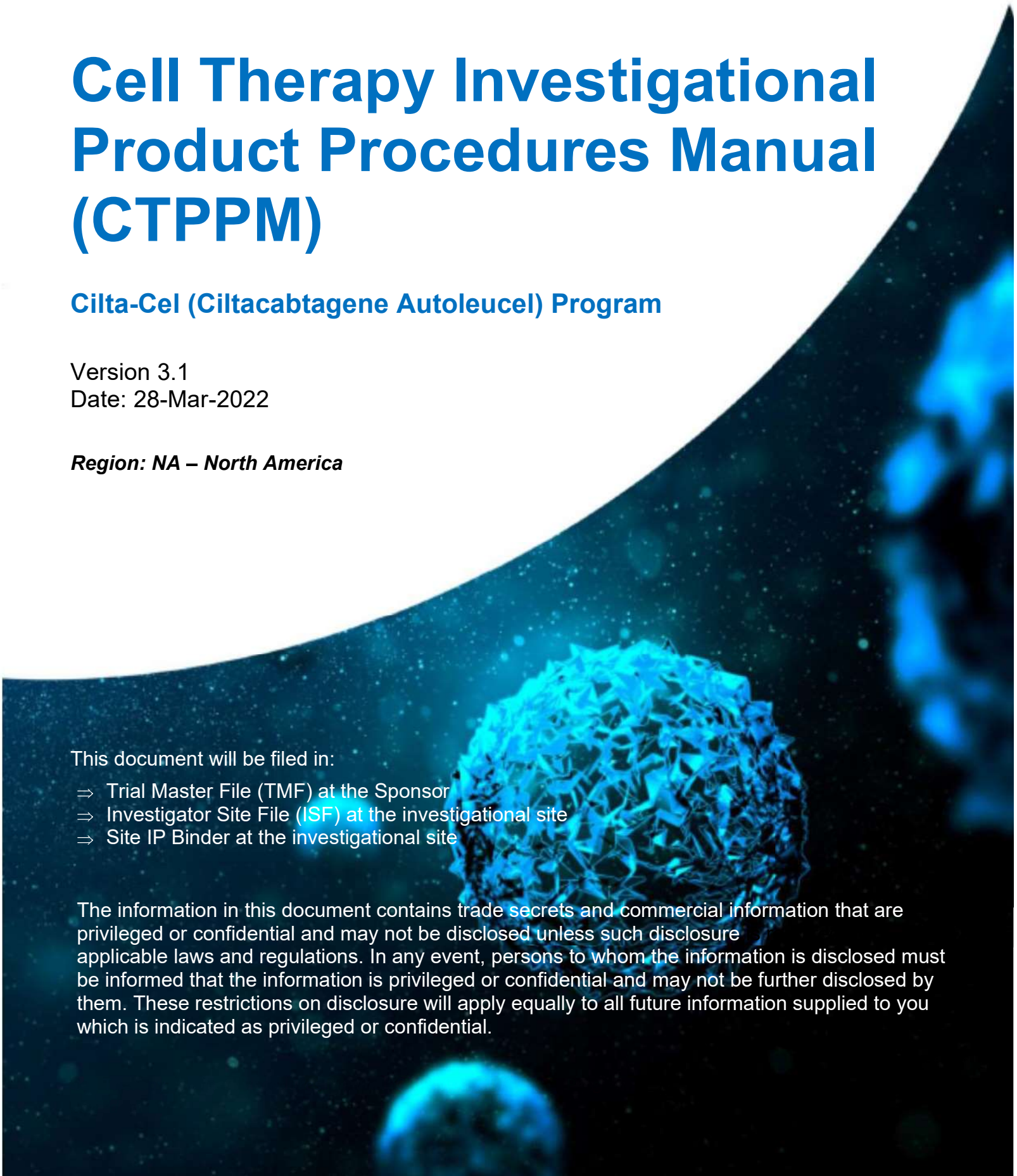
Cell Therapy Investigational Product Procedures Manual (CTPPM)

Cilta-Cel (Ciltacabtagene Autoleucel) Program

Version 3.1
Date: 28-Mar-2022

Region: NA – North America



This document will be filed in:

⇒ Trial Master File (TMF) at the Sponsor
⇒ Investigator Site File (ISF) at the investigational site
⇒ Site IP Binder at the investigational site

Program CTPPM Approval

I approve the content of this document.

Name	Role	Signature	Date (DD-MON-YYYY)
Sadaf Naz Khan	CASL	See Program CTPPM v3.1 28-Mar-2022 approval page	28-Mar-2022
Cameron Estes	GTL	See Program CTPPM v3.1 28-Mar-2022 approval page	28-Mar-2022
Gordon Gregory	CSOM	See Program CTPPM v3.1 28-Mar-2022 approval page	28-Mar-2022
John Caruolo	CSI	See Program CTPPM v3.1 28-Mar-2022 approval page	28-Mar-2022
Christopher Greenberg	CSC Systems	See Program CTPPM v3.1 28-Mar-2022 approval page	28-Mar-2022

Regional Approval

I approve the content of this document.

Name	Role	Signature	Date (DD-MON-YYYY)
Candice Powell	Global Trial Leader (GTL)	Candice Powell Digitally signed by Candice Powell DN: cn=Candice Powell, o=PDO, ou, email=cpowel@its.jnj.com, c=US Reason: I agree to specified portions of this document. Date: 2022.04.08 11:15:48 -07'00' Adobe Acrobat DC version: 2015.006.30527	
Agne Taraseviciute-Morris	Study Responsible Physician (SRP)	Agne Taraseviciute-Morris Digitally signed by Agne Taraseviciute-Morris DN: cn=Agne Taraseviciute-Morris, o=Janssen Pharmaceuticals, ou=R&D, email=atarasev@its.jnj.com, c=US Reason: I attest to the accuracy and integrity of this document. Date: 2022.04.05 06:59:34 -07'00'	

Table of Contents

Introduction

Cell Therapy Product Procedures Manual (CTPPM)

The CTPPM provides end to end instructions to investigational site personnel on the Sponsor's requirements and processes for enrollment, MNC, Apheresis collection, storage & shipment to and from the manufacturer.

Instructions provided in this document must be followed precisely. Any deviations from the instructions, whether intentional or accidental, must be documented and reported to the Site Manager.

For trials outsourced to a Contract Research Organization (CRO), references to a site manager refer to the appropriate CRO title e.g., Clinical Research Associate (CRA).

Preparation, Dispensing, and Administration of IP

See the Investigational Product Preparation Instructions (IPPI) for Sponsor instructions on preparing, dispensing, and administering the IP. The IPPI is located in the Site IP Binder.

Follow the site's standard procedures for preparation of IP in alignment with Sponsor instructions. If the site does not have written procedures, contact the Site Manager for guidance.

Two qualified staff members should be involved whenever the IP is prepared by the site; one to prepare the IP and the other to check or verify.

Guidance on the use of Sponsor provided or Site provided ancillary supplies will be provided in the IPPI.

General Principles in Conducting Clinical Studies

The conduct of clinical studies and the associated activities outlined in this Manual are subject to various local, national, and international regulations. Furthermore, each site's policies and procedures must be adhered to.

Staff Training and Delegation of Responsibilities

Only qualified individuals are permitted to perform any activities described in this document per the Quality Terms within the clinical trial agreement signed by each site. In certain instances, the necessary elements of the quality agreement have been incorporated into the site's Clinical Trial Agreement.

Any individual involved in any part of the study must be appropriately delegated those tasks on the Delegation Log and have appropriate training and/or experience to perform his/her activities. Individuals acting in the Lead Cell Lab Staff roles are responsible for ensuring that all other individuals that are performing Apheresis collection and shipping and packaging activities are appropriately trained and their training is documented.

A training record describing each individual's qualification must exist and be available for inspection by the Sponsor's representatives and regulatory agency inspectors.

Good Documentation Practices

- Documentation is required to reconstruct the events and activities of the study. In this study, documentation will be accomplished through, but not limited to, the use of forms, logs, facsimiles, and correspondence, or maintained directly within an Interactive Web Response System (IWRS).
- Any other means required to achieve the above goal (e.g., worksheets) may be used to ensure proper documentation of activities. All such documentation must be retained.
- Blank forms required for use in the procedures, as instructed in this Manual, are provided in the Site IP Binder. If you require help in using these forms, contact the Site Manager.
- When completing study documents and forms, please note the following:
  - Make entries only with a permanent (indelible) pen.
  - Corrections must be made so as not to obliterate the original text. *This is done by drawing a single line through the error and printing a legible correction as close to the error as possible. Original entries should not be erased, or otherwise obliterated (e.g., by using correction tape or fluids).*
  - All corrections must identify who made the correction, be dated, and must also include an explanation (e.g., typo, incorrect date).
  - Abbreviations or codes may be used for standard explanations, provided a list of these is included with the documentation.
  - For additional form-specific instructions refer to the form completion instructions and/or discuss with the Site Manager.
  - All spaces for entries including headers (e.g., subject ID number) must be completed. If a field should be left blank, draw a line through it.
  - Do not use “ditto” (or its equivalents) for repeated identical entries. Unless specifically directed in the completion instructions, do not use check marks or “x”s.
  - Do not add any information that is not specifically requested on the form. If for any reason there is a need to adapt the forms and/or include additional information, contact the Site Manager for the proper method.
  - The date format is: DD-MON-YYYY (e.g., 01-JAN-2010).
  - Time should be expressed in a 24-hour (or military) format (i.e., 8:30 am is recorded as 0830 and 8:30 pm is entered as 2030); otherwise, ensure that am or pm is designated.

Records

Good Documentation Practices

The site is expected to establish and maintain a records retention schedule for the identification, completion, checking, controlled storage, protection, retrieval, retention, and destruction of active and inactive records in accordance with the Sponsor requirements and the Quality Agreement.

Records shall be stored so that they can be accurately, completely, and consistently retrieved and/or accessed in a timely manner. The records shall be stored and maintained as to prevent damage or deterioration for the record retention period.

The site shall ensure that records are accessible to the Sponsor during audits and site visits.

The record retention schedule shall enable tracking of retention times for all records, including inactive stored records.

Examples of records are provided below:

- Chain of custody and chain of identity forms
- Production records
- Equipment cleaning
- Quality Assurance /Quality Control records
- Quality system records (Deviations, CAPA, Change Control)
- Complaints files
- Training records
- Validation records
- Engineering Change Orders/Notifications

The site shall follow the applicable retention period for the minimum period as outlined in the Protocol and Clinical Trial Agreement and applicable legal and regulatory requirements.

Abbreviations

APH	Apheresis
AWB	Air Waybill
CAR-T	Chimeric Antigen Receptor T
eCRF	Electronic Case Report Form
COC	Chain of Custody
COI	Chain of Identity
CPC	Cryopreservation Center
CRYO	Cryopreservation
DIN	Donor Identification Number
IDM	Infectious Disease Markers
IP	Investigational Product
ISBT	International Standard for Blood Transfusion
IWRS	Interactive Web Response System
LN_2	Liquid Nitrogen
MFG	Manufacturing
MNC	Mononuclear Cell
OBC	On Board Courier
PI	Principal Investigator
PPE	Personal Protective Equipment
PQC	Product Quality Complaint
QP	Quality Person
REC	Receipt at Site
RTN	Return of IP
SEC-DIS	Single European Code Donor Identification Sequence

SHIP	Shipment from Site
SIPPM	Site Investigational Product Procedures Manual
TIC	Thermal Isolation Chamber
TOR	Temperature Out of Range
TRN	Transfer to Shipment Facility
VIP	Vacuum Insulated Panels
WBC	White Blood Cell

Module 1:
Pre-Collection

Version: 3.1

Date: 28-Mar-2022

Module 1: Table of Contents

1.1 Study Supplies

1.2 Pre-Collection Activities (All Subjects)

Module 1: Revision History

This is a controlled document.

VERSION DATE (DD-MON-YYY)	SECTION(S) CHANGED	DESCRIPTION OF CHANGE(S)
01-Mar-2021	Initial Document	
05-Jul-2021	1.2	Updated wording outlining slot reservation process, randomization and Vineti ordering Included statement on re-treatment per protocol
10-Mar-2022	Module 1	Updated CSOM email to: Central.Scheduling@ITS.JNJ.com
	1.2.1 & 1.2.5	Reference to CQUENCE clinical trial portal added
28-Mar-2022	Module 1	Formatting changes

1.1 Study Supplies

This provides details of study supplies that will be supplied by the sponsor

Materials

Investigational Product (IP): JNJ-68284528 (ciltacabtagene autoleucel)

Refer to the protocol for a description of the IP.
Refer to the Material Data Safety Sheet in the Site IP binder for information about the IP.

Other Medications:

Refer to the protocol and non-JNJ-68284528 SIPPM for a description of other medications used in the study.

Ancillary Supplies:

See below table for ancillaries initially provided by the sponsor for use in activities documented in the CTPPM. All supplies related to packaging and shipment of MNC, Apheresis product and receipt of IP are contained in the Shipments section of the CTPPM.

Refer to the IP Preparation Instructions in the Site IP Binder for ancillary materials needed for investigational product preparation/administration.

Ensure that an adequate inventory of the below supplies is maintained, and the sponsor is alerted to any supplies that are needed in accordance with the below lead-times. If additional ancillary supplies for apheresis are needed, email Central.Scheduling@ITS.JNJ.com and specify which supplies and quantities are required.

Ancillary	Provided By	Process Utilized In	Storage Conditions	Lead-times
Bulk Label Supply: Labels, Self-laminating cards & zip ties	Sponsor	Apheresis	Room Temperature	3 weeks
Wire Cutters	Sponsor (if required)	Shipment Receipts	Room Temperature	3 weeks

1.2 Pre-Collection Activities (All Subjects)

This section outlines the steps for reserving a manufacturing slot for the production of IP per subject.

Documentation & Patient Verification		
Step	**Task**	**Responsibility**
1.2.1	**Slot Reservation** The slot reservation request process will start during the pre-screening period to reserve and obtain an approval of a slot prior to consent of a potential subject. • The site will submit a request for apheresis date approval to the Sponsor for a specific potential subject in the CQUENCE Clinical Trials portal. If the portal cannot be utilized, a pdf Slot Reservation form can be emailed to Central.Scheduling@its.jnj.com. • This request should be submitted one (1) week prior to the expected consenting date (where possible). Subject shall not be consented or screened until the slot has been approved by the Sponsor.	Clinical Site
1.2.2	The Sponsor will review the Slot Reservation request and approve or reject the slot. If approved, approval will be provided to the site along with the projected date for manufactured ciltacabtagene autoleucel to be onsite.	Sponsor
1.2.3	**Screening** Once the slot has been approved, the site may proceed with collecting informed consent and start of screening. At the time of signing consent, complete the Screening transaction in IWRS (see IWRS User Manual). **A unique 13-digit subject ID will be generated on completion of the IWRS transaction.** Example: N05US10001001 (10 digit site number + 3 digit code)	Clinical Site
1.2.4	**Eligibility Confirmation** • Enter all pertinent subject screening data in the eCRF. • Once that is completed, submit the Eligibility Approval Request transaction in IWRS, requesting sponsor approval.	Clinical Site

Documentation & Patient Verification		
Step	**Task**	**Responsibility**
	• Approve enrollment based on screening data entered in eCRF after all queries have been resolved and all data has been appropriately updated in the eCRF.	Sponsor
	Randomization *(only applicable to protocols requiring randomization)* • Once eligibility is confirmed, randomize the subject via IWRS transaction on the pre-agreed randomization date only. **NOTE: If re-treatment is permissible per protocol and an additional apheresis is required, follow the steps outlined in 'Pre-collection activities (All subjects)'**	Clinical Site
1.2.5	**Apheresis Scheduling** • If there are any changes to the date of apheresis after approval of the slot, this should be rescheduled via the CQUENCE Clinical Trials portal. If further discussion is needed beyond rescheduling the date, this should be communicated to the Sponsor by email at: Central.Scheduling@ITS.JNJ.com	Clinical Site
	• Sponsor will approve any updated apheresis date request from the site in alignment with current available capacity. In alignment with the approved date of apheresis for the assigned subject's slot, schedule the delivery of the empty CREDO CUBE shipping container to the apheresis or site's cell processing lab.	Sponsor
	If COC and COI is being maintained in the Vineti system, prior to apheresis: • Create an order in the Vineti system to register the patient details and the agreed upon Apheresis date. • Refer to the Vineti Ordering Module User Guide for guidance on the steps. *(see further instructions in Module 3 related to transfer to cell lab & Module 5 related to packing & shipment).*	Clinical Site

	**If using Vineti complete the Ordering module in the Vineti system and enter all applicable data in the eCRF.** **Refer to the "Vineti Ordering User Guide" for additional details.**	**Clinical Site** **Cell Lab Staff**

MODULE 1 COMPLETED

Module 2:
Apheresis & Cell Management

Version: 3.1

Date: 28-Mar-2022

Module 2: Table of Contents

Module 2: Revision History

This is a controlled document.

VERSION DATE (DD-MON-YYYY)	SECTION(S) CHANGED	DESCRIPTION OF CHANGE(S)
01-Mar-2021	Initial	
05-Jul-2021	2.3	Updated definitions and naming conventions for all regions Apheresis collection section updated with the following requirements. • New apheresis target collection added and changed from MNC to WBC • Note clarify anticoagulant volume is applicable to product • Note added for recommended storage temp and transport temperature • Added recommendation for plasma to be added to collection bag for shipment • Added recommendation to take mid-point samples • Removed recommendations for whole blood to be processed
10-Mar-2022	2.1.2, 2.2.2	Added statement for apheresis bag label expiration date & time to meet requirements for Janssen starting material and storage temperature requirements
	2.2.3, 2.2.4	Deleted central printed labels option added new instructions for manual label completion
	2.3.1	Added IDM instructions for KOR; Changed IDM testing requirement for AUS from 7 days to 30 days
	2.3.2	Added Vineti steps for capturing IDM sample
	2.3.6, 2.3.7, 2.3.9	Updated instructions for apheresis collection and added instructions to store the apheresis product in a monitored refrigerator or intermediary transport at 2-8^{0}C until the time of shipment occurs
28-Mar-2022	Module 2	Formatting changes

2.1 Apheresis Manual Labeling

This section is only applicable to sites that are utilizing manual forms to manage the COC/COI of the MNC, Apheresis product and Investigational product and are utilizing a CPC.

Labels		
Step	**Task**	**Responsibility**
2.1.1	**Bulk Label Supplies Binder** Your site will have been provided a bulk label supplies binder during initiation, including the following materials per study: • Sponsor-provided supplemental apheresis labels to include on the self- laminating cards • Shipper labels to be included with the AWB in the shipper • Self-laminating cards to place apheresis label onto • Zip ties to attach the labels to the apheresis bag	Sponsor
2.1.2	**APHERESIS – Bag Label** Print apheresis bag labels as per site process, following ISBT 128 and local guidelines. The apheresis bag labels should include, at a minimum, the following elements for the purpose of COI: • Date and Time of apheresis end of collection (including time zone) • Product Volume of apheresis collection • Subject Name • Date of Birth • SEC-DIS (21-digits) where applicable for some countries in EEA or DIN or Apheresis ID • Any required warnings per local standards & regulations If the apheresis expiration date & time are included in the apheresis bag label, this should follow the requirements for Janssen starting material expiration time of thirty-two (32) hours • The storage temperature on the apheresis bag label should be consistent with the supplemental label storage requirements at 2-8^{0}C	Clinical Site

2.1.3	**APHERESIS – Sponsor Supplemental Label** The sponsor-provided supplemental apheresis label will already include the sponsor and description pre-printed on the label. Complete the following information on the label: • Site Number • Subject Number • DIN or Apheresis ID • Date of collection After completing all sections of the supplemental apheresis label, place the label onto the self-laminating card and attach the self-laminating card to the apheresis bag using the zip tie provided by the sponsor. **Refer to section 2.1.5 for instructions.**	Sponsor/ Clinical Site
2.1.4	**SHIPPER – Sponsor Label** The sponsor-provided shipper label will include the sponsor and description pre-printed on the label. Complete the following information on the label: • Site Number • Subject Number • DIN or Apheresis ID The shipper label is included with the MNC apheresis product shipment to the CPC. **Specific instructions for the shipper label are outlined in Module 5.**	Sponsor/ Clinical Site

2.1.5 Instructions for Use of self-laminating card with Sponsor-provided Apheresis Label

<table>
<tr><th>Step 1</th><th>Step 2</th><th colspan="2">Steps 3.1 – 3.4</th><th>Step 4</th></tr>
<tr>
<td rowspan="2"> 
The sponsor apheresis bag Labeling Kit will contain:
• label to attach to the bag
• a self-laminating card to place the label onto
• a zip tie to attach the label to the bag</td>
<td> 
2.1 Fill out the necessary information on label.</td>
<td> 
3.1 Lift the top flap of the self-laminating card.</td>
<td> 
3.2 Place the label onto the self-laminating card. Place any additional labels (DIN) as necessary onto self-laminating card.</td>
<td rowspan="2"> 
Secure the self-laminating tag and label via zip tie to the collection bag.
  </td>
</tr>
<tr>
<td> 
2.2 Peel the paper off the label to expose the adhesive side.</td>
<td> 
3.3 Remove the paper on the self-laminating card.</td>
<td> 
3.4 Laminate and seal the labels onto the self-laminating card.</td>
</tr>
</table>

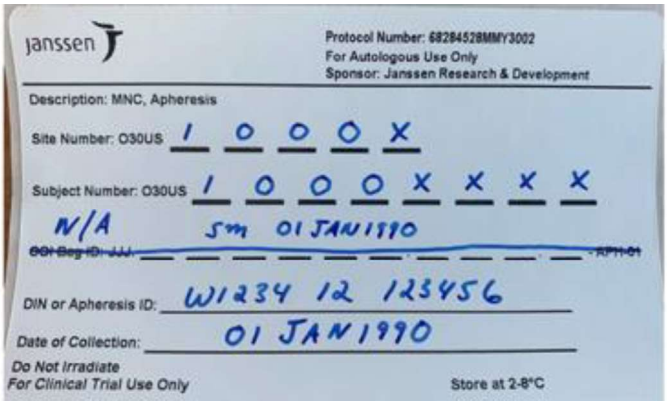
Once completed, proceed to section 2.3 Apheresis collection.

2.2 Apheresis Vineti Labeling

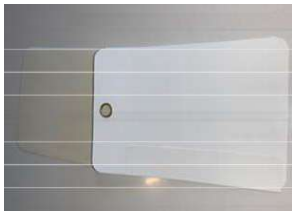
This section is only applicable to sites that are utilizing the Vineti system to manage the COC/COI of the MNC, Apheresis product and Investigational product.

Vineti Labeling		
Step	**Task**	**Responsibility**
2.2.1	**Bulk Label Supplies Binder** Your site will have been provided a bulk label supplies binder during initiation, including the following materials per study: • Sponsor-provided supplemental apheresis labels (use only as a backup when Vineti can't be used (e.g. system is down, site is not yet fully trained, technical issue with the printer)) to include on the self-laminating cards • Shipper labels (use as a backup when system is down) to include in the shipper • Self-laminating cards to place sponsor supplemental apheresis label onto • Zip ties to attach the labels to the apheresis bag	Sponsor
2.2.2	**APHERESIS – Bag Label** Print apheresis bag labels as per site process, following ISBT 128 guidelines. The apheresis bag labels should include, at a minimum, the following elements for the purpose of COI: • Date and Time of apheresis collection (including time zone) • Product volume of apheresis collection • Subject Name • Date of Birth • SEC-DIS (21-digits) where applicable for some countries in EEA or DIN or Apheresis ID • Any required warnings per local standards & regulations • If the apheresis expiration date & time are included in the apheresis bag label, this should follow the requirements for Janssen starting material expiration time of thirty-two (32) hours • The storage temperature on the apheresis bag label should be consistent with the supplemental label storage requirements at 2-8^{0}C	Clinical Site

Vineti Labeling

Step	Task	Responsibility
2.2.3	**Vineti Printing of Sponsor Supplemental labels** After entering the SEC-DIS where applicable for some countries in EEA or DIN or Apheresis ID into the Vineti system, print the following labels: One (1) Apheresis supplemental label One (1) Shipper label **Refer to the Vineti Collection User Guide.**	Clinical Site
2.2.4	**APHERESIS – Sponsor Supplemental Label** The supplemental apheresis label printed on-site will include all necessary information already pre-printed on the label from the data entry into the Vineti system. **IMPORTANT:** If using labels provided by the sponsor (use only as a backup when Vineti system can't be used (e.g. system is down, site is not yet fully trained, technical issue with the printer), you must manually complete the required information on the labels. In case the COI and COI Bag ID are not available the site needs to 'N/A' and strikethrough the COI and COI Bag ID fields on the labels, then initial and date (see example below). 	Clinical Site
2.2.5	**Label Scanning** Scan or enter the unique COI bag identifier from the Vineti apheresis label to associate the bag with the COI record in Vineti. **Refer to the Vineti Collection User Guide.**	Clinical Site 

2.2.6 Instructions for use of self-laminating card with Apheresis Label using Vineti

<table>
<tr><th>Step 1</th><th colspan="2">Steps 2.1 – 2.4</th><th>Step 3</th></tr>
<tr><td>1.1 Print off or complete all Vineti labels during Apheresis.
 
Please note: the labels can be printed on paper</td><td> 
2.1 Lift the top flap of the self-laminating card.</td><td> 
2.2 Place the label onto the self-laminating card. Place any additional labels (DIN) as necessary onto self-laminating card.</td><td rowspan="3"> 
Secure the self-laminating tag and label via zip tie to the collection bag.
  </td></tr>
<tr><td>1.2 Retrieve the appropriate label(s) to attach to the apheresis/cryo bag by noting the suffix at the end of the Bag ID.
 
1.3 Peel the paper off the label to expose the adhesive side.</td><td> 
2.3 Remove the paper on the self-laminating card.</td><td> 
2.4 Laminate and seal the labels onto the self-laminating card.</td></tr>
<tr><td>If the printed label exceeds the size of the self-laminating card, cut the excess or fold the excess label around the self-laminating card.</td><td>  </td><td>Ensure that the label content is clear and readable.</td><td>  </td></tr>
</table>

2.3 Apheresis Collection

Mononuclear cells (MNCs) will be collected from each subject via apheresis for use in the manufacture of the autologous cellular product.

Apheresis collection		
Step	**Task**	**Responsibility**
2.3.1	MNC, Apheresis collection should be performed according to the site's standard operating procedures and institutional standards targeting 9 x 10^9 Total White Blood Cells (WBCs), aka Total Nucleated Cells (TNC), containing a high % of MNC. Acceptable range: 6 to 12 x 10^9 Total WBCs. **NOTE: The blood volume processed is dependent on the protocol apheresis parameters, subject's weight, and medical status.**	Clinical Site
2.3.2	The use of Anticoagulant Citrate Dextrose solution, solution-A (ACD-A) or ACD-A plus heparin is permissible. Use of heparin alone is not permitted. **NOTE: The anticoagulant volume (mL) to be captured on the COI/COC form, should be the volume of anticoagulant in the apheresis bag.**	Clinical Site
2.3.3	If the final volume in the collection bag is less than 100 mL, add 50 mL of plasma before disconnecting the apheresis bag.	Clinical Site
2.3.4	Strip the tubing and leave a minimum of 15 cm (6 inches) of tubing when sealing off the apheresis bag from the collection kit.	Clinical Site
2.3.5	Seal tubing using triple weld/seal technique.	Clinical Site
2.3.6	MNC, Apheresis product must be transferred and placed into a 2-8^{0}C shipper within 60 minutes of collection end time. If more time is required, store the apheresis product in a monitored refrigerator or intermediary transport at 2-8^{0}C until the time of shipment occurs. **NOTE: If the MNC, Apheresis product is stored overnight at the clinical site, provide the Sponsor with a copy of the temperature data report. Upload a copy of this report to MBOX-SDX.** ***(See further instructions in Module 5, related to packing & shipment.)***	Clinical Site
2.3.7	It is recommended to perform a WBC count at the midpoint of the collection to ensure the target cell number (9 x 10^9 Total WBCs) is reached and to minimize patient apheresis time.	Clinical Site
2.3.8	**IMPORTANT:** **If a minimum of 2 x 10^9 Total WBCs is not collected on the first attempt, a second collection may be scheduled and performed to attain this target. Product bags from multiple collections should not be combined. Each apheresis collection should be performed with the goal of achieving 9 x 10^9 Total WBC target.**	Clinical Site

2.4 Cell Management

Once cell collection is completed the collection is referred to as starting material, ready to be sent for manufacturing into IP.

Enrollment		
Step	**Task**	**Responsibility**
2.4.1	After an SEC-DIS (where applicable for some countries in EEA) or DIN or Apheresis ID is assigned to the subject, enter the following in IWRS on the day of collection: Refer to IWRS manual for instructions on how to use the IWRS. • Subject Name • Date of Birth • SEC-DIS (21-digits) where applicable for some countries in EEA, or DIN or Apheresis ID • Subject weight in kg on day of apheresis. **IMPORTANT**: must be rounded to 1 decimal point, i.e., 59.0 or 59.5 kg. **NOTE: All subject identifiers & weight entered in IWRS should be double checked for accuracy and should match entries on all source documents.**	Clinical Site
2.4.2	In Vineti, enter SEC-DIS (where applicable for some countries in EEA) or DIN or Apheresis ID. When scanning the DIN on an ISBT-128 label, remove the leading "=" and the 2 check digits at the end of the DIN. The DIN should be 13 digits long.	
2.4.3	If a 2nd apheresis collection is required, perform an "Apheresis Collection" transaction in IWRS to capture the updated information under "Investigator Site" tab in IWRS.	Clinical Site

	MANUAL COC/COI ACTIONS:	
	Complete the Apheresis Chain of Custody/Chain of Identity Form (see NA_APH) and enter all applicable data in the eCRF.	**Clinical Site**
	On completion of the form, upload a signed copy of this form to MBOX-SDX on the same day (see MBOX-SDX user guide).	

OR

	VINETI COC/COI ACTIONS:	
	Complete the Collection module in the Vineti system and enter all applicable data in the eCRF. **Refer to the "Vineti Collection User Guide" for additional details**	**Clinical Site Cell Lab Staff**

If the MNC, Apheresis product will be packed-out and shipped directly from the Apheresis center, proceed to **Module 5 'packing and shipment**'. The **[NA_TRN]** form does **NOT** need to be completed.

If the MNC, Apheresis product will be transferred to cell lab to be packed-out and shipped or for local cryopreservation, proceed to **Module 3 'Cell transfer'.** The **[NA_TRN]** form needs to be completed.

MODULE 2 COMPLETED

Module 3:
Cell Transfer

Version: 3.1

Date: 28-Mar-2022

Module 3: Table of Contents

3.1 Transfer of MNC, Apheresis Product to Cell Processing Lab

Module 3: Revision History

This is a controlled document.

VERSION DATED DD-MON-YYYY	SECTION(S) CHANGED	DESCRIPTION OF CHANGE(S)
01-Mar-2021	Initial Document	
05-Jul-2021	3.1	Minor updates to regional definitions and abbreviations Note added for overnight storage of the apheresis product
10-Mar-2022	3.1.1	Changed wording to: store in a monitored refrigerator or intermediary transport at 2-8^{0}C until the time of shipment occurs
28-Mar-2022	Module 3	Formatting changes

3.1 Transfer of MNC, Apheresis Product to Cell Processing Lab

Collected MNC, Apheresis product will be transferred to the site's cell processing lab or other facility for subsequent packing and shipment to the CPC.

Transfer of MNC, Apheresis Product to Cell Processing Lab		
Step	**Task**	**Responsibility**
3.1.1	Upon completion of collection, follow the sites internal procedures to transfer the MNC, Apheresis product to the cell processing lab or other shipment facility. MNC, Apheresis product must be transferred and placed into 2-8^{0}C shipper within one hour (60 minutes) of the end of collection. If more time is required prior to the transfer, store the apheresis product in a monitored refrigerator or intermediary transport at 2-8^{0}C until the time of shipment occurs. *(See further instructions in **Module 5** related to packing & shipment, if applicable.)* **NOTE: If the MNC, Apheresis is stored overnight at the Clinical Site, provide the Sponsor with a copy of the temperature data report. Upload copy of this report to MBOX-SDX.**	Clinical Site
3.1.2	To confirm release of custody of the MNC, Apheresis product, Apheresis Operator should SCAN or enter the Apheresis bag ID and provide electronic signature in the **Vineti system,** or complete required COI/COC form **(NA_TRN)** when using Manual method.	Clinical Site
3.1.3	To confirm receipt of custody of the MNC, Apheresis product, Cell Lab Operator should SCAN or enter the Apheresis bag ID and provide electronic signature in the **Vineti system** or complete required COI/COC form **(NA_TRN)** when using Manual method.	Clinical Site

	MANUAL COC/COI ACTIONS:	
	Complete the Transfer to Cell Laboratory or Shipment Facility Chain of Custody/Chain of Identity Form (see NA_TRN) and enter all applicable data in the eCRF.	**Clinical Site**
	On completion of the form, upload a signed copy of this form to the sponsor MBOX-SDX on the same day (see MBOX-SDX user guide).	

OR

	VINETI COC/COI ACTIONS:	
	Complete the Collection module in the Vineti system and enter all applicable data in the eCRF. **Refer to the "Vineti Collection User Guide" for additional details.**	**Clinical Site Cell Lab Staff**

MODULE 3 COMPLETED

Module 4:
Local Cryopreservation Procedure

Version: 3.1

Date: 28-Mar-2022

This module is only applicable to sites who perform on-site cryopreservation.

Module 4: Table of Contents

Module 4: Revision History

This is a controlled document.

VERSION DATE DD-MON-YYYY	SECTION(S) CHANGED	DESCRIPTION OF CHANGE(S)
01-Mar-2021	Initial Document	
05-Jul-2021	4.1 4.2 4.5 4.6	Minor updates to regional definitions and abbreviations Updates to shipper label applied to batch record Updates to Vineti steps Update wording for temperature excursion and CSOM as main point of contact Updated wording for IWRS notification and temperature excursions New Cryogenic Containment Pouch added
10-Mar-2022	4.1.1 & 4.1.3	Updated labelling numbers for two bag process and corrected to read apply cryopreservation label directly to the cryo bag
	4.3.3	Added note: Site nor local team has access to the EVO-IS system temperature data
	4.4.2, 4.5.4, 4.6.2, 4.6.6 & 4.6.11	Updated packing material 3-Piece Packing Solution: Poly bags, Tyvek bags, and absorbent pads or 1-Piece Packing Solution: CryoPort envelope and foam dunnage
28-Mar-2022	Module 4	Formatting and administrative changes

4.1 Local Cryopreservation: Labeling

This section is only applicable to sites that are utilizing onsite cryopreservation lab and should be followed alongside the Sponsor Batch Record.

Local Cryopreservation: Labeling		
Steps	**Task**	**Responsibility**
4.1.1	**Labels** The following labels will accompany the MNC, Apheresis product to the cell lab: • Two (2) Cryopreservation bags labels– to be attached to the cryopreserved bags. • Two (2) Cassette labels– to be affixed to the cassettes containing cryopreserved bags. • One (1) or Two (2) Shipper label– to accompany cryopreserved products inside the LN_2 shipper. When imported into the USA, another shipper label should be included in the clear packing envelope on the outside of the LN_2 shipper with airway bill. • One (1) Shipper label for Batch Record When using Vineti: Print Sponsor Cryopreservation labels. All necessary information will be pre-printed on the label. When using the manual method: Create subject specific Sponsor cryopreservation labels with the Sponsor approved label templates.	Clinical Site 
4.1.2	**Sponsor Cryopreservation bag labels:** Apply cryopreservation bag label directly to the cryopreservation bag.	Cell Lab
4.1.3	**Sponsor Cassette Label Application:** Apply a label to each cassette under room temperature conditions **30 MINUTES BEFORE the cassette is placed into the controlled rate freezer**, otherwise, the label will not adhere properly to the cassette.	Cell Lab
4.1.4	In the Vineti system, or the **XX_CRY form,** indicate the number of bags used for cryopreservation. Then apply each label (s) to the cryo bag and corresponding cassette. The Vineti system will require you to scan each cryo bag and the associated cassette label after affixing the labels. This step will confirm the cryo bag is placed in the corresponding cassette (same COI identifier).	Cell Lab 
4.1.5	**Label Reconciliation:** Once all labels have been applied to the bags and cassettes, **complete the Batch Record** to document which labels have been used, damaged and/or destroyed.	Cell Lab

4.2 Local Cryopreservation and LN_2 Storage

This section is only applicable to sites that are utilizing an on-site cryopreservation lab and should be followed alongside the Sponsor Batch Record.

Local Cryopreservation and LN_2 Storage		
Steps	**Task**	**Responsibility**
4.2.1	Cryopreservation and storage of the MNC, Apheresis product should be performed in the site cell lab per the **Sponsor Apheresis Cryopreservation Batch Record.** • Follow the Sponsor Apheresis Cryopreservation Batch Record for instructions on cell processing and cryopreservation of the MNC, Apheresis product. • The batch record outlines the bill of materials required for cell processing and cryopreservation referenced in the section related to study supplies.	Cell Lab
	**IMPORTANT: Next steps below need to be performed as quickly as possible. It is critical to pack the cassette(s) into the LN_2 freezer quickly to avoid thawing of the apheresis product.**	
4.2.2	Upon completion of the controlled rate freezing process, the MNC, Apheresis cryopreserved product must be stored at ≤ -120°C in the vapor phase of liquid nitrogen storage system. • Remove cassette with cryo bag product from the controlled rate freezer (one at a time) and perform the next steps in Vineti. **NOTE: Transfer times must be ≤3 minutes.** ⇒ Scan or enter COI Bag identifier from cassette label to confirm the COI for the cryo bag you are moving into storage. Click confirm. ⇒ On the next screen, scan or enter COI Bag Identifier and click confirm. Move cassette inside LN_2 tank. **NOTE: After the second scan move the product into storage. Enter the per bag details after the product is safely in storage.** ⇒ Repeat for each cassette. • Complete entry of cryopreservation data for each bag in the Vineti system.	Cell Lab 

	MANUAL COC/COI ACTIONS:	
	**Complete the CAR-T Local Cryopreservation Chain of Custody/Chain of Identity Form (see XX_CRY) and enter all applicable data in the eCRF.**	**Cell Lab**
	On completion of the form, upload a signed copy of this form to the sponsor MBOX-SDX on the same day (see MBOX-SDX user guide).	

OR

	VINETI COC/COI ACTIONS:	
	**Complete the Collection module in the Vineti system and enter all applicable data in the eCRF.** **Refer to the "Vineti Cryopreservation User Guide" for additional details.**	**Cell Lab**

4.3 Local Cryopreservation Shipping: Communication Plan with Site, Courier and Sponsor

There are two types of shipments related to the packaging and shipment of MNC, Apheresis Cryopreserved to the manufacturing facility.

- Shipment of charged empty LN_2 shipper to the site (for loading of MNC, Apheresis Cryopreserved)
- Shipment of MNC, Apheresis cryopreserved product from clinical site to the manufacturing facility

Communication Plan with Site, Courier and Sponsor		
Step	**Task**	**Responsibility**
4.3.1	Sponsor will initiate order pick up with the courier.	Sponsor
4.3.2	The courier will issue an automated pre-alert/order confirmation to the site. • The notification will reference the Subject Number to track and trace the shipment from clinical site to the manufacturing facility. • The notification will also reference the Air Waybill (AWB) for the shipment. **Note:** a print-out of the same AWB will be provided in the Shipper kit pouch within the shipper.	Courier
4.3.3	The courier will send one notification to the clinical site contact(s) prior to delivery of the empty charged shipper. The notification will be: • The day of delivery, within 1 hour prior to delivery. This is a geofence notification and will trigger when the shipment is within a 15-mile radius of the clinical site. • **NOTE:** The site or Janssen local team does not have access to the EVO-IS system temperature data. • Any delays in shipment date will be communicated by the courier via e- mail or phone call to the designated site contact.	Courier
4.3.4	The charged shipper will arrive at the site in the morning between 9:00-11:00 am local time for the pack-out of MNC, Apheresis Cryopreserved.	Cell Lab
4.3.5	The Sponsor will coordinate with the courier to return that afternoon to pick up the MNC, Apheresis cryopreserved product at an agreed local time for delivery to the manufacturing facility.	Sponsor
	**IMPORTANT Notify CSOM via email: Central.Scheduling@ITS.JNJ.com and copy your site manager if the packed shipper will not be ready for pick-up by the courier by agreed local time.**	

4.4 Local Cryopreservation Shipping: Review of Packing Materials

(Refer to **Module 3** of the 'CAR-T Packaging & Shipping Video'.)

Review of Packing Materials		
Step	**Task**	**Responsibility**
4.4.1	The following tools should be utilized in preparation for site packing and unpacking of the liquid nitrogen shipper: • Cryogloves • Safety glasses • Wire cutter **NOTE: Adhere to any additional site requirements for PPE when handling cryopreserved products and equipment.** **Do not discard any contents or packaging materials until you have read these instructions.**	Cell Lab
4.4.2	Upon the receipt of shipper, you will find the following components inside the outer shipper case: • a reusable **LN_2 shipper** (Savsu DV-10) • a labeled **Shipper Kit pouch** (inside the pouch within the shipper case) • a labeled **Consignee Kit pouch** (inside the pouch within the shipper case) The **Shipper Kit Pouch** is used when shipping MNC, Apheresis cryopreserved product back to the Sponsor. The **Shipper Kit Pouch** includes: • One (1) red tamper evident seal (for use on one side of the LN_2 shipper lid, number should match the AWB) • One (1) red tamper evident seal (for use on cassette rack) • One (1) zip tie (for use on the outer shipper case lid) • One (1) zip tie (for use on one side of the LN_2 shipper lid) • 3-Piece Packing Solution: Poly bags, Tyvek bags, and absorbent pads or 1-Piece Packing Solution: CryoPort envelope and foam dunnage • One (1) clear side packing envelope • AWB for shipment The **Consignee Kit Pouch** is used by the Sponsor when shipping the empty shipper back to the courier upon receipt of the MNC, Apheresis cryopreserved product. Information is included here only for reference. • 1 zip tie (for use on the outer shipper case) • AWB for return shipment of empty shipper **Inside the shipper,** there will be an empty cassette rack. This is used to store and secure the cassettes inside the shipper during transport.	Cell Lab

Review of Packing Materials

Step	Task	Responsibility
4.4.3 	**NOTIFY CSOM email Central.Scheduling@ITS.JNJ.com and copy Site Manager IF:** • The shipping container case is not secured. • The zip tie is missing from the outer case lid. • The subject number listed on the AWB does not match the intended subject. • The EVO-IS ID (last 4 digits) listed on the AWB does not match the LN_2 shipper. • Any contents are missing or incorrect from the Shipper Kit Pouch listed above. • There is a flashing alarm indicated on the temperature display or if the alarm light indicator is not functioning. **Example of Shipping Container and Components** 	Sponsor/ Cell Lab

4.5 Local Cryopreservation Shipping: Instructions for Receipt of Empty LN_2 Shipper

The following are step-by-step instructions for receipt of the empty LN_2 shipper in anticipation of packing-out of the MNC, Apheresis Cryopreserved. (Refer to **Module 4** of the 'CAR-T Packaging & Shipping Video'.)

Instructions for Receipt of the Empty LN_2 Shipper		
Step	**Task**	**Responsibility**
4.5.1	**The shipper will arrive inside an outer corrugated case. The outer corrugated case includes wheels and luggage handle for ease of transport.** Once the shipper has been transported to the appropriate packaging location, set the shipper upright and lower the luggage handle. 	Cell Lab
4.5.2	**The outer corrugated case is secured by buckle straps.** Unclip the buckle straps. Open the outer corrugated case lid. 	Cell Lab

Instructions for Receipt of the Empty LN_2 Shipper

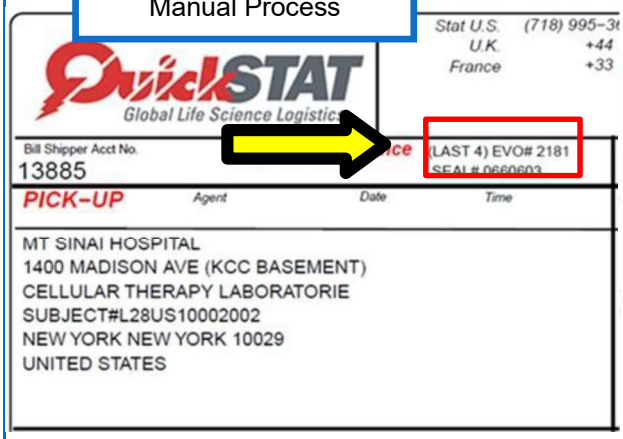
Step	Task	Responsibility
4.5.3	**The outer case shipper lid is secured by a single zip tie through the zipper pulls.** Cut and discard the zip tie then unzip the outer case lid. **NOTE: The site will need to use wire cutters (these are NOT included in the shipment).** 	Cell Lab
4.5.4	**Lift the shipper case lid.** 1. When the outer shipper case lid is opened, verify that the pouch within the outer case contains the Shipper kit pouch and Consignee kit pouch—which are labeled.  **Pouch within outer case** 2. Remove the Shipper kit pouch and its materials. These materials will be used for packing the MNC, Apheresis Cryopreserved. **There are two types of shipper kit pouches shown below:**  **3-Piece Packing Solution**  **1-Piece Packing Solution** 3. Leave the Consignee kit pouch inside the pouch. **NOTE: For the 1-Piece Packing Solution foam dunnage will be included in the Shipper kit pouch (not shown in image)**	Cell Lab

Instructions for Receipt of the Empty LN_2 Shipper

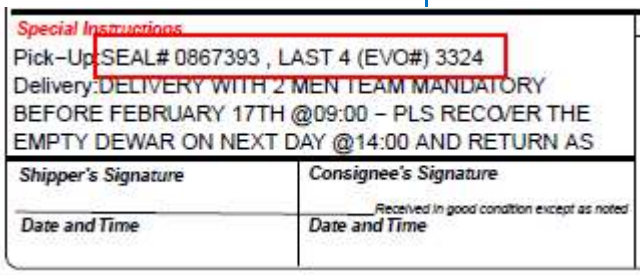
Step	Task	Responsibility
4.5.5	**Verify that the EVO-IS ID number (last 4 digits) on the AWB matches the EVO-IS ID number on the LN_2 shipper lid.**	Cell Lab

Quick Stat AWB

Manual Process



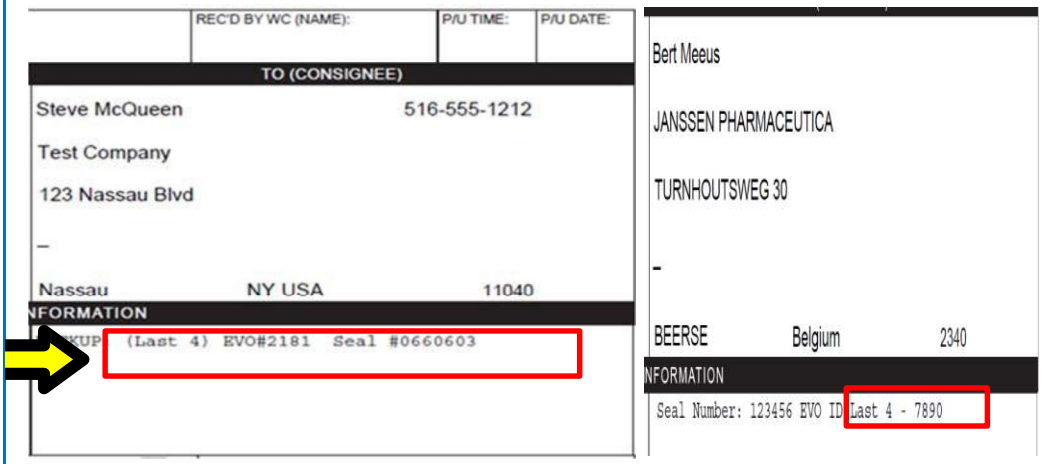
Vineti Process



Manual Process

Vineti Process

World Courier AWB



Evo-IS ID number location

Instructions for Receipt of the Empty LN_2 Shipper

Step	Task	Responsibility
4.5.6	**Confirm if there is any temperature excursion:** To determine if the temperature is within range, press the light indicator, release & wait for 5 seconds on the DV-10 lid. The indicator will emit a light. • Note the Janssen training video mentions a blue light. The light is white. • Note that a steady light indicates that the temperature is within range. Proceed to the next steps. Notify CSOM email Central.Scheduling@ITS.JNJ.com and copy Site Manager immediately and do not continue if: • A flashing light indicating a temperature excursion has occurred. • Temperature light indicator is not functioning. • **NOTE:** The site or Janssen local team does not have access to the EVO-IS system temperature data. **NOTE: Refer to Module 6, Section 6.7 Problems and Special Situation for further instructions for how to handle TOR.** **Press Indicator**  **Light Indicator** 	Cell Lab

Instructions for Receipt of the Empty LN_2 Shipper

Step	Task	Responsibility
4.5.7	**Inside the Shipper kit pouch, there are 2 tamper evident seals** • Tamper evident seal with "SECURED" and serial number listed • Tamper evident seal with "RACK" listed  Verify the tamper evident seal number (SEAL#) listed on the AWB matches the tamper evident seal from the Shipper kit pouch. **Quick Stat**  **World Courier** 	Cell Lab

4.6 Local Cryopreservation Shipping: Packing of MNC, Apheresis Cryopreserved Product into the LN_2 Shipper

The following are step-by-step instructions for packing the MNC, Apheresis Cryopreserved into the LN_2 shipper. (Refer to **Module 5** of the 'CAR-T Packaging & Shipping Video.)

REMINDER: Ensure all necessary PPE is on before the next steps.

⚠ The MNC, Apheresis Cryopreserved must be placed into the LN_2 shipper immediately following removal from the storage and verification of COC/COI.

Packing of MNC, Apheresis Cryopreserved Product into the LN_2 Shipper		
Step	**Task**	**Responsibility**
4.6.1	**Ensure that the following documents are available for reference and completion immediately after pack-out of the shipper.** 1. **XX_SHIP_CRYO Site Shipment Form for Chain of Custody/Chain of Identity Form** 2. Copy of **IWRS notification with subject information**	Cell Lab

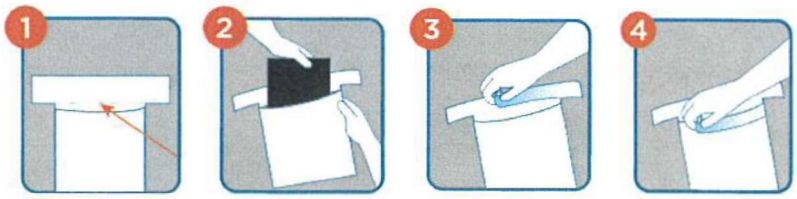
4.6.2	**Ensure all materials in the Shipper kit pouch are removed and staged for the pack-out. This includes the AWB.** **Shipper kit pouch components: 3-Piece Packing Solution**  **Shipper kit pouch components: 1-Piece Packing Solution**   **NOTE: Packing Solution foam dunnage will be included in the Shipper kit pouch (as shown above)**	Cell Lab

STOP	**IMPORTANT: The next steps need to be performed as quickly as possible. It is critical to avoid thawing of the MNC, Apheresis cryopreserved product as the cassette(s) are packed into the shipper. Co-locate all packing materials and shipper as much as possible.**

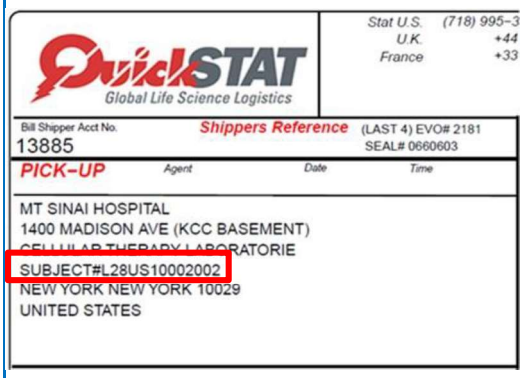
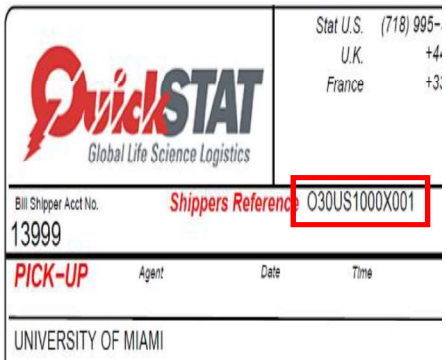
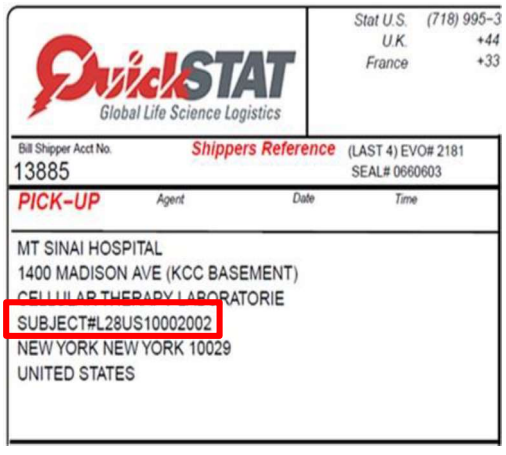
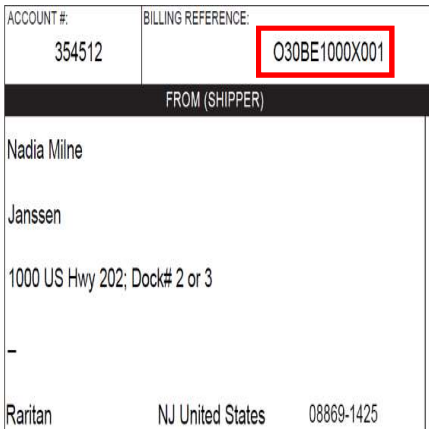
Packing of MNC, Apheresis Cryopreserved Product into the LN_2 Shipper

Step	Task	Responsibility
4.6.3	**If using the 3-piece packing solution Tyvek bag:** Place the absorbent pad into the Poly Bag. Insert the cassette into the Poly bag with the locking hinge toward the top. Remove the adhesive backing and seal the bag. Fold the poly bag and wrap tightly around cassette   	Cell Lab
4.6.4	Place the Poly bag into the Tyvek bag with locking hinge of the cassette towards top. Fold the one side of the Tyvek bag into the other. 	Cell Lab
4.6.5	Fold one side of the Tyvek bag so the cassette will fit into the rack. The cassette should now be fully placed into the Tyvek bag with locking hinge towards the top. 	Cell Lab

Packing of MNC, Apheresis Cryopreserved Product into the LN_2 Shipper

Step	Task	Responsibility
4.6.6	**<u>If using the 1-Piece Packing Solution</u>** Cryogenic Containment Pouch**:** 1) Pre-fold over the scored line shown by the arrow. The pre-fold may fold over the adhesive seal cover. 2) Insert the cassette with the locking hinge toward the top and push completely down past the adhesive seal into the Cryogenic Containment Pouch. Ensure the cassette is not behind the adhesive seal. 3) Peel off adhesive strip cover on top flap.  4) Peel off adhesive strip cover on the envelope pouch. 5) a. Seal the Cryogenic Containment Pouch. Ensure to fold flap along pre-folded scored line. b. Start sealing from center of pre-fold and work out to the sides. Seal must not have any wrinkles or gaps. 6) Fold tabs around seal with pressure. Tabs must be sealed as close as possible to the envelope.  	Cell Lab

Packing of MNC, Apheresis Cryopreserved Product into the LN_2 Shipper

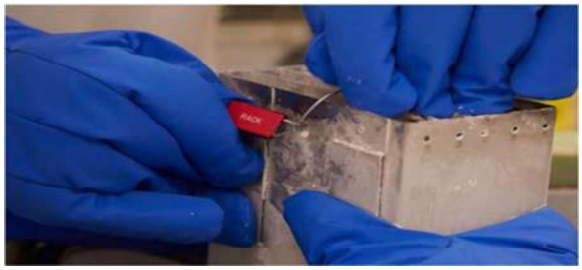
Step	Task	Responsibility
4.6.7	**Remove the first cassette (with MNC, Apheresis cryopreserved product) from LN_2 storage.** • Prior to packing the cassette, verify that the Subject Number on the **AWB** and on the copy of the **IWRS** matches the Subject Number on the cassette label. • As a reminder, the AWB is inside the Shipper kit pouch. **QuickStat AWB** Manual Process  Vineti Process  **World Courier AWB** Manual Process  Vineti Process  In Vineti for each cassette, scan or enter the COI Bag Identifier on the cassette as you remove it from storage and scan or enter the COI number on the Shipper Label once placed into shipper.	Cell Lab

Packing of MNC, Apheresis Cryopreserved Product into the LN_2 Shipper

Step	Task	Responsibility
4.6.8	Begin completing **XX_SHIP_CRYO Site Shipment Form for Chain of Custody/Chain of Identity Form.** **OR** **Complete the shipment section of the Collection module in the Vineti system and enter all applicable data in the eCRF.** **Refer to the "Vineti Cryopreservation User Guide" for additional details.**	Cell Lab
4.6.9	Remove the shipper lid and lift the cassette rack.  	Cell Lab
4.6.10	**NOTE:** Proper placement of the DV10 Smart Cap when not seated in the dewar body is **PROBE SIDE UP** on a flat surface. Serious damage to the probe may occur if placed otherwise.   	Cell Lab

Packing of MNC, Apheresis Cryopreserved Product into the LN_2 Shipper

Step	Task	Responsibility
4.6.11	Place sealed Tyvek bag or Cryogenic Containment Pouch with frozen bag/cassette into the cassette rack. Ensure proper orientation so the locking hinge of the cassette is at the top of the rack.  If using the 1-Piece Packing Solution place one piece of the foam dunnage on top of the envelope within the cassette rack. 	Cell Lab
4.6.12	Return the rack into shipper to prevent warming and close the shipper lid.  	Cell Lab

Packing of MNC, Apheresis Cryopreserved Product into the LN_2 Shipper		
Step	**Task**	**Responsibility**
4.6.13	Repeat the pack-out process for any of the remaining cassettes to be shipped. 	Cell Lab
4.6.14	After packing the final cassette, secure the cassette rack with the tamper evident seal. Feed the tamper evident seal with “RACK” through the cassette holes and secure. 	Cell Lab
4.6.15	Remove the shipper lid and place the cassette rack (with MNC, Apheresis cryopreserved product) into the shipper. Close the shipper lid.  	Cell Lab
4.6.16	Next, secure the lid and lower the shipper handle to allow for the closing of the shipper lid after tamper evident seal is attached. 	Cell Lab

Packing of MNC, Apheresis Cryopreserved Product into the LN_2 Shipper

Step	Task	Responsibility
4.6.17	Feed the tamper evident seal that contains the word **"SECURED"** and seal number through the metal hook and lid. As a reminder, this seal number needs to match the seal number listed on the AWB. On the other side of the shipper lid, wrap and secure a zip tie through the lid and around the handle.  	Cell Lab
4.6.18	Once the shipper lid is secured, place the verified shipper label into the cryogenic containment pouch. **NOTE: Only the Consignee kit pouch and the shipper label should remain inside the pouch within the shipper case.**  	Cell Lab

Packing of MNC, Apheresis Cryopreserved Product into the LN_2 Shipper

Step	Task	Responsibility
4.6.19	Obtain the second zip tie provided in the Shipper kit pouch. Zip the outer case lid closed and secure by passing the single zip tie through the zipper pulls. Fasten the lid of the outer corrugated case by fastening the buckle straps 	Cell Lab
4.6.20	Remove the existing AWB and place the new AWB (from the Shipper kit pouch) into the clear packing envelope. Place the additional shipper label with the new AWB into the clear packing envelope. Applicable to all sites **excluding USA**. Discard all leftover materials and packaging per site disposal procedures. Discard any remaining items and bags from Shipper kit pouch.  	Cell Lab

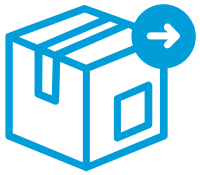
⚠ **REMINDER: The Sponsor will coordinate with the courier to pick up the LN_2 shipper packed with MNC, Apheresis cryopreserved product from the site at agreed local time. Notify CSOM via email Central.Scheduling@ITS.JNJ.com and copy the site manager immediately if there are any constraints for getting this shipment ready at agreed local time.**

	MANUAL COC/COI ACTIONS:	
	Complete the CAR-T Local Cryopreservation Chain of Custody/Chain of Identity Form (see XX_SHIP_CRYO) and enter all applicable data in the eCRF.	**Cell Lab**
	On completion of the form, upload a signed copy of this form to the sponsor MBOX-SDX on the same day (see MBOX-SDX user guide).	

OR

	VINETI COC/COI ACTIONS:	
	Complete the shipment section of the Collection Module in the Vineti system and enter all applicable data in the eCRF. **Refer to the "Vineti Cryopreservation User Guide" for additional details.**	**Cell Lab**

MODULE 4 COMPLETED



Module 5:
Packaging and Shipment

Version: 3.1

Date: 28-Mar-2022

This module is applicable for sites shipping apheresis to CPC only.

Module 5: Table of Contents

Module 5: Revision History

This is a controlled document.

VERSION DATE DD-MON-YYYY	SECTION(S) CHANGED	DESCRIPTION OF CHANGE(S)
01-Mar-2021	Initial Document	
05-Jul-2021	5.3	Minor updates to regional definitions and abbreviations throughout document Updated image for temptale ultra device
10-Mar-2022	5.1.2, 5.3.1,	Updated instructions for EEA & ISR Removed OBC shipments and updated shipping details for EEA
	5.4.1	Updated statement added for EEA & ISR Credo cube courier arrangements
28-Mar-2022	Module 5	Formatting and administrative changes

5.1 Communication Plan with Site, Courier & Sponsor

- There are two types of shipments related to the packaging and shipment of MNC, Apheresis product collections.
  - Shipment of empty CREDO CUBE shipper to the site (for packing of MNC, Apheresis product)
  - Shipment of MNC, Apheresis product from clinical site to the CPC

Communication Plan with Site, Courier & Sponsor		
Step	**Task**	**Responsibility**
5.1.1	The Sponsor will coordinate pick-up of MNC, Apheresis product collection on the day of the scheduled apheresis from the clinical site. Shipping couriers • QuickSTAT (Except Canada) • World Courier	Sponsor
5.1.2	The Courier will issue an automated pre-alert/order confirmation to the site. • The notification will reference the Subject Number to track and trace the shipment from the clinical site to the manufacturing facility. • The notification will also reference the AWB for the shipment. **Note:** a print-out of the same AWB will be provided in the **Clinical Site kit pouch** within the shipper.	Courier
5.1.3	The CREDO CUBE shipper will arrive at the site at **the agreed local time** for the packing of MNC, Apheresis product.	Courier
5.1.4	The Sponsor will coordinate with the courier to return that afternoon to pick up the MNC, Apheresis product at confirmed local time for delivery to the CPC.	Sponsor / Courier
	**REMINDER: The Sponsor will coordinate with the courier to pick up the CREDO CUBE packed with MNC, Apheresis from the site at agreed local time. Notify CSOM email Central.Scheduling@ITS.JNJ.com immediately if there are any constraints for getting this shipment ready at agreed local time.**	Clinical Site

5.2 Review of Packing Materials

This section describes the packing materials required for packing apheresis product.

Applicable for NA, except for Canada:

Review of Packing Materials		
Step	**Task**	**Responsibility**
5.2.1	Receipt of CREDO CUBE Shipper. Check that the CREDO CUBE shipment contains the following: • CREDO CUBE shipper • Labeled Clinical Site kit pouch • Labeled Central Cryopreservation kit pouch	Clinical Site
5.2.2	The Clinical Site kit pouch is used when shipping MNC, Apheresis product to the CPC. The Clinical Site kit pouch includes: • Non activated temperature monitoring device (TempTale Ultra) • Poly bag • Absorbent pad • AWB for shipment to the CPC	Clinical Site
5.2.3	The Central Cryopreservation kit pouch remains inside the brown payload box. Do not remove as it is intended for future use at the CPC. This information is included here only for reference.	Clinical Site
	**Notify CSOM via email Central.Scheduling@ITS.JNJ.com and copy your site manager if any contents are missing or temperature monitoring device activated prior to receipt at the site.**	

Applicable for Canada only:

Review of Packing Materials		
Step	**Task**	**Responsibility**

5.2.1	Receipt of CREDO CUBE Shipper
	
	Check that the CREDO CUBE shipment contains the following:
	• CREDO CUBE shipper
	• Large Polythene Bag containing:
	  • Poly Bio Bag
	  • Non activated temperature monitoring device (TempTale Ultra)
	  • Absorbent material
		Clinical Site

	**Notify CSOM via email Central.Scheduling@ITS.JNJ.com and copy your site manager if any contents are missing or temperature monitoring device activated prior to receipt at the site.**	

5.3 Packing of MNC, Apheresis Product into the CREDO CUBE Shipper [NA, except Canada]

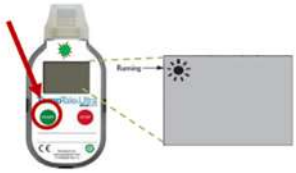
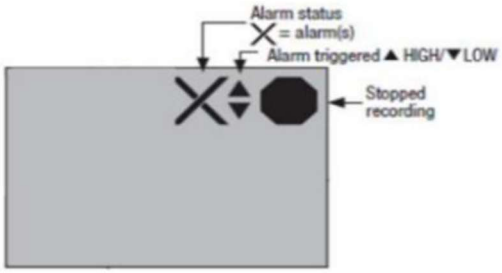
This section provides step-by-step instructions for packing the MNC, Apheresis product into the CREDO CUBE shipper.

Refer to Module 3 of the 'CAR-T Packaging & Shipping Video Central Cryo Manual' video on the Study Portal.

Packing of MNC, Apheresis Product into the CREDO CUBE Shipper		
Step	**Task**	**Responsibility**
5.3.1	Open outer corrugate of the empty CREDO CUBE shipper. 	Clinical Site
5.3.2	Open the top panel and remove the VIP panel.  	Clinical Site
5.3.3	Open brown payload box. • Remove the **Clinical Site kit pouch** and stage its components for pack- out. **IMPORTANT:** Leave the **Central Cryopreservation kit pouch** inside the shipper. This is for the CPC. 	Clinical Site

Packing of MNC, Apheresis Product into the CREDO CUBE Shipper		
Step	**Task**	**Responsibility**
5.3.4	Prior to starting packing, verify that the Subject Number on the AWB matches the Subject Number listed on the apheresis bag and Shipper Label. Manual Process  PICK-UP Agent Date Time MT SINAI HOSPITAL 1400 MADISON AVE (KCC BASEMENT) CELLULAR THERAPY LABORATORIE SUBJECT#L28US10002002 NEW YORK NEW YORK 10029 UNITED STATES Vineti Process  QuickSTAT Global Life Science Logistics Stat U.S. (718) 995- U.K. +4 France +3 Bill Shipper Acct No. 13999 Shippers Reference O30US1000X001 PICK-UP Agent Date Time UNIVERSITY OF MIAMI	Clinical Site
5.3.5	In Vineti, scan or enter the COI number on the shipper label to capture the timestamp of the packing step or document in the manual forms. Refer to Vineti module for detailed instructions.	Clinical Site 
5.3.6	Enter the AWB Number in Vineti and complete shipment checklist or document in the manual forms.	Clinical Site
5.3.7	Once the subject information is verified, place the MNC, Apheresis product bag into the poly bag with the absorbent pad. • Remove the adhesive backing and seal the bag with the MNC, Apheresis product inside.  • Gently place the MNC, Apheresis product into the shipper.	Clinical Site

Packing of MNC, Apheresis Product into the CREDO CUBE Shipper

5.3.8	Activate the TempTale: • Press on the Green Start button until the "SUN" icon appears.  **IMPORTANT**: If any of these icons appears on the screen, notify CSOM via email Central.Scheduling@ITS.JNJ.com and copy your site manager immediately:  • Once activated, place the TempTale into the shipper next to the collection bag. 	Clinical Site

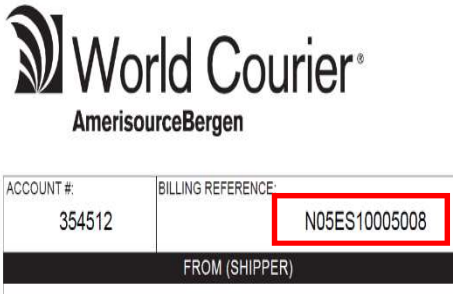
Packing of MNC, Apheresis Product into the CREDO CUBE Shipper		
Step	**Task**	**Responsibility**
5.3.9	Close and secure the top White TIC™ panel of the shipper 	Clinical Site
5.3.10	Place the VIP Panel on the top and secure the outer corrugate.  	Clinical Site
5.3.11	Once the shipper is secured, place the shipper label and AWB into the packing envelope. • Ensure the existing AWB has been removed. • The shipper is now ready for pick-up by the courier. 	Clinical Site
	IMPORTANT! In case of Emergency during the packing process, notify CSOM via email Central.Scheduling@ITS.JNJ.com and copy the Site Manager.	

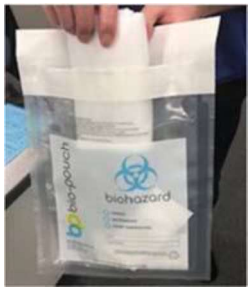
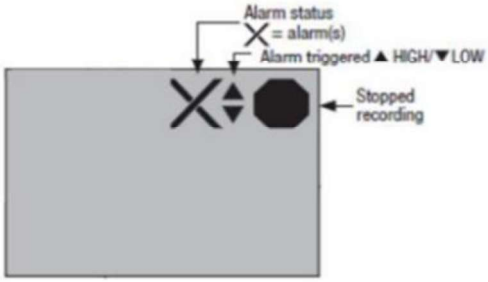
5.3 Packing of MNC, Apheresis Product into the CREDO CUBE Shipper [Canada only]

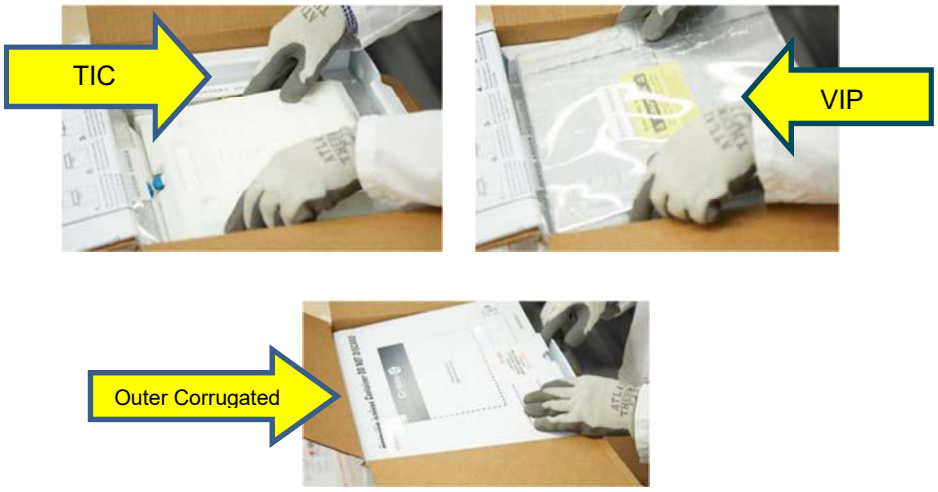
This section provides step-by-step instructions for packing the MNC, Apheresis product into the CREDO CUBE shipper. (Refer to Module 3 of the 'CAR-T Packaging & Shipping Video Central Cryo – Manual' video on the Study Portal.)

Packing of MNC, Apheresis Product into the CREDO CUBE Shipper		
Step	**Task**	**Responsibility**
5.3.1	Open outer corrugate of the empty CREDO CUBE shipper. 	Clinical Site
5.3.2	Open the top panel and remove the VIP panel. 	Clinical Site
5.3.3	Remove the White TIC™ Panel. 	Clinical Site

Packing of MNC, Apheresis Product into the CREDO CUBE Shipper

Step	Task	Responsibility
5.3.4	Check contents: • Locate the Large Polythene bag inside the CREDO CUBE shipper. • The contents needed for the packing will be inside the Polythene bag- (Poly Bio-Bag with absorbent pad, non-activated temperature monitoring device (TempTale Ultra). • Remove the Poly Bio-Bag from the Polythene bag to pack out the MNC Apheresis product. • Leave the TempTale Ultra in the shipper until ready to start the logger after the packing is completed. **NOTE: all finished contents should go inside this Polythene bag** Poly Bio-Bag  	Clinical Site
5.3.5	Prior to start packing, remove the AWB from the outer lid pouch and verify that the Subject Number on the AWB matches the Subject Number listed on the apheresis bag and shipper label. **Manual Process**  **Vineti Process** 	Clinical Site
5.3.6	Scan or enter in Vineti the COI number from the shipper label to capture the timestamp of the packing step or complete required COI/COC form. Refer to Vineti Collection module for detailed instructions. Enter the AWB in Vineti and complete shipment checklist or complete required COI/COC form.	Clinical Site

Packing of MNC, Apheresis Product into the CREDO CUBE Shipper		
Step	**Task**	**Responsibility**
5.3.7	Once the subject information is verified, place the MNC, Apheresis product bag into the poly bag with the absorbent pad. • Remove the adhesive backing and seal the bag with the MNC, Apheresis product inside. • Gently place the MNC, Apheresis product into the Polythene bag of the shipper. 	Clinical Site
5.3.8	Activate the TempTale: • Remove the logger from the Polythene bag. • Press on the Green Start button until the "SUN" icon appears.  **IMPORTANT:** If any of these icons appears on the screen, notify CSOM via email Central.Scheduling@ITS.JNJ.com and copy Site Manager immediately: 	Clinical Site
5.3.9	Once activated, place the TempTale into the Polythene bag of the shipper next to the packed Poly-Bio-Bag.  	Clinical Site

Packing of MNC, Apheresis Product into the CREDO CUBE Shipper		
Step	**Task**	**Responsibility**
5.3.10	Close & secure the top White TIC™ panel of the shipper. • Place the VIP Panel on the top and secure the outer corrugate. 	Clinical Site
5.3.11	Once the shipper is secured, place the shipper label and the existing AWB (from Step 5.3.5) into the packing envelope. The shipper is now ready for pick-up by the courier. 	Clinical Site

5.4 Courier Pick Up of the Packed CREDO CUBE Shipper

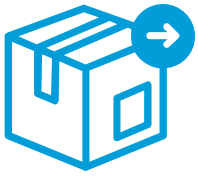
Courier Pick Up of Packed CREDO CUBE Shipper		
Step	**Task**	**Responsibility**
5.4.1	The Sponsor will coordinate with the courier to return that afternoon to pick up the MNC, Apheresis product collection at **agreed local time** for delivery to CPC.	Sponsor
⚠	**IMPORTANT** Notify CSOM via email **Central.Scheduling@ITS.JNJ.com** if the packed shipper will not be ready for pick-up by the courier by agreed local time. Should the pickup time be delayed, alternate plans may need to be implemented based on flight or ground transportation constraints.	

🔗	**MANUAL COC/COI ACTIONS:**	
✎	**Complete the CAR-T Central Cryo Site Shipment Form for Chain of Custody/Chain of Identity Form (see NA_SHIP_APH) and enter all applicable data in the eCRF.**	**Clinical Site**
⬆	On completion of the form, upload a signed copy of this form to the MBOX-SDX on the same day (see MBOX-SDX user guide).	

OR

🔗	**VINETI COC/COI ACTIONS:**	
🖥	**Complete the Collection module in the Vineti system and enter all applicable data in the eCRF.** **Refer to the "Vineti Collection User Guide" for additional details.**	**Clinical Site** **Cell Lab Staff**

MODULE 5 COMPLETED



Module 6:

Receipt and Storage of the Investigational Product

Version: 3.1

Date: 28-Mar-2022

Module 6: Table of Contents

Module 6: Revision History

This is a controlled document.

VERSION DATE DD-MON-YYYY	SECTION(S) CHANGED	DESCRIPTION OF CHANGE(S)
01-Mar-2021	Initial Document	
05-Jul-2021	6.3 6.4 6.7	Updated information for temperature excursions Updated instructions on placement of DV10 smart cap Section related to PQC's has been updated to include damage to secondary container 'Cassette' Cryogenic Containment Pouch added as scheduled for August 2021 roll out
10-Mar-2022	6.1.1	Step updated to include CQUENCE clinical trials portal process
	6.2.2, 6.4.5	Added Certificate of Compliance & CAR-T Final Release Form to be edited per region
	6.3.4	Edited shipper documents provided per region
	6.6	Updated requirements for onsite transport between two locations
	6.7	Updated statement for PQC to include bag and or cassette
28-Mar-2022	Module 6	Formatting and administrative changes

6.1 Communication Plan with Site, Courier & Sponsor

There are two types of shipments related to the receipt and handling of IP. If a situation falls outside of the shipments listed below, or the shipments related to the packaging and shipment of MNC, Apheresis product, notify CSOM via Central.Scheduling@ITS.JNJ.com and copy site manager for further instructions.

1. Shipment of IP from manufacturing facility
2. Shipment of empty LN_2 shipper back to Sponsor (for recharge/reuse).

Communication Plan with Site, Courier & Sponsor		
Step	**Task**	**Responsibility**
6.1.1	Once manufacturing has started, the site will be able to book the IP on-site date within the CQUENCE Clinical Trials portal. If the IP on-site date needs to be rescheduled, the site should reach out to Central.Scheduling@its.jnj.com to alert the CSOM to schedule a new date.	Clinical Site
	The Sponsor will review the initially scheduled IP on-site date (as well as any potential rescheduled dates) and approve the shipment date. The currently approved date of IP on site will always be visible on the specific Patient Journey page in the CQUENCE Clinical Trials portal.	Sponsor
6.1.2	In alignment with the approved IP on-site date, the Sponsor will initiate order pick up once the IP has been released from Manufacturing Quality. Shipping couriers are either: • Quick Stat • World Courier	Sponsor
6.1.3	The courier will issue an automated pre-alert/order confirmation to the site. • The notification will reference the Subject Number to track and trace the shipment from manufacturing facility to the site. The notification will also reference the AWB for the shipment. **NOTE: A print-out of the same AWB will be provided in the Consignee kit pouch within the shipper.**	Courier
6.1.4	The courier will send one notification to the clinical site contact(s) prior to delivery of the shipper. The notification will be: • The day of delivery, within 1 hour prior to delivery. This is a geofence notification and will trigger when the shipment is within a 15 mile radius of the clinical site. • **NOTE:** The site or the Janssen local team does not have access to the EVO-IS system temperature data. • Any delays in shipment date will be communicated by the courier via e-mail or phone call to the designated site contact.	Sponsor/Courier
6.1.5	The shipper will arrive at the site at the agreed local time for the receipt of the IP.	Courier

Communication Plan with Site, Courier & Sponsor		
6.1.6	The Sponsor will coordinate with the courier to pick up the empty shipper that afternoon at the agreed local time.	Sponsor
	**IMPORTANT! Notify the CSOM via Central.Scheduling@ITS.JNJ.com and copy Site Manager immediately if the empty shipper will not be ready for pick-up by the courier by agreed local time. Should the pick-up time be delayed, alternate plans may need to be implemented based on flight or ground transportation constraints.**	

6.2 Review of Packing Materials

This section describes the packing materials required for unpacking IP.

Refer to Module 2 of the 'CAR-T Packaging & Shipping Video Central Cryo – Manual' video on the Study Portal.

Review of Packing Materials		
Step	**Task**	**Responsibility**
6.2.1	Upon receipt of the IP, check to ensure all necessary contents and packaging materials (below) are present. As a reminder, the following tools should be utilized in preparation for site unpacking of liquid nitrogen shipper: • Cryogloves • Safety glasses • **Site will need to use wire cutters (these are NOT included in the shipment).** **NOTE: Adhere to any additional site requirements for PPE when handling cryopreserved products and equipment.** **Do not discard any contents or packaging materials until you have read these instructions.**	Clinical Site

6.2.2	Upon the receipt of the shipper, you will find the following components inside the outer shipper case:
	
	• a reusable **LN_2 shipper** (Savsu DV-10)
	• a labeled **Consignee Kit pouch** (inside the pouch within the shipper case)
	• Certificate of Compliance
	• **Cassette rack with IP:** located inside of LN_2 shipper, secured with red tamper evident seal and wire (can be verified once LN_2 shipper is opened).
	
	The **Consignee kit pouch** includes:
	
	• Materials used by the site when shipping the empty LN_2 shipper:
	  • 1 zip tie (for use on the outer shipper case). A back-up zip tie will be included.
	  • AWB for return shipment of empty shipper
		Clinical Site

Review of Packing Materials

Step	Task	Responsibility
6.2.3 	**NOTIFY CSOM via Central.Scheduling@ITS.JNJ.com and cc site manager IF:** • The shipping container case is not secured. • The zip tie is missing from the outer case lid. • The Subject Number listed on the AWB does not match the intended subject. • The EVO-IS ID (last 4 digits) listed on the AWB does not match the LN_2 shipper. • The tamper evident seal number (SEAL#) listed on the AWB does not match the tamper seal on the shipper lid. • Any contents are missing from the consignee kit pouch listed above. • There is a flashing alarm indicated on the temperature display. • The temperature light indicator is not functioning. **Shipping Container and Components** 	Clinical Site

6.3 Receipt of the LN_2 Shipper Containing IP

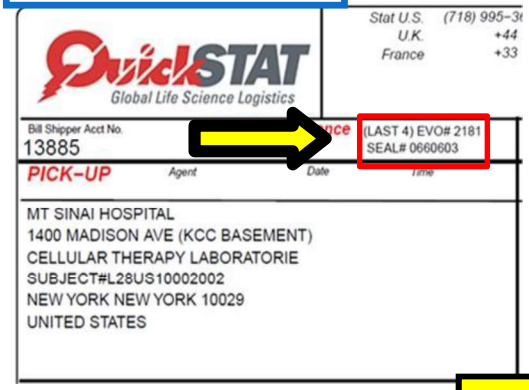
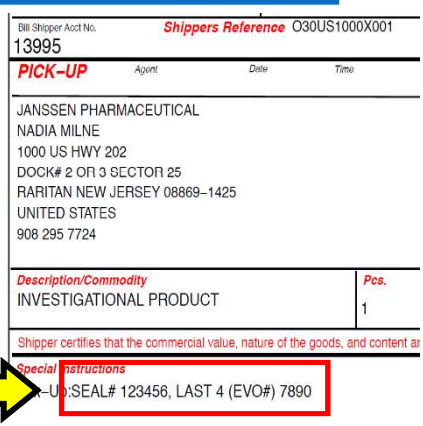
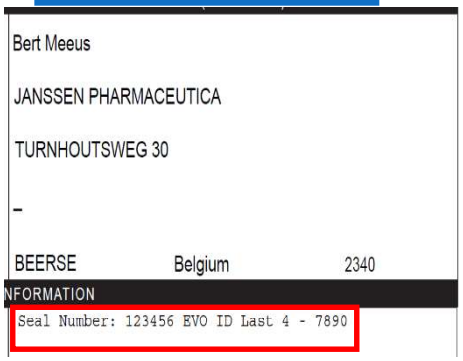
This section outlines step-by-step instructions for receipt of the packed LN_2 shipper containing IP. (Refer to Module 4 of the 'CAR-T Packaging & Ship- ping Video Central Cryo – Manual' video on the study Portal.)

Receipt of the LN_2 Shipper Containing IP		
Step	**Task**	**Responsibility**
6.3.1	The shipper will arrive inside an outer corrugated case. The outer corrugated case includes wheels and luggage handle for ease of transport. 1. Once the shipper has been transported to the appropriate unpackaging location, set the shipper upright and lower the luggage handle. 2. Remove the AWB. 	Clinical Site
6.3.2	The outer corrugated case is secured by buckle straps. Unclip the buckle straps. Open the outer corrugated case lid. 	Clinical Site
6.3.3	The outer case shipper lid is secured by a single zip tie through the zipper pulls. Cut and discard the zip tie then unzip the outer case lid. **NOTE: The site will need to use wire cutters (these are NOT included in the shipment.** 	Clinical Site

Receipt of the LN_2 Shipper Containing IP

Step	Task	Responsibility
6.3.4	Lift the shipper case lid. • When the outer shipper case lid is opened, verify that the pouch within the outer case contains the consignee Kit Pouch. The pouch contains: o One (1) shipper label o One (1) zip-tie to secure the outer shipper lid prior to return o AWB use to return the empty LN_2 shipper. o Certificate of Compliance If using Vineti select the COI number on the Infusion tab, then scan or enter in Vineti the COI Number found on the Shipper Label. If using the manual process, complete the required COC/COI form. • For each item on the Shipment Receipt Checklist, click **Yes or No** to indicate the state of the shipment as it arrived and enter the requested information. • Remove the consignee kit pouch and its materials. **Pouch within outer case**  **Consignee Kit pouch** 	Clinical Site 

Receipt of the LN_2 Shipper Containing IP

Step	Task	Responsibility
6.3.5	Verify that the EVO-IS ID number (last 4 digits) on the AWB matches the EVO-IS ID number on the LN_2 shipper lid. **Quick Stat AWB** Manual Process  Vineti Process  **World Courier AWB** Manual Process  Vineti Process  **EVO-IS ID number location**  	Clinical Site

Receipt of the LN_2 Shipper Containing IP

Step	Task	Responsibility

6.3.6	Confirm if there is any temperature excursion:
	• To determine if the temperature is within range, press the light indicator, release & wait for 5 seconds on the DV-10 lid. The indicator will emit a light. Note: The Sponsor training video mentions a blue light. The light is white.
	• Note that a steady light indicates that the temperature is within range. You can proceed to the next steps.
	• If any of the following occurs, remove the IP from the LN_2 shipper, place in the proper storage condition, and notify CSOM via Central.Scheduling@ITS.JNJ.com and copy Site Manager:
	  • A flashing light indicating a temperature excursion has occurred.
	  • Temperature light indicator is not functioning (does not turn on)
	Press Indicator **Light Indicator**
	  	

6.3.7	Verify the tamper evident seal number (SEAL#) listed on the AWB matches the tamper evident seal number on the LN_2 shipper. 	Clinical Site

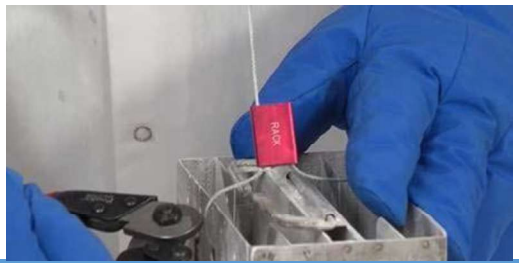
6.4 Unpacking and Storage of IP

The following are step-by-step instructions for unpacking the IP from the shipper. It is recommended that two personnel work together during this process.

REMINDER: Ensure all necessary PPE is on before the next steps. Also, ensure that the form is available for reference and completion.

IMPORTANT: IP must be placed into storage immediately following removal from the LN_2 and verification of COC/ COI.

Unpacking and Storage of IP		
Step	**Task**	**Responsibility**
6.4.1	**Make sure AWB, Certificate of Compliance and copy of IWRS are available to conduct COC/COI checks.** Cut and discard the zip tie and tamper seal on the shipper lid so it can be opened when necessary. **NOTE: The site will need to use wire cutters (these are NOT included in the shipment).** 	Clinical Site
STOP	**NOTE:** Proper placement of the DV10 Smart Cap when not seated in the dewar body is **PROBE SIDE UP** on a flat surface. Serious damage to the probe may occur if placed otherwise. 	Clinical Site
STOP	**IMPORTANT: Next steps below need to be performed as quickly as possible. It is critical to pack the cassette(s) into the LN_2 freezer quickly to avoid thawing of the IP.**	Clinical Site

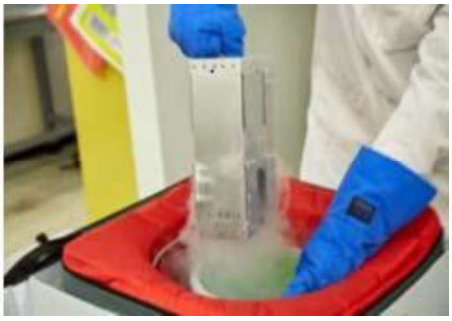
Unpacking and Storage of IP		
Step	**Task**	**Responsibility**
6.4.2	Remove the shipper lid and lift the cassette rack. Close the shipper lid once the rack is removed.  	Clinical Site
6.4.3	Using a wire cutter, cut and discard the tamper evident seal wire on the cassette rack and remove dunnage (only when using 1-Piece Cryogenic Pouch) located on top of the envelope within the cassette rack. 	Clinical Site

Unpacking and Storage of IP

Step	Task	Responsibility
6.4.4	Remove the bag(s) containing the IP from the rack slots.  Cut open the pouch and remove the cassette.  	Clinical Site

Unpacking and Storage of IP

Step	Task	Responsibility
6.4.5	Prior to placing the cassette into LN_2 storage, verify the following on each **bag and cassette:** • Subject # on bag and cassette label matches the Subject # on the AWB, **IWRS, shipper label and Certificate of Compliance**. • DIN or Apheresis ID or SEC-DIS (where applicable in some EEA countries) on the bag and cassette label matches IWRS, shipper label and Certificate of Compliance. • IP Lot # on bag and cassette label matches the Lot # on the IWRS, Shipper Label and **Certificate of Compliance** In Vineti for each cassette, scan or enter the COI number on the Shipper Label while removing it from the shipper. Then, scan the COI Bag Identifier on the cassette as the IP is placed into local storage. Place the cassette with IP immediately into the LN_2 storage. **IP cassette(s) should not be exposed to ambient temperature greater than 3 minutes.** **IMPORTANT: If 3 mins is exceeded, notify CSOM via Central.Scheduling@ITS.JNJ.com and copy Site Manager.** **Complete the Product Receipt Checklist on Vineti or complete the required COI/ COC form.**	Clinical Site 
6.4.6	Place empty cassette rack inside shipper. Remove the shipper lid and use correct placement of the DV10 Smart Cap **PROBE SIDE UP** on a flat surface. 	Clinical Site

Unpacking and Storage of IP		
Step	**Task**	**Responsibility**
6.4.7	Place the empty cassette rack into the shipper. Lower the shipper handle to allow for the closing of the shipper lid.  Close the LN_2 shipper lid. 	Clinical Site

	MANUAL COC/COI ACTIONS:
	Complete the IP Shipment Receipt Checklist for Site (see NA_REC) and enter all applicable data in the eCRF.
	On completion of the form, upload a signed copy of this form to MBOX-SDX on the same day (see MBOX-SDX user guide).

OR

	VINETI COC/COI ACTIONS:
	Complete the Infusion module in the Vineti system and enter all applicable data in the eCRF. **Refer to the "Vineti Infusion User Guide" for additional details.**

6.5 Prepare Empty LN_2 Shipper for Shipment

After completion of the IP Shipment Receipt Checklist for Site, the site will prepare the empty shipper for shipment.

Prepare Empty LN_2 Shipper for Shipment		
Step	**Task**	**Responsibility**
6.5.1	• Obtain the second zip tie provided in the consignee kit pouch • Zip the outer case lid closed and secure by passing the single zip tie through the zipper pulls. • Fasten the lid of the outer corrugated case by fastening the buckle straps.  	Clinical Site
6.5.2	• Place the AWB into the clear packing envelope for courier pick-up. • Discard all leftover materials and packaging per site disposal procedures. 	Clinical Site
	REMINDER: The Sponsor will coordinate with the courier to pick up the empty LN_2 shipper from the site at the agreed local time. Notify CSOM via Central.Scheduling@ITS.JNJ.com and copy Site Manager immediately if there are any constraints for getting this shipment ready for agreed local time.	Clinical Site

6.6 Storage and Monitoring of IP

IP must be stored according to the conditions on the label, in a secure location with limited access.

Storage

During on-site storage and during any internal transportation between sites, IP must not be separated from the cassette. The packaging is designed to protect the drug from breakage and damage and parts should not be separated.

JNJ-68284528 (ciltacabtagene autoleucel) must be kept frozen at ≤-120°C vapor phase of liquid nitrogen. For frozen IP, maintenance records for the liquid nitrogen storage system must be available for Sponsor review.

Storage Temperature Monitoring of IP

Temperature conditions during on-site storage and any internal transportation between sites of IP must be monitored and recorded (e.g., temperature logs or data, charts or graphs from temperature monitoring equipment or devices). The use of a temperature monitoring device is required for the storage of all IP. Upon removal of IP from storage for transport, the time of removal must be documented. Documentation of the temperature is required for transport of IP from the storage location to the administration site. All documentation/data of the storage temperature must be retained in accordance with the records retention policy outlined in the Protocol and Clinical Trial Agreement, and applicable legal and regulatory requirements.

Frequency of Temperature Monitoring Verification

The output of the temperature monitoring device must be verified, and this verification recorded on a temperature log/ temperature alarm log, at a minimum, daily, during site working days.

It is not necessary to check the temperature monitoring equipment on weekends and holidays. If a temperature out- of-range (TOR) occurs during the weekend or holiday, report it on the morning of the first working day following the weekend or holiday.

A blank Temperature Log and a Temperature Alarm Log can be found in the Blank Forms section of the Site IP Binder; the Site Manager will advise you on which form(s) apply to your site. Temperature Logs must identify or link to (e.g., through the serial number or unique identifier) the temperature monitoring device and, if applicable, the liquid nitrogen storage system.

In the event of a TOR occurrence during on-site storage, appropriate actions are described in the Problems and Special Situations section 6.7. If a Sponsor-provided device is used, first correct the cause of the excursion (e.g., restore power in case of failure) and wait for the temperature to come back within range. Then stop the alarmed device and proceed with downloading the data for reporting the TOR.

Storage temperature monitoring with a site's own monitoring equipment

To ensure that the temperature monitoring equipment continues to meet expectations throughout the study, it must be calibrated in accordance with the manufacturer's recommendations. Calibration documentation, and maintenance documentation for the liquid nitrogen storage system must be filed and made available for inspection.

When the site's temperature monitoring device is equipped with audible and visible alarms to attract immediate attention in the event of a TOR, the proper functioning of these alarms must also be periodically tested and documented.

Storage and Monitoring of IP

Periodic checking of the temperature measurements

The temperature monitoring device must be checked to verify that temperatures have stayed within the acceptable range. Depending on the type of temperature monitoring device that the site uses, there are different options:

⇒ **Temperature monitoring device with audible/visible alarms:**

The audible and/or visible alarm will alert the cell processing laboratory staff of a temperature out-of-range situation and the procedure for reporting a TOR must be followed.

Even when the system has not alarmed, the temperature records generated by the system should be periodically reviewed to verify that all temperature measurements were within range. The Site Manager will check the temperature records at periodic monitoring visits.

⇒ **Temperature monitoring equipment without audible/visible alarms:**

When temperature monitoring equipment is not equipped with an audible or visible alarm, then the temperature monitoring equipment must be checked according to the frequencies in the previous section to verify that no TOR has occurred. This check must be documented on a Temperature Alarm Log or Temperature Log.

Replacing site-owned temperature management equipment

When the equipment used to store (liquid nitrogen storage system) or used to monitor storage temperature (e.g., temperature probe) of IP is replaced, the new equipment must undergo an assessment to determine whether it is acceptable for use in the study. Before the equipment is replaced, contact the Site Manager for an assessment and acceptance of the new equipment.

The same requirement applies if the IP will be permanently moved to another liquid nitrogen storage system that has not been assessed and determined to be acceptable for storage of the IP. Assessment does not apply to emergency situations (power outage or equipment failure).

6.7 Problems and Special Situations

This section applies to both LN_2 shipping container and site's LN_2 storage TORs.

Problems and Special Situations

Temperature Out-of-Range (TOR) Events

Immediately upon discovery of a TOR, via the temperature light indicator built into the LN_2 shipper lid, take the following steps:

- Quarantine the affected IP supplies. It is important not to use supplies that have experienced a temperature excursion. (Refer to Quarantining)
- Remove the product from the cryoshipper and place the product in the LN_2 storage following the instructions provided in the Shipping section above.
- Immediately notify CSOM via Central.Scheduling@ITS.JNJ.com and copy Site Manager of the TOR and discuss the potential impact, providing them with the last 4 digits of the EVO-IS # and Subject #.
  - Immediately following contact with the Site Manager, complete a TOR report, and send it to the TOR team electronically, copying the Site Manager/Local Trial Manager. If unable to reach the Site Manager, move forward with completing the TOR report, send to the TOR team and then resume attempts to escalate to the Site Manager.
  - Include the Protocol Number and Site Number in the subject line of the email when submitting a TOR.
  - Be sure to include the last 4 digits of the EVO-IS # and Subject # in the body of the email.
  - Regional fax numbers are listed on the TOR Report Form in the event that the site is not able to e-mail the form.

NOTE: For LN_2 shipper TORs, you do not need to attach the temperature reports to the TOR Report Form, as the TOR team will be pulling these from the EVO-IS shipper readout. For TORs that occur while the IP is in storage on site, the temperature report MUST be attached with the TOR Report Form.

- The Sponsor will complete the bottom of the TOR Report and indicate whether the IP is acceptable for use or not. In general, you should expect a response within hours, but not longer than 1 working day after sending the report, which may either be a final verdict or a request for more information. If you have not received any response within 24 hours, contact your Site Manager.
- The Sponsor will send the completed TOR Report to the email address from which the TOR Report was sent. The completed TOR Form is the documentation provided by the Sponsor to indicate if the IP is acceptable for use or not. File the completed TOR Report from the Sponsor with the originally submitted TOR Report in the Site IP Binder.

Problems and Special Situations

Quarantining

If it is necessary to quarantine any IP (e.g., damaged, TOR, product quality complaint) the following steps should be followed.

- Notify the Site Manager/Local Trial Manager – immediately.
- Physically separate the IP being quarantined if possible.
- Ensure that the quarantined IP is temporarily identified as "Quarantined" to ensure that it is not used.
- While in quarantine, the IP must be stored and handled according to the study requirements (e.g., LN_2 storage) and procedures. This will prevent further deterioration or damage to the IP while the viability of the IP is being assessed.
- Once quarantined, the IP should ideally remain separated until further notification is received from the Sponsor (if IP was quarantined because of a TOR, the completed TOR Form is the notification provided by the Sponsor to indicate if the IP is acceptable for use or not).
- If the IP has been quarantined because of a product quality complaint, be ready to provide details and a photograph of the drug and/or packaging to the Site Manager regarding the complaint so that the Site Manager can further report the issue to the Sponsor.
- After the assessment, the Sponsor will inform you of the outcome.
    - If the Sponsor indicates that the IP is acceptable for use: Remove the temporary "Quarantined" identification and return it to usable inventory.
    - If IP was quarantined because of a TOR, the completed TOR Form is the notification provided by the Sponsor to indicate if the IP is acceptable for use or not.
    - If the Sponsor indicates that the IP is not acceptable: Identify the IP as 'for return to Sponsor'; return it to the LN_2 liquid nitrogen storage system and await instructions on return to Sponsor

Problems and Special Situations

Damaged IP

If the IP is damaged while stored at the site, follow the instructions for Quarantining. Notify the Site Manager and await instructions on the final disposition of the IP.

Lost IP

Loss of IP is considered a critical situation by regulatory authorities. If IP is lost while stored at the site, immediately upon discovery of the shortage:

- Contact the Site Manager;
- Conduct an investigation;
- Submit a written report, signed by the Investigator, to the Site Manager.

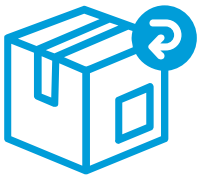
Product Quality Complaints (PQC)

Do not dispense the IP to a subject if there is a concern about the quality of the product.

PQC can include:

- Dramatically unexpected appearance or condition of the IP (e.g., apparent visible particles, dramatically unexpected coloration);
- IP primary container with leak(s)
- Damage to secondary container (cassette)
- Labeling of the IP bag and/or cassette is incorrect (e.g., incorrect protocol number, or incorrect subject information).
- If a potential PQC is identified, the following steps should be followed:
- Quarantine the affected product (see Quarantine section above). Do not discard it.
- Immediately contact the Site Manager to report the problem and to provide the details. Email a photograph of the IP and/or packaging to the Site Manager.
- If the PQC is associated with a serious adverse event (SAE), a SAE Report must also be submitted with 24 hours of becoming aware of the event.
- Assist with the investigation of the problem, when requested.
- File the Complaint Resolution Letter in the Site IP Binder.

MODULE 6 COMPLETED



Module 7:

Return and On-site Destruction of IP

Version: 3.1

Date: 28-Mar-2022

Module 7: Table of Contents

Return

Destruction

Module 7: Revision History

This is a controlled document.

VERSION DATE DD-MON-YYYY	SECTION(S) CHANGED	DESCRIPTION OF CHANGE(S)
01-Mar-2021	Initial Document	
05-Jul-2021	7.1 7.2 7.4 7.6	Updated information for temp excursions and packing materials Updated instructions on placement of DV10 smart cap Added Cryogenic Containment Pouch scheduled for August 2021 roll out Changes to section 7.6 Onsite destruction of IP to align with process IWRS 'subject information'
10-Mar-2022	7.2.2, 7.3.4, 7.4.8, 7.4.10,	Updated step to include new packing materials
	7.7	Removed section as not applicable to BCMA CAR-T
28-Mar-2022	Module 7	Formatting and administrative changes
	7.6.1	Updated step to clarify CAR-T IP destruction process

7.1 Communication Plan with Site, Courier, and Sponsor

There are two types of shipments related to the packaging and shipment of IP back to the Sponsor:

- Shipment of charged empty LN_2 shipper to the site (for loading of IP)
- Shipment of IP from clinical site to the Sponsor

Communication Plan with Site, Courier and Sponsor		
Step	**Task**	**Responsibility**
7.1.1	The sponsor will initiate order pick up upon notification by the site that one is needed.	Sponsor
7.1.2	The courier will issue an automated pre-alert/order confirmation to the site. • The notification will reference the Subject Number to track and trace the shipment from clinical site to the Sponsor. • The notification will also reference the Air Waybill (AWB) for the shipment. **Note:** a print-out of the same AWB will be provided in the Shipper kit pouch within the shipper.	Courier
7.1.3	The courier will send one notification to the clinical site contact(s) prior to delivery of the empty charged shipper. The notification will be: • The day of delivery, within 1 hour prior to delivery. This is a geofence notification and will trigger when the shipment is within a 15 mile radius of the clinical site. • **NOTE:** The site or the Janssen local team does not have access to the EVO-IS system • Any delays in shipment date will be communicated by the courier via	Courier
7.1.4	The charged shipper will arrive at the site at the agreed local time for the pack-out of IP.	Clinical Site
7.1.5	The Sponsor will coordinate with the courier to return that afternoon to pick up the IP at the agreed local time for delivery to the manufacturing facility.	Sponsor
	**IMPORTANT:** Notify CSOM via Central.Scheduling@ITS.JNJ.com and copy the Site Manager if the packed shipper will not be ready for pick-up by the courier by agreed local time.	

7.2 Review of Packing Materials

(Refer to **Module 5** of the 'CAR-T Packaging & Shipping Video'.)

Review of Packing Materials		
Step	**Task**	**Responsibility**
7.2.1 	The following tools should be utilized in preparation for site packing and unpacking of the liquid nitrogen shipper: • Cryogloves • Safety glasses • Wire cutter • **NOTE: The site will need to use wire cutters (these are NOT included in the shipment).** **NOTE: Adhere to any additional site requirements for PPE when handling cryopreserved apheresis products and equipment.** **Do not discard any contents or packaging materials until you have read these instructions.**	Clinical Site
7.2.2	3-Piece Packing Solution: Poly bags, Tyvek bags, and absorbent pads or 1-Piece Packing Solution: CryoPort envelope and foam dunnage Upon the receipt of shipper, you will find the following components inside the outer shipper case: • a reusable **LN_2 shipper** (Savsu DV-10) • a labeled **Shipper Kit pouch** (inside the pouch within the shipper case) • a labeled **Consignee Kit pouch** (inside the pouch within the shipper case) The **Shipper Kit Pouch** is used when shipping IP back to the Sponsor. The **Shipper Kit Pouch** includes: • One (1) red tamper evident seal (for use on one side of the LN_2 shipper lid, number should match the AWB) • One (1) red tamper evident seal (for use on cassette rack) • One (1) zip tie (for use on the outer shipper case lid) • One (1) zip tie (for use on one side of the LN_2 shipper lid) • 3 - Piece Packing Solution: Poly bags, Tyvek bags, and absorbent pads or 1-Piece Packing Solution: CryoPort envelope and foam dunnage • One (1) clear side packing envelope • AWB for the IP shipment The Consignee Kit Pouch is used by the Sponsor when shipping the empty shipper back to the courier upon receipt of the IP. Information is included here only for reference.	Clinical Site

Review of Packing Materials

Step	Task	Responsibility
	• One (1) zip tie (for use on the outer shipper case) • AWB for return shipment of empty shipper **Inside the shipper,** there will be an empty cassette rack. This is used to store and secure the cassettes inside the shipper during transport.	
7.2.3 	**NOTIFY CSOM via Central.Scheduling@ITS.JNJ.com and copy Site Manager IF:** • The shipping container case is not secured • The zip tie is missing from the outer case lid • The subject number listed on the AWB does not match the intended subject • The EVO-IS ID (last 4 digits) listed on the AWB does not match the LN_2 shipper • Any contents are missing or incorrect from the Shipper Kit Pouch listed above • There is a flashing alarm indicated on the temperature display **Example of Shipping Container and Components** 	Sponsor/ Clinical Site

7.3 Instructions for Receipt of Empty LN_2 Shipper

The following are step-by-step instructions for receipt of the empty LN_2 shipper in anticipation of packing-out of the IP. (Refer to **Module 5** of the 'CAR-T Packaging & Shipping Video'.)

Instructions for Receipt of the Empty LN_2 Shipper		
Step	**Task**	**Responsibility**
7.3.1	The shipper will arrive inside an outer corrugated case. The outer corrugated case includes wheels and luggage handle for ease of transport. Once the shipper has been transported to the appropriate packaging location, set the shipper upright and lower the luggage handle. 	Clinical Site
7.3.2	The outer corrugated case is secured by buckle straps. 1. Unclip the buckle straps. Open the outer corrugated case lid. 2. The outer case shipper lid is secured by a single zip tie through the zipper pulls. 	Clinical Site

Instructions for Receipt of the Empty LN_2 Shipper		
Step	**Task**	**Responsibility**
7.3.3	Cut and discard the zip tie then unzip the outer case lid. **NOTE: The site will need to use wire cutters (these are NOT included in the shipment).** 	Clinical Site

Instructions for Receipt of the Empty LN_2 Shipper

Step	Task	Responsibility
7.3.4	Lift the shipper case lid. 1. When the outer shipper case lid is opened, verify that the pouch within the outer case contains the shipper kit pouch and consignee kit pouch which are labeled.  **Pouch within outer case** 2. Remove the Shipper kit pouch and its materials. These materials will be used for packing the IP.  **3-Piece Packing Solution**   **1-Piece Packing Solution** 3. Leave the consignee kit pouch inside the pouch. **NOTE: For the 1-Piece Packing Solution and foam dunnage will be included in the Shipper kit pouch (shown in image)**	Clinical Site

Instructions for Receipt of the Empty LN_2 Shipper

Step	Task	Responsibility
7.3.5	**Verify that the EVO-IS ID number (last 4 digits) on the AWB matches the EVO-IS ID number on the LN_2 shipper lid.** **Quick Stat AWB Example** **Manual Process** QuickSTAT Global Life Science Logistics Stat U.S. (718) 995– U.K. +4 France +3 Bill Shipper Acct No. 13885 (LAST 4) EVO# 2181 SEAL# 0660603 PICK–UP Agent Date Time MT SINAI HOSPITAL 1400 MADISON AVE (KCC BASEMENT) CELLULAR THERAPY LABORATORIE SUBJECT#L28US10002002 NEW YORK NEW YORK 10029 UNITED STATES **Vineti Process** Bill Shipper Acct No. 13995 Shippers Reference O30US1000X001 PICK–UP Agent Date Time JANSSEN PHARMACEUTICAL NADIA MILNE 1000 US HWY 202 DOCK# 2 OR 3 SECTOR 25 RARITAN NEW JERSEY 08869–1425 UNITED STATES 908 295 7724 Description/Commodity INVESTIGATIONAL PRODUCT Pcs. 1 Shipper certifies that the commercial value, nature of the goods, and content ar Special Instructions –Up:SEAL# 123456, LAST 4 (EVO#) 7890 **World Courier AWB Example** **Manual Process** REC'D BY WC (NAME): P/U TIME: P/U DATE: TO (CONSIGNEE) Steve McQueen 516-555-1212 Test Company 123 Nassau Blvd – Nassau NY USA 11040 ORMATION UP (Last 4) EVO#2181 Seal #0660603 **Vineti Process** Bert Meeus JANSSEN PHARMACEUTICA TURNHOUTSWEG 30 – BEERSE Belgium 2340 NFORMATION Seal Number: 123456 EVO ID Last 4 - 7890 **EVO-IS ID number location** evois information system 990005120002181 View data : evois.savsu.com Contact us : 1 . 505 . 466 . 1962 info@savsu.com 2630 Alamo Ave. SE Suite 101 Albuquerque, NM 87106 USA	Clinical Site

Instructions for Receipt of the Empty LN_2 Shipper		
Step	**Task**	**Responsibility**
7.3.6	**Confirm if there is any temperature excursion:** To determine if the temperature is within range, press the light indicator, release & wait for 5 seconds on the DV-10 lid. The indicator will emit a light. • Note the training video mentions a blue light. The light is white. • Note that a steady light indicates that the temperature is within range. Proceed to the next steps. Notify CSOM via email Central.Scheduling@ITS.JNJ.com and copy Site manager immediately and do not continue if: • A flashing light indicating a temperature excursion has occurred. • Temperature light indicator is not functioning (does not turn on). **Press Indicator**  **Light Indicator** 	Clinical Site

Instructions for Receipt of the Empty LN_2 Shipper

Step	Task	Responsibility
7.3.7	**Inside the Shipper kit pouch, there are 2 tamper evident seals** • tamper evident seal with "SECURED" and serial number listed • tamper evident seal with "RACK" listed  Verify the tamper evident seal number (SEAL#) listed on the AWB matches the tamper evident seal from the Shipper kit pouch. **Quick Stat**  **World Courier** 	Clinical Site

7.4 Packing of IP into LN_2 Shipper

The following are step-by-step instructions for packing the IP into the LN_2 shipper.
(Refer to **Module 5** of the 'CAR-T Packaging & Shipping Video central Cryo.)

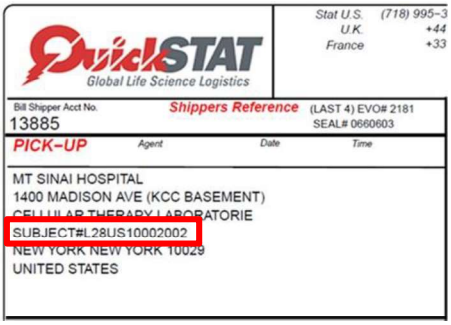
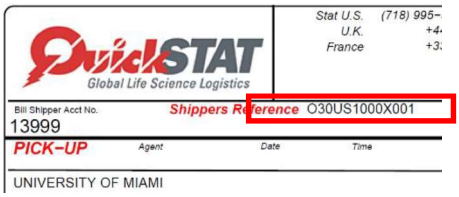
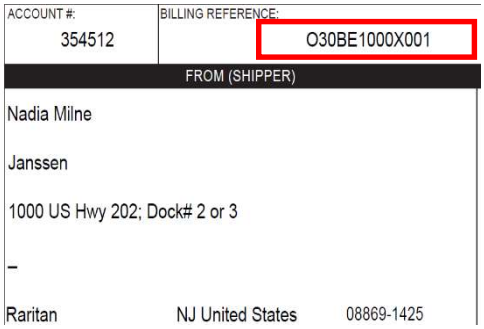
REMINDER: Ensure all necessary PPE is on before the next steps.

The investigational product must be placed into the LN_2 shipper immediately following removal from the storage and verification of COC/COI.

Packing of IP into LN_2 Shipper		
Step	**Task**	**Responsibility**
7.4.1	Ensure that the following documents are available for reference and completion immediately after pack-out of the shipper. 1. **NA_RTN Site IP Return Shipment Form for Chain of Custody/ Chain of Identity** 2. Copy of **IWRS**	Clinical Site
7.4.2	Ensure all materials in the Shipper kit pouch are removed and staged for the pack-out. This includes the AWB. **There are two types of packing solutions as shown below**  **3-Piece Packing Solution**  **1-Piece Packing Solution**	Clinical Site

STOP	**IMPORTANT: Next steps need to be performed as quickly as possible. It is critical to avoid thawing of the IP as the cassette(s) are packed into the shipper. Co-locate all packing materials and shipper as much as possible.**

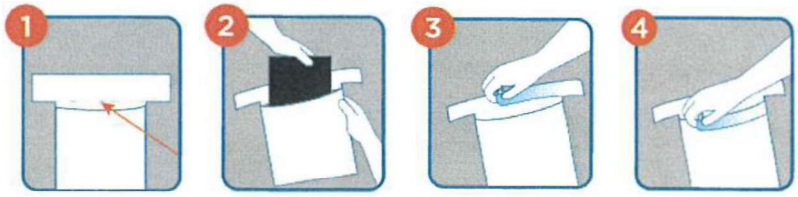
Packing of IP into LN_2 Shipper

Step	Task	Responsibility
7.4.3	Remove the first cassette (with IP) from LN_2 storage. • Prior to packing the cassette, verify that the Subject Number on the **AWB** and on the copy of the **IWRS** matches the Subject Number on the cassette label. • As a reminder, the AWB is inside the Shipper kit pouch. **Quick Stat AWB Example** **Manual Process**  QuickSTAT Global Life Science Logistics Stat U.S. (718) 995-3 U.K. +44 France +33 Bill Shipper Acct No. 13885 Shippers Reference (LAST 4) EVO# 2181 SEAL# 0660603 PICK-UP Agent Date Time MT SINAI HOSPITAL 1400 MADISON AVE (KCC BASEMENT) CELLULAR THERAPY LABORATORIE SUBJECT#L28US10002002 NEW YORK NEW YORK 10029 UNITED STATES **Vineti Process**  QuickSTAT Global Life Science Logistics Stat U.S. (718) 995- U.K. +4 France +3 Bill Shipper Acct No. 13999 Shippers Reference O30US1000X001 PICK-UP Agent Date Time UNIVERSITY OF MIAMI **World Courier AWB example** **Manual Process**  World Courier AmerisourceBergen ACCOUNT #: 098765 BILLING REFERENCE: Shipment Reference FROM (SHIPPER) Scheduling Team 212-555-1212 Sample Company 123 Main Street Subject # L28US10002002 New York NY USA 10001 SHIPMENT Finished Product UN3245 GMO 50mL **Vineti Process**  ACCOUNT #: 354512 BILLING REFERENCE: O30BE1000X001 FROM (SHIPPER) Nadia Milne Janssen 1000 US Hwy 202; Dock# 2 or 3 – Raritan NJ United States 08869-1425	Clinical Site
7.4.4 	Complete Section 1 of the **Site IP Return Shipment Form for Chain of Custody/Chain of Identity (NA_RTN).** This is completed prior to inserting the cassette (with IP) into the cassette rack and LN_2 shipper.	

Packing of IP into LN_2 Shipper

Step	Task	Responsibility
7.4.5	<u>If using **3-Piece Packing** (Tyvek bag):</u> Place the absorbent pad into the Poly Bag. Insert the cassette into the Poly bag with the locking hinge toward the top. Remove the adhesive backing and seal the bag. Fold the poly bag and wrap tightly around cassette.   	Clinical Site
7.4.6	Place the Poly bag into the Tyvek bag with locking hinge of the cassette towards top. Fold the one side of the Tyvek bag into the other.  	Clinical Site
7.4.7	Fold one side of the Tyvek bag so the cassette will fit into the rack. The cassette should now be fully placed into the Tyvek bag with locking hinge towards the top. 	Clinical Site

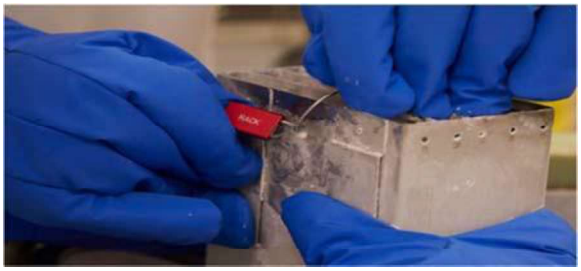
Packing of IP into LN_2 Shipper

Step	Task	Responsibility
7.4.8	**<u>If using the 1-Piece Packing (Cryogenic Containment Pouch):</u>** 1. Pre-fold over the scored line shown by the arrow. The pre-fold may fold over the adhesive seal cover. 2. Insert the cassette with the locking hinge toward the top and push completely down past the adhesive seal into the Cryogenic Containment Pouch. Ensure the cassette is not behind the adhesive seal. 3. Peel off adhesive strip cover on top flap. 4. Peel off adhesive strip cover on the on the envelope pouch.  5. a Seal the Cryogenic Containment Pouch. Ensure to fold flap along pre-folded scored line. b Start sealing from center of pre-fold and work out to the sides. Seal must not have any wrinkles or gaps. 6. Fold tabs around seal with pressure. Tabs must be sealed as close as possible to the envelope. 	Clinical Site
7.4.9	Remove the shipper lid and lift the cassette rack.  	Clinical Site

Packing of IP into LN_2 Shipper

Step	Task	Responsibility
7.4.9	**NOTE:** proper placement of the DV10 Smart Cap when not seated in the dewar body is **PROBE SIDE UP** on a flat surface. Serious damage to the probe may occur if placed otherwise. 	Clinical Site
7.4.10	Place sealed Tyvek bag or Cryogenic Containment Pouch with frozen bag/cassette into the cassette rack. Ensure proper orientation so the locking hinge of the cassette is at the top of the rack.  If using the 1-Piece Packing Solution (Cryogenic Containment Pouch) place one piece of the foam dunnage on top of the envelope within the cassette rack. 	Clinical Site

Packing of IP into LN_2 Shipper

Step	Task	Responsibility
7.4.11	Return the rack into shipper to prevent warming and close the shipper lid.  	Clinical Site
7.4.12	   Repeat the pack-out process for any of the remaining cassettes to be shipped.	Clinical Site
7.4.13	After packing the final cassette, secure the cassette rack with the tamper evident seal. Feed the tamper evident seal with “RACK” through the cassette holes and secure. 	Clinical Site
7.4.14	Remove the shipper lid and place the cassette rack (with IP) into the shipper. Close the shipper lid.  	Clinical Site

Packing of IP into LN_2 Shipper		
Step	**Task**	**Responsibility**
7.4.15	Next, secure the lid and lower the shipper handle to allow for the closing of the shipper lid after tamper evident seal is attached. 	Clinical Site
7.4.16	Feed the tamper evident seal that contains the word **"SECURED"** and seal number through the metal hook and lid. As a reminder, this seal number needs to match the seal number listed on the air waybill. On the other side of the shipper lid, wrap and secure a zip tie through the lid and around the handle.  	Clinical Site
7.4.17	Once the shipper lid is secured, place the verified shipper label into the pouch. NOTE: Only the Consignee kit pouch and the shipper label should remain inside the pouch within the shipper case.  	Clinical Site

Packing of IP into LN_2 Shipper

Step	Task	Responsibility
7.4.18	Zip close the outer shipper case lid and secure by passing the remaining zip tie through the zipper pulls. Secure the outer corrugated case by clipping the buckle straps.  	Clinical Site
7.4.19	Remove the existing AWB and place the new AWB (from the Shipper kit pouch) into the clear packing envelope. Place the additional shipper label with the new AWB into the clear packing envelope. Applicable to all sites excluding USA. Discard all leftover materials and packaging per site disposal procedures. Discard any remaining items and bags from Shipper kit pouch.  	Clinical Site

⚠ **REMINDER:** The Sponsor will coordinate with the courier to pick up the LN_2 shipper packed with IP from the site at **agreed local time**.

Notify CSOM via email Central.Scheduling@ITS.JNJ.com and copy Site Manager immediately if there are any constraints for getting this shipment ready by local agreed time.

	MANUAL COC/COI ACTIONS:	
	Complete the Return Chain of Custody/Chain of Identity Form (see NA_RTN) and enter all applicable data in the eCRF.	**Clinical**
	On completion of the form, upload a signed copy of this form to MBOX-SDX on the same day (see MBOX-SDX user guide).	

7.5 Discontinuing or Withdrawing a Subject from Investigational Product

Preparation, Dispensing and Administration of IP

See the Investigational Product Preparation Instructions (IPPI) for Sponsor instructions on preparing, dispensing and administering the IP. The IPPI is located in the Site IP Binder.

Follow site's standard procedures for preparation of IP in alignment with Sponsor instructions. If the site does not have written procedures, contact the Site Manager for guidance.

Two qualified staff members should be involved whenever the IP is prepared by the site; one to prepare the IP and the other to check or verify.

Guidance on the use of Sponsor provided or Site provided ancillary supplies will be provided in the IPPI.

Discontinuing or Withdrawing a Subject from Investigational Product

See the Protocol for information on the process for discontinuing study treatment (e.g., JNJ-68284528 (ciltacabtagene autoleucel) is not administered) or for a subject's withdrawal from the study following treatment with the IP (e.g., JNJ-68284528 (ciltacabtagene autoleucel) administered).

See Protocol for information on retention of apheresis product and JNJ-68284528 (ciltacabtagene autoleucel) that was manufactured but not administered.

In the event JNJ-68284528 (ciltacabtagene autoleucel) is manufactured, but not administered, follow site standard procedures for return of cellular therapy products to the cellular therapy lab and store at ≤ -120°C. Contact the Sponsor Site Manager.

7.6 On-Site Destruction of IP

Any IP that is unused, assigned but not dispensed, expired, was damaged, and/or that the Sponsor deems to be unusable, can be destroyed on-site **AFTER** sponsor approval for destruction is obtained. Prior to the first destruction, site processes and SOPs will be reviewed by the Sponsor.

On-Site Destruction of IP		
Step	**Task**	**Responsibility**
7.6.1	Prior to the **first IP destruction** at the site, obtain approval from Sponsor. • Contact Site Manager and request approval for onsite CAR-T Investigational Product Destruction. • If approval is obtained, proceed to step 7.6.2. • If approval is denied proceed to section 7.1 for instructions on the return of IP.	Sponsor/ Clinical Site
7.6.2	**Ensure that the following documents are available for reference and completion before starting the destruction procedure.** 1. CAR-T IP On-Site Destruction Form (TV-FRM-57192). 2. Copy of the **IWRS.**	Clinical Site
7.6.3	Complete Page 1 of Form CAR-T IP On-Site Product Destruction Form (TV-FRM-57192). Obtain PI signature for destruction approval.	
7.6.4	Proceed to IP identification and destruction and complete page 2 of Form CAR-T IP On Site Product Destruction Form (TV-FRM-57192). Follow institutional SOPs. **NOTE**: Ensure all necessary PPE is on before performing the procedure.	Clinical Site

	MANUAL COC/COI ACTIONS:	
	Complete the CAR-T IP On-Site Destruction Form (see TV-FRM-57192**).**	**Clinical Site**
	On completion of the form, upload a signed copy of this form to sponsor MBOX-SDX on the same day (see MBOX-SDX user guide).	

MODULE 7 COMPLETED

Module 8:
COI/COC Maps & Forms

Version: 3.1

Date: 28-Mar-2022

Module 8: Table of Contents

Module 8: Revision History

This is a controlled document.

VERSION DATE DD-MON-YYYY	SECTION(S) CHANGED	DESCRIPTION OF CHANGE(S)
01-Mar-2021	Initial Document	
05-Jul-2021	8.4	Updated definitions and naming conventions for all regions and minor wording changes throughout document Updated COC/COI Map with new countries · USA and Vineti map updated to include the following regions North America/Latin America/Australia/Korea/Singapore · Additional Vineti maps added · New Saudi Arabia onsite cryopreservation map added
10-Mar-2022	8.1	Updated the summary of COC/COI documents
28-Mar-2022	Module 8	Formatting and administrative changes
	8.3	Added correct form CAR-T IP On-Site Destruction Form TV-eFRM-57192

8.1 Summary of Site Facing Chain of Custody and Chain of Identity Documents

Site Facing Chain of Custody and Chain of Identity Documents		
Timepoint	**Site Action & Critical COC/COI Step**	**COC/COI Document**
Subject Screened (signs consent form)	Site enters subject information into IWRS: • Date of consent **And when using Vineti:** • Complete Vineti Ordering Module	13-digit subject number is generated IWRS screening notification email sent
Subject Randomized	Site completes randomization transaction for the subject in IWRS: *(Only applicable to protocols requiring randomization)*	IWRS randomization notification email
Apheresis Collection	Site enters subject information into IWRS: • Name • DOB • SEC-DIS (21-digits) (where applicable for countries in EEA) or DIN or Apheresis ID • Weight in kg on Day of Apheresis (rounded to 1 decimal point)	NA_APH
	Subject completes apheresis: • Site completes NA_APH (Apheresis Chain of Custody/Chain of Identity Form) using the IWRS screening notification and uploads the completed NA_APH to sponsor MBOX-SDX on the day of the Apheresis. **OR** • Complete Vineti **Collection** Module.	

Site Facing Chain of Custody and Chain of Identity Documents

Timepoint	Site Action & Critical COC/COI Step	COC/COI Document
Transfer to shipment facility for Shipment to CPC	Site transfers custody of MNC, Apheresis product to cell processing lab or other department (named here in the document as "shipment facility") for packing and shipment to CPC: • Site completes NA_TRN CTPPM (Transfer to Cell Laboratory or Shipment Facility Chain of Custody/Chain of Identity Form) using the IWRS screening notification and uploads the completed NA_TRN form to Sponsor MBOX-SDX on the same day. **NOTE: If MNC, Apheresis product is being packed for shipment to the CPC in the Apheresis center, this step and form are not necessary to complete. Document on NA_SHIP_CRYO that no transfer of the MNC, Apheresis product occurred.** **OR** • Complete Vineti **Collection** Module.	NA_TRN (if applicable)
Shipment of cells: Site → CPC	Site packs MNC, Apheresis product in CREDO CUBE shipper and ships to CPC: • Site completes NA_SHIP_APH from CTPPM (Site Shipment Form for Chain of Custody/Chain of Identity) using the IWRS screening notification and uploads the completed NA_SHIP_APH to Sponsor MBOX-SDX on the day of the shipment. **NOTE: MNC, Apheresis product must be transferred and placed into 2-8^{0}C shipper within 60 minutes of collection end time.** **OR** • Complete Vineti **Collection** Module.	NA_SHIP_APH
Receipt of IP: Manufacturing facility→site	Site receives cryopreserved IP in LN_2 shipper from manufacturing facility and stores IP on site in anticipation of dosing: • Site completes NA_REC from CTPPM (Site Receipt Form for Chain of Custody/Chain of Identity) and uploads to Sponsor MBOX-SDX on the day of the receipt. **OR** • Complete Vineti **Infusion** Module.	NA_REC

8.2 Chain of Custody/Chain of Identity Central Cryo Forms

The table below provides an overview of the COC/COI form number, form description and form name. The COI/COC form naming convention will be used throughout the document to identify the COC/COI forms. COI/COC forms for your region can be found in your IP binder and on the study portal.

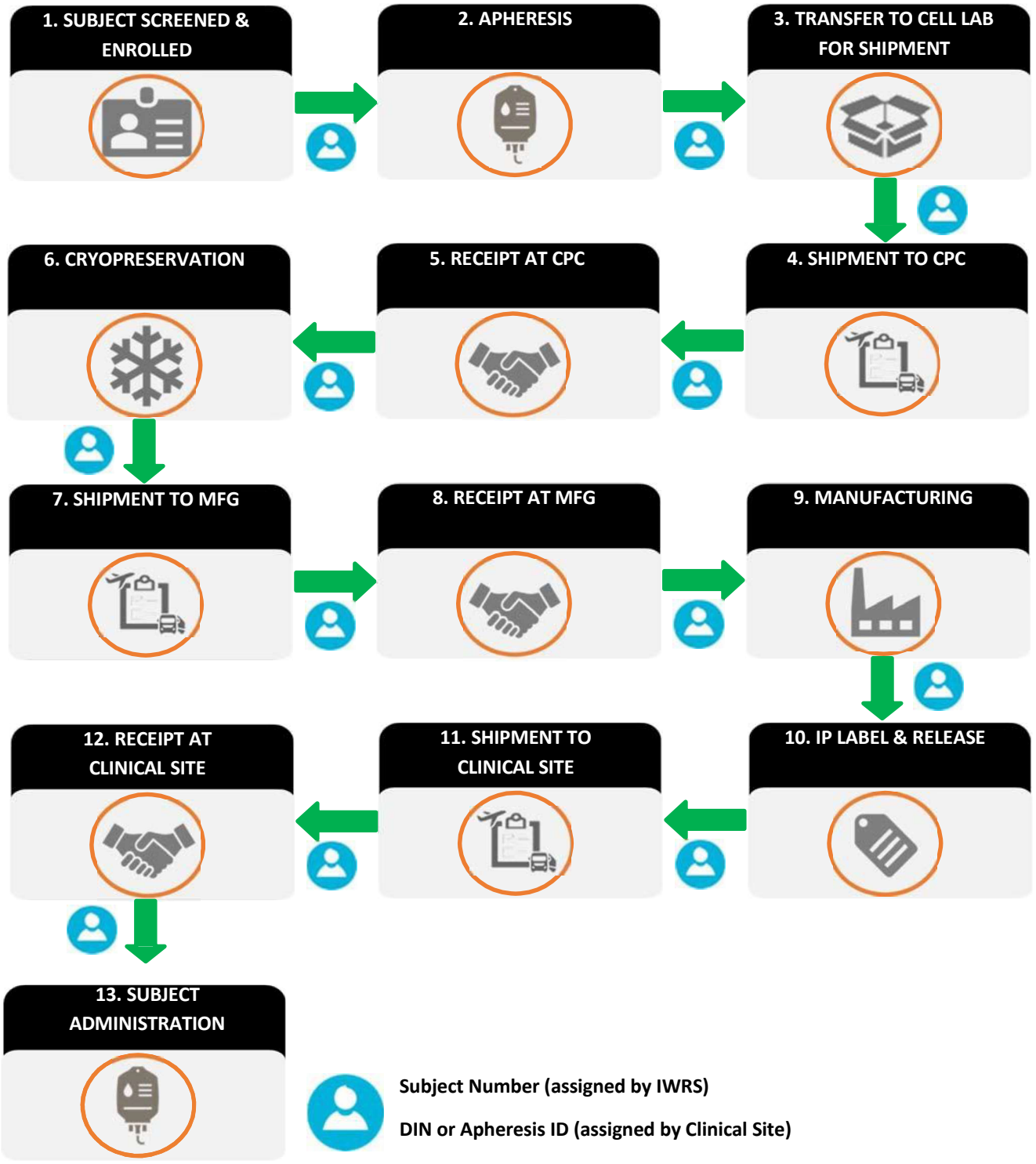
COC/COI Form Number	Form Description	Form Name
TV-eFRM-10456	CAR-T Apheresis Chain of Custody/Chain of Identity Form	NA_APH
TV-eFRM-10454	CAR-T Transfer to Cell Laboratory or Shipment Facility Form	NA_TRN
TV-eFRM-10455	CAR-T Central Cryo Site Shipment Form for Chain of Custody/Chain of Identity	NA_SHIP_APH
TV-eFRM-10449	CAR-T IP Shipment Receipt Checklist for Site	NA_REC
TV-eFRM-10450	CAR-T IP Return Shipment Form	NA_RTN
TV-FRM-57192	CAR-T IP On-Site Destruction Form	N/A

8.3 Chain of Custody/Chain of Identity Local Cryo Forms

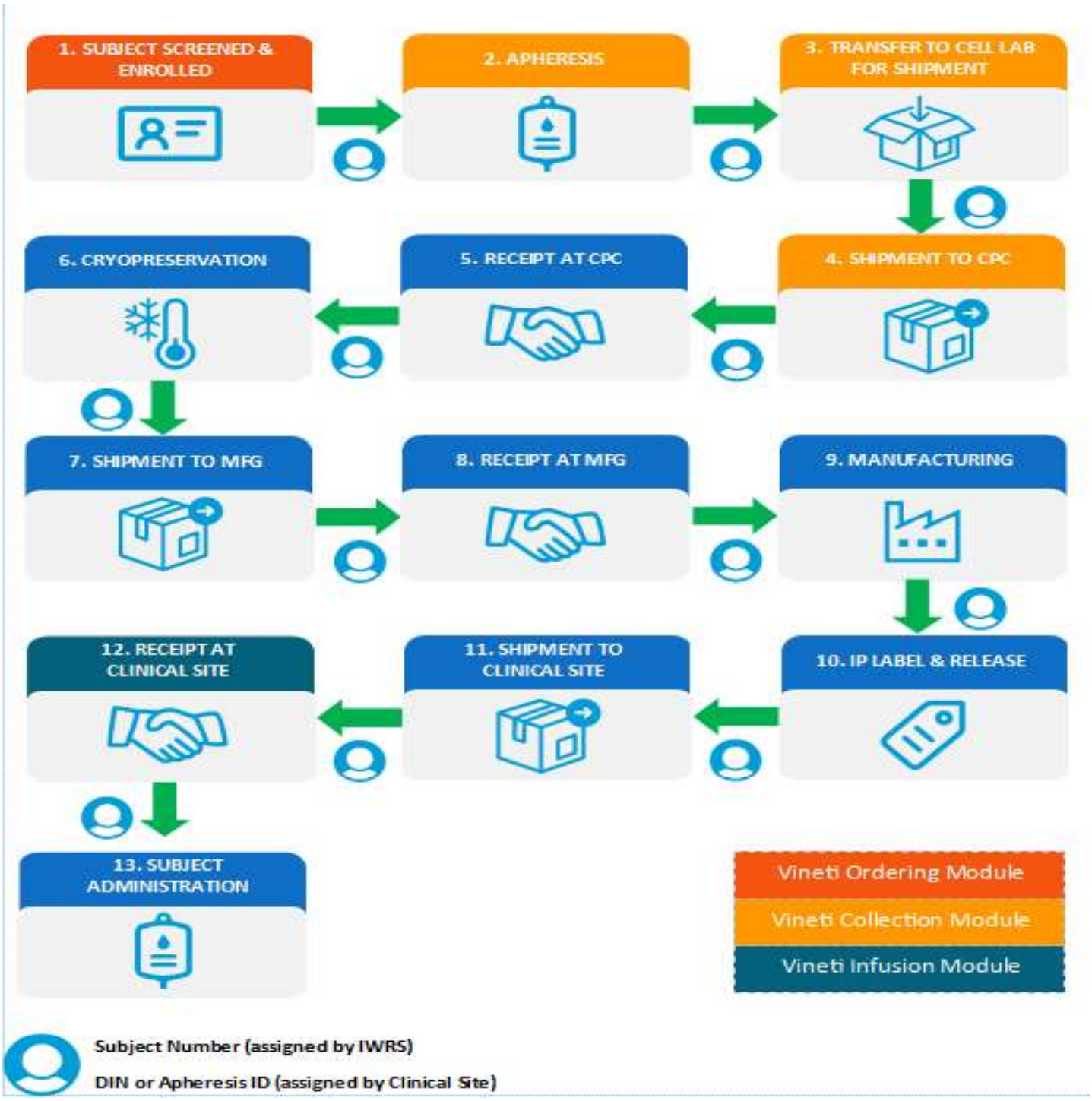
The table below provides an overview of the COC/COI form number, form description and CTPPM form name. The COC/COI form naming convention will be used throughout the document to identify the COC/COI forms. COI/COC forms for your region can be found in your IP binder and on the study portal.

COC/COI Form Number	Form Description	Form Name
TV-eFRM-10456	CAR-T Apheresis Chain of Custody/Chain of Identity Form	XX_APH
TV-eFRM-10454	CAR-T Transfer to Cell Laboratory or Shipment Facility Form	XX_TRN
TV-eFRM-10452	CAR-T Local Cryopreservation Chain of Custody/Chain of Identity Form	XX_CRY
TV-eFRM-10451	CAR-T Local Cryo Site Shipment Form for Chain of Custody/Chain of Identity	XX_SHIP_CRYO
TV-eFRM-10449	CAR-T IP Shipment Receipt Checklist for Site	XX_REC
TV-eFRM-10450	CAR-T IP Return Shipment Form	XX_RTN
TV-FRM-57192	CAR-T IP On-Site Destruction Form	N/A

8.4 Chain of Custody/Chain of Identity Map



8.5 Chain of Custody/Chain of Identity Vineti Map



8.6 Study/Region Specific Attachments

Applicable attachments for the study/region will be provided in the IP binder.