringe.
	• **Cema-cel Administration:** To be used for administration of cema-cel. Stainless steel needles with bore size 20 Gauge (G) x 1 inch or longer for administration.
	  ○ **Preferred Administration Option:** A needleless luer lock connection between the syringe and IV connector is preferred as a primary option for administration.
	  ○ **Alternative Administration Option:** If a needless connection is not available, the secondary option, only if safety IV catheter line cannot be secured and subcutaneous venous port is the only IV line, 20G or smaller # G dispensing needle can be used to stick into the port and infuse cema-cel.
	• **DO NOT USE A FILTER AT ANY PART OF IV INFUSION LINE.**
	Important Note: Always confirm the appropriate gauge of dispensing needles are being used with luer lock. For the port or long extension infusion of cema-cel, ensure the entire IV line is flushed with normal saline after cema-cel infusion is complete.

Thawing equipment	37°C water bath (or Plasmatherm) or 37°C dry bead bath with a calibrated thermometer or thermo-probe.
Plastic bag	If using a water bath to thaw cema-cel vials, a **flexible plastic bag** (e.g. Nasco Whirl-Pak®: Material of Construction-Polyethylene blend) is required. Frozen cema-cel vials will be placed in the plastic bag prior to placing in the water bath for thawing.
Important Note: Closed System Transfer Devices (CSTDs) designed to connect to traditional glass vials are not compatible with cema-cel vials. Therefore, these type of CSTDs are not allowed for cema-cel transfer to the syringe.	

9.2. IP THAW

Ensure that all the materials and required equipment are available before starting dose preparation. **Do not remove vials from frozen storage until immediately prior to preparing the dose.**

Ensure the frozen storage for the vials is in the vicinity of the thawing equipment. The temperature of the thawing equipment should have achieved setpoint of 37 °C **prior to start of thaw.**

Important Note: Vials of cema-cel must be stored frozen in a vapor phase liquid nitrogen (vLN_2) freezer at ≤ -135 °C and kept in the original packaging prior to use in dose preparation.

9.2.1. THAWING BY WATER BATH

1. Obtain the vials required for dose preparation from LN_2 storage. Reference **APPENDIX 7.** CALCULATION OF DOSE NUMBER AND VIALS.
2. Immediately place the vials at the bottom of the required plastic bag, removing all air from the bag, and fully submerge the closed bag with the vials in the 37 °C water bath.
    a. **Note:** No more than 6 vials should be placed in a single plastic bag. Use separate bags for thawing more than 6 vials
    b. **Do not** leave vials unattended in the 37 °C bath.
3. Visually observe the vials during thaw and immediately remove from the bath when only a small ice crystal is observed or no more ice is visible in the vials.
4. Total thaw time should take approximately 12 to 14 minutes, and **no more than 16 minutes.**
    a. Individual vial thaw times may vary slightly but should not vary greater than 2 minutes.
    b. After 7 minutes of thaw duration, vials should be checked every few minutes.
    c. Individual vial should be removed promptly from the bath once the thaw is complete.
    d. Vials should **not** be stored in 37 °C bath after complete thaw.
5. Wipe the outside of thawed vials with alcohol wipes and place in the dose preparation area.

9.2.2. THAWING BY DRY BEAD BATH

1. Obtain the vials required for dose preparation from LN_2 storage. Reference **APPENDIX 7.** CALCULATION OF DOSE NUMBER AND VIALS.
2. Immediately place the vials completely submerged in the beads.
    a. **Note:** No bag is required for thawing via dry bead bath.
    b. **Do not** leave vials unattended in the 37 °C bath.
3. Visually observe the vials during thaw and immediately remove from the bath immediately when only a small ice crystal is observed, or no more ice is visible in the vials.
4. Thawing of vials in dry bead bath should take approximately 10 minutes, **and no more than 14 minutes**.
    a. Individual vial thaw times may vary slightly but should not vary greater than 2 minutes.
    b. After 7 minutes of thaw duration, vials should be checked every few minutes.
    c. Individual vial should be removed promptly from the bath once the thaw is complete.
    d. Vials should **not** be stored in 37 °C bath after complete thaw.
5. Wipe the outside of thawed vials with alcohol wipes and place in the dose preparation area.

9.2.3. THAWING BY PLASMATHERM

1. Obtain the vials required for dose preparation from LN_2 storage. Reference **APPENDIX 7.** CALCULATION OF DOSE NUMBER AND VIALS.
2. Immediately place the vials in between the two pre-warmed, sealed water bags.
    a. **Do not** leave vials unattended in the 37 °C Plasmatherm.
6. Visually observe the vials during thaw and immediately remove from the Plasmatherm when only a small ice crystal is observed, or no more ice is visible in the vials.
7. Thawing of vials in Plasmatherm should take approximately 11-15 minutes, **and no more than 17 minutes**.
    a. Individual vial thaw times may vary slightly but should not vary greater than 2 minutes.
    b. Vials should be monitored closely throughout the thaw.

c. Individual vial should be removed promptly from the Plasmatherm once the thaw is complete.

d. Vials should **not** be stored in 37 °C Plasmatherm after complete thaw.

8. Wipe the outside of thawed vials with alcohol wipes and place in the dose preparation area.

9.3. POST THAW IP REQUIREMENTS

Vials should be inverted 180° clockwise and then anticlockwise 3 times to mix cell suspensions **(DO NOT SHAKE).** Clinical site staff should verify that there are no large visible clumps in the suspension and rotate 3 additional times to disperse clumps, if needed.

Vials that are thawed and **not used immediately** should be inverted 180° clockwise and then anticlockwise 3 times to mix cell suspension **(DO NOT SHAKE)** immediately prior to dose withdrawal into the syringe in addition to initial inversion after thaw.

Note: If large clumps are still visible after mixing by inversion, the vial must be retained and not used for administration. Notify Allogene via study distribution inbox immediately so that a re-supply order may be initiated.

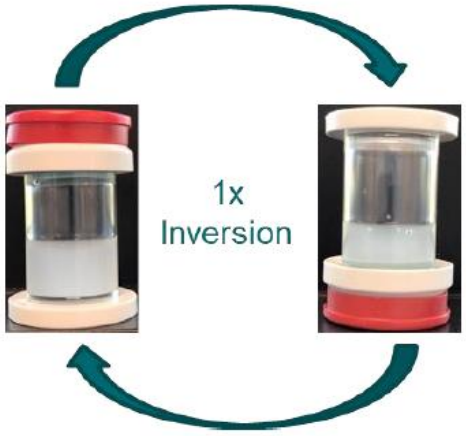


Figure 2. Illustration of vial inversion to mix cell suspension immediately prior to dose withdrawal into single syringe.

Once the vial caps are removed, dose preparation must continue to completion **without interruption.**

10. CEMA-CEL DOSE GUIDANCE

10.1. PREPARED IP DOSE GUIDANCE

Avoid cema-cel vial exposure to direct sunlight and ultraviolet light. Preparation and administration may take place under normal room lighting conditions.

Prepared dosing solutions, including thawed vials **should be used immediately**.
If they cannot be used immediately, the thawed vials or prepared dosing solution may be kept at room temperature for a **maximum of 2 hours*** (up to 25 °C (77 °F)) from the removal of IP from LN_2 storage, e.g. start of thaw, until the start of administration, including any line flush.

***Note:** The maximum "in-use time" for cema-cel is 2 hours from thaw. "In-use time" is defined as the time from when cema-cel vials are removed from LN_2 storage/shipper until the start of IP administration.

Important: Do not refrigerate prepared dosing solution and do not re-freeze thawed vials.

If the dosing solution is left at room temperature for more than the in-use period of 2 hours from the start of thaw time, discard and do not use the solution.

If the in-use time has been exceeded, new vials will need to be ordered and the preparation of the dosing solutions will need to be repeated.

Unused (unopened) cema-cel product vials that have been thawed cannot be returned to storage and **should** be discarded following institutional and local guidelines.

Dosing solutions should be allowed to reach room temperature prior to administration. Clinical site staff should ensure the prepared dosing solution in its container is not cold to the touch.

10.2. CALCULATION OF DOSE VOLUME AND NUMBER OF VIALS

For calculation of dose volume and number of vials, please reference **APPENDIX 7.** CALCULATION OF DOSE NUMBER AND VIALS

10.3. DOSE MODIFICATIONS

There is no dose modification from the assigned dose for cema-cel. Every effort should be made to administer cema-cel at the planned dose and per the schedule defined within the study protocol.

11. CEMA-CEL DOSE PREPARATION

The preparation and administration of all sterile products must be performed using aseptic technique, including but not limited to: ensuring the work area is clean, minimizing contact with nonsterile surfaces, minimizing introduction of particulate matter or biological fluids and preventing mix-ups of materials.

All handling and preparations of products are, although not required, but recommended to be carried out in a ClassIIA1 or higher-level Biological Safety Cabinet (BSC).

Note: Handling and preparations without BSC are allowed only after being endorsed by the sponsor.

11.1. IP DOSE PREPARATION SUPPLIES REQUIRED:

- cema-cel vials (no more than required for dose preparation)
- Alcohol wipes
- Sterile 10 ml polypropylene syringe
- 18G sterile needle, 1 ½ inch or longer needed.
- Institutional label(s) required per clinical site's institutional requirements to label prepared syringe.
    - If an institutional label cannot be provided, please notify Allogene for alternative labeling options.
- Discard container, as needed.
- cema-cel (ALLO-501A) Administration Form **(APPENDIX 8.** CEMA-CEL ADMINISTRATION FORM
- cema-cel (ALLO-501A) Accountability Log **(APPENDIX 9.** CEMA-CEL ACCOUNTABILITY LOG

11.2. DOSE PREPARATION INSTRUCTIONS

The following dose preparation instructions should be completed using aseptic techniques, including minimizing contact with nonsterile surfaces, avoiding the introduction of particulate matter or biological fluids and preventing material mix-ups.

Note: Prior to preparing dose, ensure the working area is clean. All vials will be drawn up (pooled) into a single syringe.

1. Obtain and assemble a sterile 10 mL polypropylene syringe and 18G, 1½ inch or longer needles for withdrawing the required dose volume (6 mL) (leaving the needle cap **on** until withdrawal).

2. Invert each vial 3 times to mix cell suspension (**DO NOT SHAKE**) immediately prior to dose withdrawal into the syringe.
    a. Verify that there are no large visible clumps in the suspension of each vial.
3. Remove the plastic vial cap **on all six vials** and wipe the rubber stoppers with alcohol wipes.
    a. **IMPORTANT:** Once the vial caps are removed, dose preparation must continue to completion **without** interruption or delay to minimize risk of contamination.
4. Place the vial in the upright position first and gently insert the needle through the rubber stopper.
5. Invert the vial (Figure 2) and carefully position the tip of the needle just beneath the liquid surface.
6. 

Figure 3. *Image of cema-cel vial positioned upside down while withdrawing dose*

7. Gradually and steadily withdraw the vial contents while ensuring the needle remains submerged to prevent the formation of air bubbles.
8. Withdraw the contents of each vial using the **same syringe and 18G needle.**
9. Prior to transitioning to the next vial, expel as much air as possible from the syringe.
    a. Six vials will be required and will be drawn up (pooled) into a single syringe consecutively without delay.
10. After the last vial contents are withdrawn and before removal of the 18G needle, ensure the residual hold-up of the needle is pulled into the syringe. Ensure the required total dose volume of 6 mL is in the syringe.
11. Remove and discard the 18G needle.
12. Use a sterile cap to cover the tip of the syringe until ready for administration.
13. Record the dose volume in the syringe on the cema-cel (ALLO-501A) Administration Form.
14. Adhere applicable institutional label(s) to the prepared syringe as per clinical site's institutional requirements.

12. CEMA-CEL ADMINISTRATION

12.1. INTRAVENOUS (IV) ADMINISTRATION PREPARATION

Prior to dosing the participant, adhere to normal standard of care and aseptic techniques per site policies and procedures. Ensure the prepared dosing solution is at room temperature prior to administration.

Cema-cel should be administered by bolus IV injection over a period of approximately 5 -10 minutes. Cema-cel must be administered within 2 hours of the start of thaw (i.e. removal from LN_2 storage or shipper).

12.2. IV ADMINISTRATION INSTRUCTIONS

1. Obtain the prepared dose syringe and connect to luer lock IV connector (in the case of administration via subcutaneous venous port), or assemble a 20G x 1 inch or longer needle for administration (in the case of administration via subcutaneous IV).
2. Administer the entire contents of IV syringe containing the dosing solution intravenously via peripheral or central line over approximately 5 minutes through a needleless connector (alternatively through subcutaneous venous port with 20G needle).
3. Record the infusion start time on the cema-cel (ALLO-501A) Administration Form.
4. Subsequently flush the port with 0.9% sodium chloride in accordance with local site policies and procedures to ensure complete delivery of the dose.
    a. Flush time should be over approximately the same time or per institutional standard, but no more than 25 minutes.
    b. End flush time should be no longer than 2 hours of IP start of thaw time (that is, removal from LN_2 storage or shipper).
5. After the line flush is complete, record the infusion stop time on the cema-cel (ALLO-501A) Administration Form.

13. CEMA-CEL DOSING AND DISPENSING ERRORS

Any error in the dispensation or administration of Allogene IP that may cause or lead to inappropriate medication use, or participant harm must be reported to Allogene via the study distribution list and the site monitor/CRA immediately. Medication errors associated with an SAE are to be reported to Allogene or designee within 24 hours. Errors may result from the administration of the IP to the wrong participant, or at the wrong time, or at the wrong dosage strength, etc.

14. CEMA-CEL ACCOUNTABILITY

The investigator, or site designee, is responsible for maintaining accurate and complete records associated with cema-cel receipt, storage, applicable transfer, administration, accountability/ reconciliation, and return/destruction of IP.

Allogene or designee will supply product accountability forms for site use on this study. Sites may use their own accountability logs as long as they capture the information required by the Allogene forms, and the monitor/CRA approves their use.

Sample product accountability forms are provided in **APPENDIX 9.** CEMA-CEL ACCOUNTABILITY LOG

14.1. IP RETURN

If cema-cel remains in the LN_2 shipper with the tamper evident seal intact, it may be possible to return the product if it will not be used (e.g., in cases where the participant can no longer receive the intended dose).

If cema-cel is to be returned, please notify Allogene via the study distribution list to assist in coordinating product return and providing additional guidance for documentation completion.

14.2. IP DESTRUCTION

IP destruction must be approved by Allogene prior to each onsite destruction. Please notify the study distribution list of the intended destruction of unused, damaged and/or expired product.

Unused (unopened) IP vials that have been thawed cannot be returned to storage and should be discarded following institutional and local guidelines.

Destruction of drug product that is remaining or expiring at the clinical sites is the responsibility of the clinical site staff. Destruction may be performed by the appropriate site personnel (e.g. Pharmacist or Study Nurse/Coordinator) following local environmental requirements and institutional policies. The site procedure or SOP for IP destruction must be available for monitor/CRA review and Allogene approval before any unused IP can be destroyed by the clinical site.

All destruction must be fully documented on the product accountability log at the time of destruction. Ensure all accountability documentation has been completed, is filed in the ISF or Pharmacy binder and is available for monitoring by the monitor/CRA.

All IP destruction certificates (or alternative documentation if no certificate is available) must be filed in the ISF or Pharmacy Binder.

Sample product accountability forms are provided in **APPENDIX 9.** CEMA-CEL ACCOUNTABILITY LOG

15. TEMPERATURE EXCURSIONS

The acceptable temperature range for cema-cel is -135 °C or colder (≤-135 °C).

If any of the following occur for cema-cel, the clinical site must immediately quarantine the supply in the appropriate storage conditions as indicated on the product label and in such a way that prevents inadvertent dispensing until disposition instructions are received from Allogene. **Immediately notify Allogene via the study distribution list.**

Examples of temperature excursions or concerns include, but are not limited to:

- Any temperature excursion that occurs from either shipping conditions while in transit to the clinical site or storage conditions while product is at the clinical site.
- The temperature is not monitored continuously (for example, a temperature monitoring device malfunctions).

Designated staff will be required to submit FRM-0014, Temperature Excursion Notification Form **(APPENDIX 10. FRM-0014** TEMPERATURE EXCURSION NOTIFICATIONto Allogene via the study distribution list. The clinical site should indicate if the documented temperatures and/or duration of an excursion are not available for any reason in Section A of FRM-0014.

When reporting an excursion, include the following information at a minimum:

- Site Name/Site number where excursion occurred.
- Site contact information
- Product name/number (i.e., cema-cel)
- Lot and vial number(s) of impacted supplies
- Recorded temperature data showing the date and duration of an individual excursion.
- List of affected kits that have been dispensed/administered to participants (if applicable)

The quarantined product must not be used until further instruction is received from Allogene.

If it is determined that the product should not be used, the materials must continue to be physically quarantined in a way that prevents inadvertent dispensing until the product is destroyed or returned. Allogene will initiate a replacement shipment to the site, as necessary.

16. PRODUCT COMPLAINTS

Upon identification of any product complaint immediately notify Allogene and the monitor/CRA. Designated staff must submit the Clinical Product Complaint Intake Form **(APPENDIX 11. FRM-0017** CLINICAL PRODUCT COMPLAINT INTAKEto Allogene via the study distribution list. Allogene will evaluate the information provided.

Cema-cel product complaints include, but are not limited to the following:

- Vials are damaged (cracked/broken/chipped/scratched vial or broken seal/flip-off cap)
- Vials are missing from the kit
- Product in the vials appears discolored
- Volume of the vials is not consistent throughout the kit
- Labels on the kit or vials are inconsistent or illegible

IMPORTANT: Until further guidance is provided to the clinical site, it is critical to follow the guidance below:

- Quarantine the IP in the appropriate storage conditions and wait for further instructions.
- Allogene will notify the clinical site if additional information or action is needed. **Do not destroy the product unless instructed to do so by Allogene, as it may need to be returned for further evaluation.**
- As part of the complaint reporting process, the clinical site may be asked to provide digital photographs of the product.
- If requested to ship the product in question back to Allogene, or its distribution vendor, further instructions regarding the logistics of this shipment will be provided.

If a participant received the product involved in the complaint and there were adverse events associated with receiving the product, ensure that the appropriate adverse event reporting process has been followed. **Please refer to the current protocol for instructions on Safety Reporting requirements.**

Allogene will review the complaint and complete an investigation, as needed. Once the review/investigation is complete, the clinical site will be provided with a final response by Allogene, or designee.

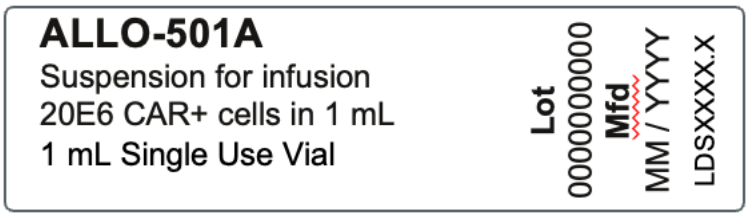
CEMA-CEL IPM APPENDICES

APPENDIX 1. CEMA-CEL LABELS

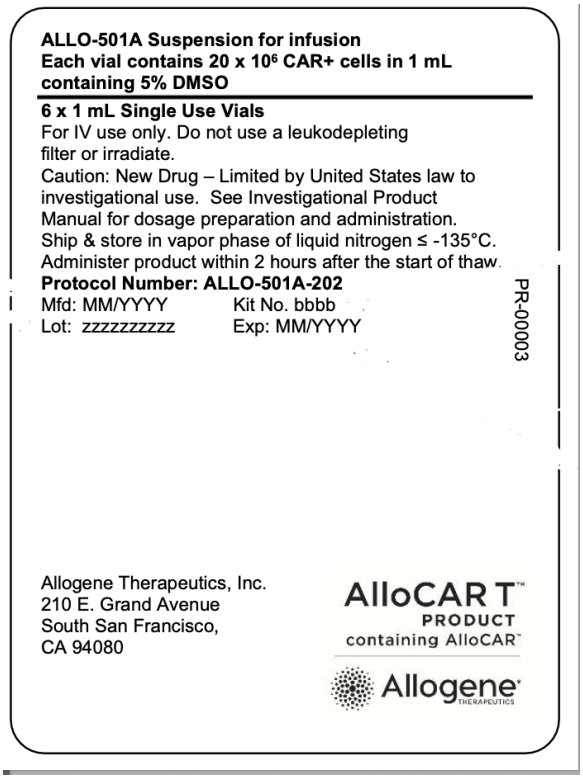
Please note, the label images provided below are examples of cema-cel labels. There may be regional differences due to respective regulatory requirements.

Cema-cel Representative Label (Examples)

Primary representative vial label (2 ml vial; 1 ml extractable volume):



Secondary representative packaging (carton) label:



APPENDIX 2. CEMA-CEL PACKING SLIP

Allogene - US Trial

***** Packing Slip *****

Distributed By
Fisher BioServices
Production and Distribution
14665 Rothgeb Drive
Rockville, MD 20850 USA
Phone: 240-618-1391
Email: FBSCustomer.Service@thermofisher.com

Shipment #:
Ship To:

Date Shipped : 21-Nov-2023
Due at Site: 22-Nov-2023
Protocol #: N/A
Client Order/IVRS
Purchase Order #: N/A
Carrier: BIOCAIR OVERNIGHT

Site ID#: SS000
Investigator:
Comments: Biocair Job#

Tracking #:

Product Name Packaging Unit	Lot # or ID # Range	Quantity	Unit
ALLO-501A-EXPAND 20E6 CAR + cells/mL, 1mL, 6 Vials, US 1 KIT **Exp./Retest Date:** 28-Feb-2024 (E)	Lot: ID:	1.000	KIT
C .k Carton CMP-01618 1 EACH	Lot:21OCT22	1.000	EACH

APPENDIX 3. UNPACKING AND RETURN INSTRUCTIONS

Allogene THERAPEUTICS

Site Unpacking Cryo-Shipper and Return Instructions

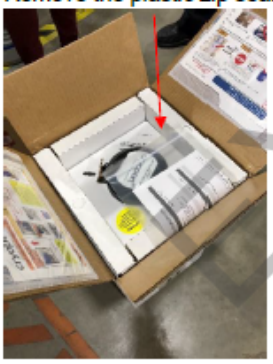
Please note the following:

- Please do not discard any contents or packaging materials until you have read these instructions.
- The IP must not be removed from the Cryo-Shipper until ready for preparation for infusion or until ready to be directly transferred to an Allogene qualified LN2 freezer.
- Return the shipper within the same day IMP is removed including the temperature logger to avoid unnecessary charges
- Email Fisher Bioservices at FBSCustomer.Service@thermofisher.com or call 240-618-1391 and email the Allogene Study Team (contact found in the study specific Investigational Product Manual) for any issues with the product

INSTRUCTIONS

1. Follow the Cryoport ***CXST1 Standard Shipper: Unloading Instructions*** to open the shipment.
   a. A copy of instructions ***How to Unload Samples*** will be included along with the shipment; reference this document at Step 8 once you are ready to unload the samples, which will be done immediately prior to dose administration.

2. Remove the plastic zip seal bag inside the case containing paperwork and FedEx Return label.



Please ensure the shipment paperwork includes the following:

☐ Packing Slip

☐ FOR NON IRT ORDERS ONLY - IMP Chain of Custody Form (FRM-0088)

- Section A of the Form will already be completed and **must match the packing slip**

☐ photocopy of the carton label(s)

APPENDIX 4. COURIER RETURN LABEL

APPENDIX 5. COMMERCIAL INVOICE (INTERNATIONAL SHIPMENTS ONLY)

Allogene THERAPEUTICS	Allogene Therapeutics 210 E Grand Avenue South San Francisco, CA 94080 United States	Date: November 29, 2023 Invoice#:	**COMMERCIAL INVOICE**

Consignee	Importer of Record	Broker

STUDY/PROTOCOL:		COURIER:	
EXPORT REFERENCE:		TRACKING/AWB#'s:	
INCOTERMS:		EIN:	

ITEM #	CLASSIFICATION	DESCRIPTION OF GOODS	COUNTRY OF MANUFACTURE	QTY	UNIT VALUE	SUBTOTAL
1 - 1	3002510000	ALLO-501A 20E6 CAR+ cells/mL, 1mL, 6 Vials, CA Phase II, Lot# Date of Manufacture: Expiry	US		$	$

Type of Packaging, Dimensions:	1 x CXST1 LN2 Dewar @ 14.75 IN x 14.75 IN x 26.75 IN			Freight: $ Total Value (USD): $
Total Gross Weight:	26.00 LBS	11.34 KGS		
Total Net Weight:	25.00 LBS			
Total # Pieces:	1		Conditions:	LN2 (-150°C -195°C)

No Commercial Value; Not for Resale; Value for Customs purposes only.

These items are controlled by the U.S. Government and authorized for export only to the country of ultimate destination for use by the ultimate consignee or end-user(s) herein identified. They may not be resold, transferred, or otherwise disposed of, to any other country or to any person other than the authorized ultimate consignee or end-user(s), either in their original form or after being incorporated into other items, without first obtaining approval from the U.S. government or as otherwise authorized by U.S. law and regulations.

I/we hereby certify that the information on this invoice is true and correct and that the contents of this shipment are as stated above.

I/we hereby authorize the freight forwarder listed above to execute any additional documents necessary for the export of merchandise described herein on my/our behalf.

NAME: _____ TITLE: _____

SIGNATURE: _____

APPENDIX 6. FRM-0088, CLINICAL PRODUCT CHAIN OF CUSTODY | VLN$_2$ SHIPMENTS

Allogene THERAPEUTICS	**Form**	Number: FRM-0088
		Version: 4.0
Title: Clinical Product Chain of Custody | vLN2 Shipments		Effective: 07 Jun 2023

Section A	Shipment Information – (Completed by CMO/Supplier)		
Subject ID Number:		Shipment Number:	Courier:
Courier Tracking/Job Number:			Seal Number:
Shipper ID Number:		Condition Monitor Number (Temperature Monitor):	

Line Item #	Product Lot #	Kit #	
1			☐ N/A
2 ☐ N/A			☐ N/A
3 ☐ N/A			☐ N/A

Internal Temperature:	Time and Date Shipper Closed:

Prepared By - Name	Signature	Date
Verified By - Name	**Signature**	**Date**

APPENDIX 7. CALCULATION OF DOSE NUMBER AND VIALS

The volume of the investigational product will be 6 vials (total of 6 mL). See calculation below:

- **Dose of investigational product:** 120 x 10^6 CAR+ cells
- **Dose Volume of Investigational Product (mL) =** $\frac{120 \times 10^6 \text{ CAR+ cells}}{20 \times 10^6 \text{ CAR+ cells/mL}}$ = **6.0 mL**
- **Extractable Volume per vial:** 1.0 ml/vial
- **Vials of investigational product =** 6 vials

APPENDIX 8. CEMA-CEL ADMINISTRATION FORM

Allogene THERAPEUTICS	**CEMA-CEL (ALLO-501A) ADMINISTRATION FORM** **Protocol: [ADD]**

Principal Investigator Name:		**Site Name & Number:**	
Subject ID:		**Lot Number:**	
Instructions: Delegated clinical site staff to complete designated fields during dose preparation and administration. After administration, clinical site to email completed form to study distribution list (reference IPM Study Appendix). Ensure completed form is filed in investigator site files.			

Dose Preparation Information							Dose Administration Information		
Date of Dose Preparation (DD/MMM/YY)	**Vial Number (according to label)**	**Time removed from LN2 shipper/freezer for administration (HH:MM)**	**Water Bath or Dry Bead Bath (37°)**	**Water/Dry Bath Temperature (°C)**	**Thaw Start Time (HH:MM)**	**Thaw Stop Time (HH:MM)**	**Date of Administration (DD/MMM/YY)**	**Infusion Start Time (HH:MM)**	**Infusion Stop Time (HH:MM)**
01/JAN/24	001	09:02	☒Water Bath ☐Dry Bead Bath	37°C	09:05	09:35	01/JAN/24	10:05	10:10
			☐Water Bath ☐Dry Bead Bath						
			☐Water Bath ☐Dry Bead Bath						
			☐Water Bath ☐Dry Bead Bath						
			☐Water Bath ☐Dry Bead Bath						
			☐Water Bath ☐Dry Bead Bath						
Total Volume of Administered Product (i.e. 6.0 mL):									

Printed name of individual preparing **CEMA-CEL:** _____ Signature of individual preparing **CEMA-CEL:** _____

Printed name of individual administering **CEMA-CEL:** _____ Signature of individual administering **CEMA-CEL:** _____

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APPENDIX 9. CEMA-CEL ACCOUNTABILITY LOG

Allogene THERAPEUTICS	**CEMA-CEL (ALLO-501A) ACCOUNTABILITY LOG**
	Protocol: [ADD]

Principal Investigator Name:		**Site Name & Number:**	
Instructions: Delegated clinical site staff to complete designated fields.			

			Pharmacy Dispensing Information						
Vial Number (according to label)	**Lot Number (XXXXXX)**	**Date Received (DD/MMM/YY)**	**Date Dispensed (DD/MMM/YY)**	**Subject ID (501A-201-PHX-XXX-XXX)**	**Initials of Dispenser (ABC)**	**Verified by CRA (initials (ABC)**	**Final Product Disposition: Administered Returned to Sponsor Onsite Destruction**	**Date of product disposition (DD/MMM/YY)**	**Signature & Date of Staff disposing cema-cel**
001	1234DA	01/JAN/24	01/06/24	501A-201-PH2-000-000	AS	ABC	☒ Administered ☐ Returned to Sponsor ☐ Onsite Destruction	01/06/24	*ADOE*
							☐ Administered ☐ Returned to Sponsor ☐ Onsite Destruction		
							☐ Administered ☐ Returned to Sponsor ☐ Onsite Destruction		
							☐ Administered ☐ Returned to Sponsor ☐ Onsite Destruction		
							☐ Administered ☐ Returned to Sponsor ☐ Onsite Destruction		
							☐ Administered ☐ Returned to Sponsor ☐ Onsite Destruction		
							☐ Administered ☐ Returned to Sponsor ☐ Onsite Destruction		

APPENDIX 10. FRM-0014 TEMPERATURE EXCURSION NOTIFICATION

Allogene THERAPEUTICS	Form	Number: FRM-0014
		Version: 3.0
Title: Temperature Excursion Notification		Effective: 10 Apr 2020

Section A	Initial Assessment (Clinical Site)						
Date & Time Excursion Identified:				Site Name:		Site Number:	
Excursion Occurred: ☐ During Transport ☐ During Storage ☐ Other: Please Explain							
Shipper ID Number: ☐ N/A				Temperature Controlled Unit/Monitor Asset Number: ☐ N/A			
Line Item #	Product Lot #	Kit #	Product Name	Vial ID Numbers	Storage Condition	Highest or Lowest Temperature Value Reached During Excursion	Duration of Excursion (Hrs : Minutes)
1							
2 ☐ N/A							
3 ☐ N/A							
4 ☐ N/A							

Description of Event, Including Root Cause (if Known) and Corrective Actions Taken to Remediate		
Note: Please attach temperature read-out from monitoring system; include photos if necessary (e.g., damaged shipper)		
Completed By - Name	Signature	Date
Contact Number	Contact Number	

APPENDIX 11. FRM-0017 CLINICAL PRODUCT COMPLAINT INTAKE

Allogene THERAPEUTICS	Form	Number: FRM-0017
		Version: 2.0
Title: Clinical Product Complaint Intake		Effective: 30 Aug 2021

Clinical Product Complaint Intake Information

Product Name:	Protocol Number#:
Is this a Blinded Study? ☐ Yes ☐ No If Yes, Kit Number:	Lot/Batch Number: (N/A if Blinded)
Contact Information: ☐ Subject ☐ Site Personnel ☐ Other:	
Contact Name: Clinical Site Name: Address: Phone:	Date of complaint event/detection: Method of Contact: Date & Time of initial contact (complaint received):
☐ Yes ☐ No Is tampering suspected? ☐ Yes ☐ No Is counterfeiting suspected? If yes to either, notify Allogene QA representative immediately to determine next steps in the investigation.	
Description of defect/problem:	
List any materials returned and attach documentation/photos if necessary:	
☐ Yes ☐ No Did a study patient receive the product involved in the complaint? ☐ Yes ☐ No If yes, were any adverse events associated with patient receiving the product? ☐ Yes ☐ No If yes, was this a Serious Adverse Event? ☐ Yes ☐ No If a Serious Adverse Event, confirm that this has been reported to Allogene via the study safety reporting process. If an adverse event, briefly describe as documented in the study EDC system:	

Signature (Information recorded by)	**Date**	**Print Name**
For Allogene Quality Assurance Use Only:		
Product Complaint Number: PC -	If associated with adverse event, AE Number:	
Quality Signature	**Date**	**Print Name**

APPENDIX 12. FRM-0151, CLINICAL PRODUCT RETURN CHAIN OF CUSTODY | VLN_2 SHIPMENTS

Allogene THERAPEUTICS	Form	Number: FRM-0151
		Version: 2.0
Title: Clinical Product Return Chain of Custody | vLN2 Shipments		Effective: 06 Jan 2021

Section A	Shipment Information – (Completed by Clinical Site)		
Courier:	Courier Tracking/Job Number:		Shipper ID Number:
Seal Number:		Seal intact: ☐ Yes ☐ No	
Condition Monitor Number (Temperature Monitor):			Internal Temperature:

Line Item #	Product Lot #	Kit #	Vial ID Numbers
1			
2 ☐ N/A			
3 ☐ N/A			
4 ☐ N/A			

Prepared By - Name	Signature	Date
Verified By - Name	Signature	Date

Comments
☐ N/A

APPENDIX 13. CEMA-CEL IPM APPROVALS

FUNCTIONAL APPROVER	SIGNATURE
Name: Audrey Kennedy **Title**: Director, Clinical Operations Allogene Therapeutics	*Electronically signed by: Audrey Kennedy* *Reason: I Approve this document* *Date: Apr 28, 2025 15:25 MDT*
Name: John Le Gall, MD, MBA, MS **Title:** Vice President, Clinical Development Allogene Therapeutics	*Electronically signed by: John Le Gall* *Reason: I Approve this document* *Date: May 1, 2025 09:48 PDT*
Name: Omid Abtahi **Title:** Associate Director, Clinical Supply Chain Allogene Therapeutics	*Electronically signed by: Omid Abtahi* *Reason: I Approve this document* *Date: Apr 30, 2025 10:57 PDT*
Name: Todd Luman **Title:** Senior Director, Process and Product Development Allogene Therapeutics	*Electronically signed by: Todd Luman* *Reason: I Approve this document* *Date: May 5, 2025 12:31 PDT*
Name: Karen Ho **Title:** Senior Director of External Quality Allogene Therapeutics	*Electronically signed by: Karen Ho* *Reason: I Approve this document* *Date: Apr 25, 2025 16:43 PDT*

APPENDIX 14. CEMA-CEL IPM SUMMARY OF CHANGES

VERSION	VERSION DATE	SUMMARY OF CHANGES
1.0	16-FEB-2024	Not applicable – first version
2.0	24-APR-2024	Throughout • Administrative changes, corrections and updates for clarity and brevity. • Introduction of ALLO Participant Pathway and associated IP shipment requirements. • Inclusion of IRT language requirements vs. manual (paper) documentation process for IP management.
		Special Handling • Updated BSL level and handling requirement due to change in cema-cel level classification to Risk Group 1. • Incorporate of updated handling and preparation activities.
		IP Storage and Handling • Addition of Environmental Exposure guidance
		IP Preparation and Administration • Updated Supplies Section – Clarification for withdrawal and administration needles. • Updated Dose Preparation and Intravenous Administration steps for clarity and readability.
		Intravenous Administration Instructions • Clarification of administration documentation completion for clarity and readability.
		Inclusion of appendices with examples of relevant forms/templates.

VERSION	VERSION DATE	SUMMARY OF CHANGES
3.0	25-APR-2025	Throughout • Administrative changes, corrections and updates for clarity and brevity. • Removal of BSL2 handling / disposal requirement language based on updated IP classification.
		IP Storage: Onsite LN_2 Vapor Phase Freezer • Clarification of documents required for review to allow for sponsor approval of onsite storage.
		cema-cel Dose Preparation • Inclusion of Plasmatherm in equipment and supplies required. • Addition of language to support sponsor-provided label option.
		Prepared IP Dose Guidance • Clarification regarding start of thaw time.
		IP Thaw • Addition of Plasmatherm thaw guidance.
		cema-cel Dose Preparation • Updated preparation requirement for recommendation, but not requirement, of use of Class IIA1 / higher-level BSC, or dose preparation without BSC (sponsor approval requirement) due to change in Allogene requirements for IP preparation.
		Dose Preparation Instructions • Updated for clarity and brevity to allow dose preparation under either condition, e.g. preparation with a BSC and without a BSC. • Removal of language to allow withdrawal with upright vials.

VERSION	VERSION DATE	SUMMARY OF CHANGES
3.0	25-APR-2025	cema-cel IPM Appendices • Appendix 1 – Updated label example • Appendix 12 – Addition of FRM-0151, Clinical Product Return Chain of Custody | vLN_2 shipments