

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

# Cell Therapy Investigational Product Procedures Manual (CTPPM)

## Cilta-Cel (Ciltacabtagene Autoleucel) Program

Version 5.0 **Final**  
Date: 12-APR-2024

**Region: NA - North America**

# Program CTPPM Approval



I approve the content of this document.

<b>Name</b>	<b>Role</b>	<b>Signature</b>	<b>Date (DD-MON-YYYY)</b>
Sadaf Naz Khan	CTL	See Program CTPPM V5.0 12-April-2024 Approval Page	12-April-2024
Kristen Wightman	GTL	See Program CTPPM V5.0 12-April-2024 Approval Page	12-April-2024
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<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
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## Regional Approval

I approve the content of this document.

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# Table of Contents

<b>Table of Contents</b> .....	<b>4</b>
Introduction .....	6
Records .....	8
<b>Module 1: Pre-Collection</b> .....	<b>11</b>
1.1 Study Supplies.....	14
1.2 Pre-Collection Activities (All Subjects) .....	15
<b>Module 2: Apheresis &amp; Cell Management</b> .....	<b>17</b>
2.1 Apheresis Labeling .....	21
2.2 Apheresis Collection .....	24
2.3 Cell Management .....	25
<b>Module 3: Cell Transfer</b> .....	<b>26</b>
<b>Module 4: Cryopreservation Procedure</b> .....	<b>30</b>
4.1 Cryopreservation: Labeling.....	34
4.2 Cryopreservation and LN <sub>2</sub> Storage.....	35
4.3 Cryopreservation Shipping: Communication Plan with Site, Courier and Sponsor.....	36
4.4 Cryopreservation Shipping: Review of Packing Materials.....	37
4.5 Cryopreservation Shipping: Instructions for Receipt of Empty LN <sub>2</sub> Shipper.....	39
4.6 Cryopreservation Shipping: Packing of cryopreserved apheresis material into the LN <sub>2</sub> Shipper .....	44
<b>Module 5: Packaging and Shipment</b> .....	<b>52</b>
5.1 Communication Plan with Site, Courier & Sponsor .....	56
5.2 Review of Packing Materials .....	57
5.3 Packing of Apheresis Material into the CREDO CUBE Shipper for USA only .....	59
5.3 Packing of Apheresis Material into the CREDO CUBE Shipper for Canada only .....	63
5.4 Courier Pick Up of the Packed CREDO CUBE Shipper.....	67
<b>Module 6: Receipt and Storage of the Investigational Product</b> .....	<b>68</b>
6.1 Communication Plan with Site, Courier & Sponsor .....	72
6.2 Review of Packing Materials .....	73
6.3 Receipt of the LN <sub>2</sub> Shipper Containing Investigational Product .....	75
6.4 Unpacking and Storage of Investigational Product .....	80
6.5 Prepare of Empty LN <sub>2</sub> Shipper for Shipment.....	87
6.6 Storage and Monitoring of IP.....	89
6.7 Problems and Special Situations.....	91
<b>Module 7: Return and On-site Destruction of IP</b> .....	<b>94</b>
7.1 Communication Plan with Site, Courier, and Sponsor .....	97
7.2 Review of Packing Materials .....	98
7.3 Instructions for Receipt of Empty LN <sub>2</sub> Shipper .....	100
7.4 Packing of Investigational Product into LN <sub>2</sub> Shipper .....	105

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

7.5 Discontinuing or Withdrawing a Subject from Investigational Product .....113

7.6 On-Site Destruction of Investigational Product.....114

**Module 8: COI/COC Maps & Forms..... 115**

8.1 Summary of Chain of Custody and Chain of Identity Documents .....118

8.2 Chain of Custody/Chain of Identity Forms.....119

8.3 Chain of Custody/Chain of Identity Cryo Forms .....120

8.4 Chain of Custody/Chain of Identity Map – NA.....121

8.5 Study/Region Specific Attachments .....122

Johnson & Johnson	Cell Therapy Product Procedures Manual		
	Document No.:	TV-eFRM-13010	Version: 3.0

# 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, apheresis collection, storage, and 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 (SM).

For trials outsourced to a Contract Research Organization (CRO), references to a site manager (SM) 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 the sponsor instructions. If the site does not have written procedures, contact the SM 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 must adhere to its internal policies and procedures.

## Staff Training and Delegation of Responsibilities

**Only qualified individuals are permitted to perform 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, packaging, and shipping 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.

Johnson&Johnson	Cell Therapy Product Procedures Manual		
	Document No.:	TV-eFRM-13010	Version: 3.0

## 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 Response Technology (IRT).
- 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 SM.
- 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 SM.
  - 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 SM for the proper method.
  - The date format is: DD-MMM-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.

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

# 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 health authority inspections, 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 cell
eCRF	Electronic Case Report Form
COC	Chain of Custody
COI	Chain of Identity
CPC	Cryopreservation Center
CRYO	Cryopreservation
CSOM	Clinical Supply Operations Manager
DIN	Donation Identification Number
IP	Investigational Product
IPPI	Investigational Product Preparation Instruction
ISBT	International Standard for Blood Transfusion
IRT	Interactive Response Technology
LN <sub>2</sub>	Liquid Nitrogen
MFG	Manufacturing
MNC	Mononuclear Cell
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

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

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

Key definitions	
MNC, Apheresis	A cell product containing a high percentage of mononuclear cells (MNCs) obtained by apheresis. Also known as apheresis material.
Consignee kit pouch	Used by the sponsor when shipping the empty shipper back to the courier upon receipt of the cryopreserved apheresis material. Information is included here only for reference.
Shipper kit pouch	Used when shipping cryopreserved apheresis material back to the sponsor.
Cryogenic containment envelope pouch	Envelope containing absorbent material capable of absorbing 100 ml of fluid used as a secondary containment.

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0



# Module 1: Pre-Collection

**Version: 5.0**

**Date: 12-APR-2024**

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

# 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-YYYY)	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
06-Mar-2023	1.2.1	Updated details on the importance of data entered for scheduling and criticality of slot approval process
	1.2.5	Removed Vineti steps
12-APR-2024	1.1	Added IDM testing kits for EEA & ISR in ancillary supplies
	1.2	Minor wording updates & numbering of steps

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

## 1.1 Study Supplies

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

Materials
<p><b>Investigational Product (IP):</b> JNJ-68284528 (ciltacabtagene autoleucel)</p> <p>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.</p>
<p><b>Other Medications:</b></p> <p>Refer to the protocol and non-JNJ-68284528 SIPPM for a description of other medications used in the study.</p>
<p><b>Ancillary Supplies:</b></p> <p>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 material and receipt of IP are contained in the Shipments section of the CTPPM.</p> <p>Refer to the IP Preparation Instructions in the Site IP Binder for ancillary materials needed for investigational product preparation/administration.</p> <p>Ensure that an adequate inventory of the below supplies is maintained, and the sponsor is alerted of any supplies needed in accordance with the below lead times below. If additional ancillary supplies for apheresis are needed, email <a href="mailto:Central.Scheduling@ITS.JNJ.com">Central.Scheduling@ITS.JNJ.com</a> and specify which supplies and quantities are required.</p>

Ancillary	Provided By	Process Utilized In	Storage Conditions	Lead-times
Bulk Label Supply: Labels, Self-laminating cards & zip ties	Sponsor	Module 2 Apheresis	Room Temperature	3 weeks
Wire Cutters	Sponsor (if required)	Module 6 Shipment Receipts	Room Temperature	3 weeks

Johnson & Johnson	Cell Therapy Product Procedures Manual		
	Document No.:	TV-eFRM-13010	Version: 3.0

## 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	<p><b>Slot Reservation</b></p> <p>The slot reservation request process will start during the pre-screening period to reserve and obtain an approval of a slot <b>prior to consent</b> of a potential subject.</p> <ul style="list-style-type: none"> <li>A slot request must be submitted once a potential subject has been identified. Submitting a slot request means cryopreservation and manufacturing capacity are checked for the subject.</li> <li>The site must 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 <a href="mailto:central.scheduling@its.jnj.com">central.scheduling@its.jnj.com</a>. Site personnel can reach out to the sponsor (SM) for a blank copy of the paper slot reservation.</li> <li>This slot request must be submitted at least two (2) business days (but preferably one (1) week) prior to the expected consenting date.</li> </ul> <p><b>IMPORTANT:</b> Subject MUST not be consented or screened until the slot has been approved by the Sponsor.</p>	Clinical Site
1.2.2	<p>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.</p>	Sponsor
1.2.3	<p><b>Screening</b></p> <p>Once the slot has been approved, the site may proceed with collecting informed consent and screening.</p> <p>At the time of signing consent, complete the Screening transaction in IRT (see IRT site user Manual).</p> <p><b>A unique 13-digit subject ID will be generated on completion of the IRT transaction.</b></p> <p><u>Example:</u> N05US10001001 (10-digit site number + 3-digit subject code)</p>	Clinical Site
1.2.4	<p><b>Eligibility Confirmation</b></p> <ul style="list-style-type: none"> <li>Enter all pertinent subject screening data in the eCRF.</li> <li>Then, submit the Eligibility Approval Request transaction in IRT, requesting sponsor approval.</li> </ul>	Clinical Site

Johnson&Johnson	Cell Therapy Product Procedures Manual		
	Document No.:	TV-eFRM-13010	Version: 3.0

Documentation & Patient Verification		
Step	Task	Responsibility
1.2.5	<ul style="list-style-type: none"> <li>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.</li> </ul>	Sponsor
1.2.6	<p><b>Randomization</b> <i>(only applicable to protocols requiring randomization)</i></p> <ul style="list-style-type: none"> <li>Once eligibility is confirmed, randomize the subject via IRT on the pre-agreed randomization date <u>only</u>.</li> </ul> <p><b>NOTE: If an additional apheresis is requested by sponsor, follow the steps outlined in 'Pre-collection activities (All subjects)'.</b></p>	Clinical Site
1.2.7	<p><b>Apheresis Scheduling</b></p> <p>In case of changes to the date of apheresis after slot approval, this needs rescheduling via the CQUENCE Clinical Trials portal. If further discussion is needed beyond rescheduling the date, contact: <a href="mailto:central.scheduling@ITS.JNJ.com">central.scheduling@ITS.JNJ.com</a></p>	Clinical Site
1.2.8	<ul style="list-style-type: none"> <li>Approve any updated apheresis date request from the site in alignment with available capacity.</li> <li>Per the approved date of apheresis for the assigned subject's slot, schedule the delivery of the empty CREDO CUBE shipping container to the clinical site.</li> </ul>	Sponsor

## MODULE 1 COMPLETED



<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0



## Module 2:

# Apheresis & Cell Management

**Version: 5.0**

**Date: 12-APR-2024**

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

# Module 2: Table of Contents

## **2.1 Apheresis Labeling**

## **2.2 Apheresis Collection**

## **2.3 Cell Management**

## 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 Document	
05-Jul-2021	2.3	Updated definitions and naming conventions for all regions Apheresis collection section updated with the following requirements. <ul style="list-style-type: none"> <li>• New apheresis target collection added and changed from MNC to WBC</li> <li>• Note clarify anticoagulant volume is applicable to product</li> <li>• Note added for recommended storage temp and transport temperature</li> <li>• Added recommendation for plasma to be added to collection bag for shipment</li> <li>• Added recommendation to take mid-point samples</li> <li>• Removed recommendations for whole blood to be processed</li> </ul>
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°C until the time of shipment occurs
28-Mar-2022	Module 2	Formatting changes and deleted 13 and 21 digits when mentioned for unique identifier
06-Mar-2023	2.1.1, 2.1.3	Changed supplemental label to sponsor label
	2.1.2	Edited requirements for site bag label
	2.1.3, 2.1.4	Added instructions critical to hang tag completion between shipper and apheresis label
	2.2	Removed section related Vineti

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

	2.3	Updated to section 2.2
	2.2.2	Adjusted wording for using institution SOPs Added recommendation for quantity of whole blood processed
	2.2.3	Added clarification to capture quantity of heparin used with ACD-A on COC/COI form
	2.2.4	Added autologous to clarify adding plasma
	2.2.7	Updated wording of apheresis product to apheresis material
	2.2.9	Removed min collection requirement 2x10e9
	2.4.1	Added for Israel sites only to enter patient ID specific to requirement from MoH
	2.4.2	Adjusted wording for possible second collection
12-APR-2024	2.1.2	Further details included & re-ordered label items
	2.2	Added IDM requirements for the UK
	2.2.1	Added IDM results communication method for South Korea
	2.2.4	Removed the addition of 50mL autologous plasma to the final collection bag if less than 100mL
	2.2.7	Clarified that only one sampling bulb may be used by the clinical site
	2.1.2, 2.3.1	Updated wording for unique identifier of apheresis collection
	Module 2	Replaced NA_APH form with new NA_APH-TRN form
	Module 2	Updated wording for MBOX system & responsibility

## 2.1 Apheresis Labeling










This section describes the labeling and forms to manage the COC/COI of the Apheresis material.

Labels		
Step	Task	Responsibility
2.1.1	<p><b>Bulk Label Supplies Binder</b></p> <p>Your site will have been provided a bulk label supplies binder during site initiation, including the following materials per study:</p> <ul style="list-style-type: none"> <li>• Sponsor-provided apheresis labels</li> <li>• Sponsor-provided shipper labels</li> <li>• Self-laminating cards</li> <li>• Zip ties</li> </ul>	Sponsor
2.1.2	<p><b>APHERESIS – Site bag label</b></p> <p>Print apheresis bag labels as per site process. It is recommended to follow ISBT 128 guidelines and local requirements.</p> <p>The site apheresis bag label must include, at a minimum, the following elements:</p> <ul style="list-style-type: none"> <li>• Type of collection: MNC, Apheresis</li> <li>• Date and time of apheresis end of collection (including time zone)</li> <li>• Volume of apheresis collection</li> <li>• Volume of anti-coagulant in the collection bag</li> <li>• Subject Name (including middle name or initial as documented in medical records)</li> <li>• Date of Birth</li> <li>• Unique identifier for apheresis collection: <ul style="list-style-type: none"> <li>• DIN where applicable for countries in NA</li> </ul> </li> <li>• Storage temperature 2-8°C. The storage temperature on the apheresis bag label should be consistent with the sponsor label requirements.</li> <li>• Any required warnings per local standards &amp; regulations</li> </ul> <p>If the apheresis expiration date &amp; time are included in the apheresis bag label, this must follow the requirements for sponsor starting material expiration time of <b>thirty-two (32) hours</b> from end of collection time.</p>	Clinical Site

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

<b>Labels</b>		
<b>2.1.3</b>	<p><b>APHERESIS – Sponsor label</b></p> <p>The sponsor-provided apheresis label is pre-printed with the sponsor name and a description. Complete the following information on the sponsor label:</p> <ul style="list-style-type: none"> <li>• Site Number</li> <li>• Subject Number</li> <li>• DIN or Apheresis ID</li> <li>• Date of collection</li> </ul> <p>After completing all sections of the sponsor apheresis label, ensure that information is accurate and complete, by performing a double-check.</p> <p>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.</p> <p><b>Refer to section 2.1.5 for instructions.</b></p>	Clinical Site
<b>2.1.4</b>	<p><b>SHIPPER – Sponsor Label</b></p> <p>The sponsor-provided shipper label is pre-printed with the sponsor name and a description. Complete the following information on the label:</p> <ul style="list-style-type: none"> <li>• Site Number</li> <li>• Subject Number</li> <li>• DIN or Apheresis ID</li> </ul> <p>After completing all sections of the sponsor shipper label, ensure that the information is accurate and complete by performing a double-check. The shipper label is included with the apheresis material shipment to the CPC.</p> <p><b>Specific instructions for the shipper label are outlined in Module 5.</b></p>	Clinical Site

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

Step 1	Step 2	Steps 3.1 – 3.4		Step 4
 <p>Bulk label supplies binder will contain:</p> <ul style="list-style-type: none"> <li>• Sponsor apheresis Label to attach to the bag</li> <li>• A self-laminating card to place the label onto</li> <li>• A zip tie to attach the label to the bag</li> </ul>	 <p>2.1 Fill out the necessary information on the label.</p>	 <p>3.1 Lift the top flap of the self-laminating card.</p>	 <p>3.2 Place the label onto the self-laminating card.</p>	 <p>Secure the self-laminating tag and label via zip tie to the collection bag.</p>
	 <p>2.2 Peel the paper off the label to expose the adhesive side.</p>	 <p>3.3 Remove the paper on the self-laminating card.</p>	 <p>3.4 Laminate and seal the labels onto the self-laminating card.</p>	

**Once completed, proceed to section 2.2 Apheresis collection.**

## 2.2 Apheresis Collection

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



Apheresis collection		
Step	Task	Responsibility
2.2.1	<p>MNC, apheresis collection should be performed according to the site's standard operating procedures following instructions from the sponsor:</p> <ul style="list-style-type: none"> <li>- <b>Target cell count: <math>9 \times 10^9</math> Total WBC, aka Total Nucleated Cells (TNC)</b>, containing a high % of MNC.</li> <li>- <b>Acceptable range: 6 to <math>12 \times 10^9</math> Total WBCs.</b></li> </ul> <p><u>NOTE:</u> Approximately 9-12 liters of whole blood should be processed. The blood volume processed is dependent on the protocol apheresis parameters, subject's weight, and medical status.</p>	Clinical Site
2.2.2	<p>The use of Anticoagulant Citrate Dextrose solution, solution-A (ACD-A) or ACD-A plus heparin is permissible.</p> <p>If both ACD-A and heparin are used; the quantity of heparin should be added to comment section of the <b>NA_APH-TRN COC/COI</b> form. Use of heparin alone is not permitted.</p> <p><u>NOTE:</u> The anticoagulant volume (mL) to be captured on the <b>NA_APH-TRN COC/COI</b> form, should be the volume of anticoagulant in the apheresis collection bag.</p>	Clinical Site
2.2.3	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
2.2.4	Seal tubing using triple weld/seal technique.	Clinical Site
2.2.5	<p><b>The apheresis material must be transferred and placed into a 2-8°C shipper within 60 minutes of the collection end time.</b></p> <p>If more time is required, store the apheresis material in a monitored refrigerator or intermediary transport at 2-8°C until the time of shipment occurs.</p> <p><u>NOTE:</u> If the apheresis material 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.</p>	Clinical Site
2.2.6	<p>It is recommended to perform a WBC count at the midpoint of the collection to ensure the target cell number (<math>9 \times 10^9</math> Total WBCs) is reached and to minimize patient apheresis time.</p> <p>When collecting midpoint sample, do not spike the bag. Use only one of the available sampling bulbs and aseptic technique.</p>	Clinical Site
2.2.7	<p><b>IMPORTANT:</b>  <b>If the minimum total WBCs are not collected on the first attempt, the sponsor may request a second collection. Each apheresis collection should be performed with the goal of achieving <math>9 \times 10^9</math> Total WBC target.</b></p>	Clinical Site



## 2.3 Cell Management

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

Cell Management		
Step	Task	Responsibility
2.3.1	<p>Once the unique identifier is assigned to the donation, enter the following details in IRT on the day of collection as soon as the unique identifier is available: This is <u>critical</u> information required for packing the apheresis material and for the creation of the cryopreservation labels.</p> <p>Refer to IRT manual for instructions.</p> <ul style="list-style-type: none"> <li>Subject Name (to include middle name or initial as documented on medical records and site bag label)</li> <li>Date of Birth</li> <li>Unique identifier for apheresis collection:               <ul style="list-style-type: none"> <li>DIN where applicable for countries in NA</li> </ul> </li> <li>Subject weight in kg on day of apheresis. <b>IMPORTANT:</b> must be rounded to 1 decimal point, i.e., 59.0 or 59.5 kg</li> </ul> <p><u>NOTE:</u> All subject identifiers &amp; weight entered in IRT should be double-checked for accuracy and should match entries on all source documents and labels.</p>	Clinical Site
2.3.2	If a 2 <sup>nd</sup> apheresis collection is requested by the sponsor, perform an “Apheresis Collection” transaction in IRT.	Clinical Site

Icon	COC/COI ACTIONS:	Responsibility
	<b>Complete the Apheresis Chain of Custody/Chain of Identity Form (see NA_APH-TRN) and enter all applicable data in the eCRF.</b>	Clinical Site
	Upload a signed copy of this form to MBOX on the same day.	Clinical Site



If the apheresis material will be packed and shipped directly from the collection center, proceed to **Module 5 ‘packing and shipment’**.

If the apheresis material will be transferred to cell lab or shipment facility to be packed and shipped or for onsite cryopreservation, proceed to **Module 3 ‘Cell transfer’**.

## MODULE 2 COMPLETED

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0



## Module 3:

# Cell Transfer

***Version: 5.0***

***Date: 12-APR-2024***

**This module is only applicable to sites who perform transfer of apheresis material from collection location to be packed at a different location.**

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

# Module 3: Table of Contents

## **3.1 Transfer of apheresis material to cell processing lab**

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

## 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°C until the time of shipment occurs
28-Mar-2022	Module 3	Formatting changes
06-Mar-2023	3.1	Updated wording to refer to apheresis material and remove references to Vineti
12-APR-2024	Module 3	Replaced NA_TRN form with new NA_APH-TRN form Updated wording for MBOX system & responsibility

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

### 3.1 Transfer of apheresis material to cell processing lab

Collected apheresis material when is transferred to the site’s cell processing lab or other facility for subsequent packing and shipment to the CPC or for cryopreservation.

Transfer of apheresis material to cell processing lab		
Step	Task	Responsibility
3.1.1	<p>Upon completion of collection, follow the sites internal procedures to transfer the apheresis material to the cell processing lab or other shipment facility.</p> <ul style="list-style-type: none"> <li><b>Apheresis material must be transferred and placed into 2-8°C shipper within one hour (60 minutes) of the end of collection.</b> If more time is required prior to the transfer, store the apheresis material in a monitored refrigerator or intermediary transport at 2-8°C until the time of shipment occurs.</li> </ul> <p><u>NOTE:</u> If the apheresis material 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.</p>	Clinical Site
3.1.2	The chain of custody of the apheresis material must be documented in the required section of the COC/COI form (NA_APH-TRN).	Clinical Site

	MANUAL COC/COI ACTIONS:	Responsibility
	Document the chain of custody from apheresis unit to Cell laboratory or shipment facility on the Apheresis Chain of Custody/Chain of Identity form (see NA_APH-TRN)	Clinical Site
	Upload a signed COC/COI form to the sponsor MBOX on the same day.	Clinical Site

## MODULE 3 COMPLETED

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0



## Module 4:

# Cryopreservation Procedure

***Version: 5.0***

***Date: 12-APR-2024***

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

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

## **Module 4: Table of Contents**

### **4.1 Cryopreservation: Labeling**

### **4.2 Cryopreservation and LN<sub>2</sub> Storage**

### **Cryopreservation: Shipping**

### **4.3 Communication Plan with Site, Courier and Sponsor**

### **4.4 Review of Packing Materials**

### **4.5 Instructions for Receipt of Empty LN<sub>2</sub> Shipper**

### **4.6 Packing of cryopreserved apheresis material into LN<sub>2</sub> Shipper**

## 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 IRT 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
06-Mar-2023	4.1, 4.2	Removed local from cryopreservation process Adjusted wording to refer to apheresis material, cryopreserved apheresis material and revised the required cryopreservation labels Removed references to Vineti
	4.1.4	COC/COI form referenced 'XX_CRY' is now a global form and the name of form is now referred to as 'CRY' (an abbreviation of the term cryopreservation)
	4.3	Adjusted wording to refer to apheresis material, cryopreserved apheresis material
	4.4, 4.5	Edited outer shipper to align with other modules and added instructions for QR code
	4.6	Removed 3-piece packing solution and removed Vineti steps
	4.6.1	COC/COI form referenced 'XX_SHIP_CRYO' is now a global form and the name of form is now referred to as 'SHIP_CRYO' (an abbreviation of the term cryopreservation)
12-APR-2024	4.1.2	Clarified that 2 shipper labels are required for cryopreserved apheresis material import to the USA



	4.3.4	Updated charged shipper arrival time
	4.5.5, 4.5.7, 4.6.4	Updated pictures
	4.6.2	Added details on shipping materials expected
	4.4, 4.5, 4.6	Removed references to obsolete videos Updated wording for MBOX system & responsibility


## 4.1 Cryopreservation: Labeling




This section is only applicable to sites that have completed a technical transfer of the sponsor cryopreservation method and these steps must be followed alongside the sponsor batch record.

Cryopreservation: Labeling		
Steps	Task	Responsibility
4.1.1	<p>The following labels will accompany the apheresis material to the cell lab:</p> <ul style="list-style-type: none"> <li>One (1) sponsor apheresis label attached to the apheresis material bag</li> <li>One (1) site apheresis bag label affixed to the apheresis bag</li> </ul> <p>Create subject specific sponsor cryopreservation labels with the sponsor approved label templates.</p>	Clinical Site
4.1.2	<p>Prepare the following labels that will accompany the cryopreserved apheresis material inside the LN<sub>2</sub> shipper:</p> <ul style="list-style-type: none"> <li>One (1) or Two (2) sponsor shipper label(s). <i>When imported into the USA, a second shipper label must be included in the clear packing envelope on the outside of the LN<sub>2</sub> shipper with AWB.</i></li> <li>One (1) sponsor shipper label for batch record</li> </ul>	Clinical Site
4.1.3	<p>Sponsor cryopreservation labels:</p> <p>Prepare and affix sponsor cryopreservation label directly to the cryopreservation bag.</p>	Cell Lab
4.1.4	<p>Sponsor cassette label:</p> <p>Prepare and affix a sponsor cassette label to each cassette under room temperature conditions <b><u>30 MINUTES BEFORE the cassette is placed into the controlled rate freezer</u></b>, otherwise, the label will not adhere properly to the cassette.</p>	Cell Lab
4.1.5	<p>In the <b>CRYO form</b>, indicate the number of bags used for cryopreservation. Then apply each label(s) to the cryo bag and corresponding cassette</p>	Cell Lab
4.1.6	<p>Label Reconciliation:</p> <p>Once all labels have been applied to the bags and cassettes, <b>complete the Batch Record</b> to document which labels have been used, damaged and/or destroyed.</p>	Cell Lab

## 4.2 Cryopreservation and LN<sub>2</sub> 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.


Cryopreservation and LN <sub>2</sub> Storage		
Steps	Task	Responsibility
4.2.1	<p>Cryopreservation and storage of the apheresis material should be performed in the site cell lab per the sponsor apheresis cryopreservation batch record.</p> <ul style="list-style-type: none"> <li>Follow the sponsor apheresis cryopreservation batch record for instructions on cell processing and cryopreservation of the apheresis material.</li> <li>The batch record outlines the bill of materials required for cell processing and cryopreservation referenced in the section related to study supplies.</li> </ul>	Cell Lab
	<p><b>IMPORTANT:</b> Next steps below need to be performed as quickly as possible. It is critical to pack the cassette(s) into the LN<sub>2</sub> freezer quickly to avoid thawing of the cryopreserved apheresis material.</p>	Cell Lab
4.2.2	<p>Upon completion of the controlled rate freezing process, the cryopreserved apheresis material must be stored at ≤ -120°C in the vapor phase of liquid nitrogen storage system.</p> <ul style="list-style-type: none"> <li>Remove cassette with cryopreserved apheresis material from the controlled rate freezer (one at a time) and place each cassette inside LN<sub>2</sub> tank.</li> </ul> <p><b>NOTE: Transfer times must be ≤3 minutes.</b></p>	Cell Lab

	COC/COI ACTIONS:	Responsibility
	Complete the CAR-T Cryopreservation Chain of Custody/Chain of Identity Form (see CRYO)	Cell Lab
	Upload a signed copy of the COC/COI form to the sponsor MBOX on the same day.	Cell Lab

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

There are two types of shipments related to the packaging and shipment of cryopreserved apheresis material to the manufacturing facility.



- Shipment of charged empty LN<sub>2</sub> shipper to the site
- Shipment of cryopreserved apheresis material from clinical site to the manufacturing facility

Communication Plan with Site, Courier and Sponsor		
Step	Task	Responsibility
4.3.1	The sponsor will initiate order pick up with the courier.	Sponsor
4.3.2	<p>The courier will issue an automated pre-alert/order confirmation to the site.</p> <ul style="list-style-type: none"> <li>• The notification will reference the subject number to track and trace the shipment from clinical site to the manufacturing facility.</li> <li>• The notification will also reference the Air Waybill (AWB) for the shipment. <b>NOTE:</b> a print-out of the same AWB will be provided in the shipper kit pouch within the shipper.</li> </ul>	Courier
4.3.3	<p>The courier will send one notification to the clinical site contact(s) prior to delivery of the empty charged shipper. The notification will be:</p> <ul style="list-style-type: none"> <li>• The day of delivery, within 1 hour prior to delivery. This is a geofence notification and will trigger when the shipment is within a 5-mile radius of the clinical site.</li> <li>• <b>NOTE:</b> The site or sponsor local team does not have access to the EVO-IS system temperature data.</li> <li>• Any delays in shipment will be communicated by the courier via e- mail to the designated site contact.</li> </ul>	Courier
4.3.4	The charged shipper will arrive at the site in the morning at the agreed local time to pack the cryopreserved apheresis material.	Courier
4.3.5	The sponsor will coordinate with the courier to return that afternoon to pick up the cryopreserved apheresis material at an agreed local time for delivery to the manufacturing facility.	Sponsor
	<b>IMPORTANT</b> Notify CSOM via email: <a href="mailto:Central.Scheduling@ITS.JNJ.com">Central.Scheduling@ITS.JNJ.com</a> and copy your SM if the packed shipper will not be ready for pick-up by the courier by agreed local time.	Cell Lab

## 4.4 Cryopreservation Shipping: Review of Packing Materials



Review of Packing Materials		
Step	Task	Responsibility
4.4.1	<p>The following tools should be utilized in preparation for packing the LN<sub>2</sub> shipper:</p> <ul style="list-style-type: none"> <li>• Cryogloves</li> <li>• Safety glasses</li> <li>• Wire cutter</li> </ul> <p><b>NOTE: Adhere to any additional site requirements for PPE when handling cryopreserved products and equipment.</b></p> <p><b>Do not discard any contents or packaging materials until you have read these instructions.</b></p>	Cell Lab
4.4.2	<p>Upon the receipt of shipper, you will find the following components inside the outer shipper case:</p> <ul style="list-style-type: none"> <li>• <b>LN<sub>2</sub> shipper</b> (Savsu DV-10)</li> <li>• <b>Shipper Kit pouch</b> (inside the pouch within the shipper case)</li> <li>• <b>Consignee Kit pouch</b> (inside the pouch within the shipper case)</li> </ul> <p>The <b>shipper Kit Pouch</b> is used when shipping cryopreserved apheresis material to the sponsor. The <b>shipper Kit Pouch</b> includes:</p> <ul style="list-style-type: none"> <li>• One (1) red tamper evident seal (for use on one side of the LN<sub>2</sub> shipper lid, number should match the AWB)</li> <li>• One (1) red tamper evident seal (for use on cassette rack)</li> <li>• One (1) zip tie (for use on the outer shipper case lid)</li> <li>• One (1) zip tie (for use on one side of the LN<sub>2</sub> shipper lid)</li> <li>• 1-Piece Packing Solution: Cryogenic containment envelope pouch and foam dunnage</li> <li>• One (1) clear side packing envelope</li> <li>• AWB for shipment</li> </ul> <p>The <b>consignee Kit Pouch</b> is used by the sponsor when shipping the empty shipper back to the courier upon receipt of the apheresis cryopreserved material. Information is included here only for reference.</p> <ul style="list-style-type: none"> <li>• 1 zip tie (for use on the outer shipper case)</li> <li>• AWB for return shipment of empty shipper</li> </ul> <p><b>Inside the shipper</b>, there will be an empty cassette rack. This is used to store and secure the cassettes inside the shipper during transport.</p>	Cell Lab

## Review of Packing Materials



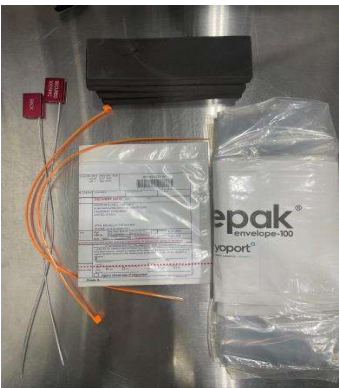
Step	Task	Responsibility
4.4.3	<p><b>NOTIFY CSOM email <a href="mailto:Central.Scheduling@ITS.JNJ.com">Central.Scheduling@ITS.JNJ.com</a> and copy SM IF:</b></p> <ul style="list-style-type: none"> <li>The shipping corrugated case is not secured.</li> <li>The zip tie is missing from the outer case lid.</li> <li>The subject number listed on the AWB does not match the intended subject.</li> <li>The EVO-IS ID (last 4 digits) listed on the AWB does not match the LN<sub>2</sub> shipper.</li> </ul>  <ul style="list-style-type: none"> <li>Any contents are missing or incorrect from the shipper kit pouch listed on 4.4.2.</li> <li>There is a flashing alarm <b>indicating</b> the temperature is out of range on the display.</li> <li>The temperature light indicator is not functioning.</li> <li>The temperature is unable to be confirmed using the QR code on the LN<sub>2</sub> shipper lid when the temperature light indicator is not functioning.</li> </ul> <p><b>Example of Shipping Corrugated Case and Components</b></p> 	Sponsor/ Cell Lab

## 4.5 Cryopreservation Shipping: Instructions for Receipt of Empty LN<sub>2</sub> Shipper

The following are step-by-step instructions for receipt of the empty LN<sub>2</sub> shipper in anticipation of packing of the cryopreserved apheresis material.

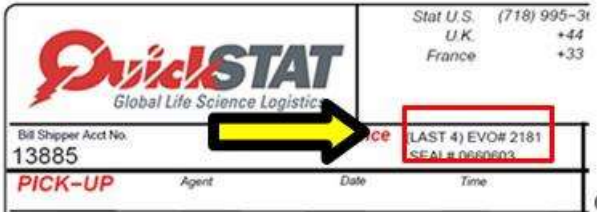


Instructions for Receipt of the Empty LN <sub>2</sub> Shipper		
Step	Task	Responsibility
4.5.1	<p>The shipper will arrive inside an outer corrugated case. The outer corrugated case includes wheels and luggage handle for ease of transport.</p> <ul style="list-style-type: none"> <li>Once the shipper has been transported to the appropriate packaging location, set the shipper upright and lower the luggage handle.</li> </ul> 	Cell Lab
4.5.2	<p>The outer corrugated case is secured by buckle straps.</p> <ul style="list-style-type: none"> <li>Unclip the buckle straps. Open the outer corrugated case lid.</li> </ul> 	Cell Lab

### Instructions for Receipt of the Empty LN<sub>2</sub> Shipper

Step	Task	Responsibility
4.5.3	<p>The outer case shipper lid is secured by a single zip tie through the zipper pulls.</p> <ul style="list-style-type: none"> <li>Cut and discard the zip tie then unzip the outer case lid.</li> </ul>  <p><b>NOTE: The site will need to use wire cutters (these are NOT included in the shipment).</b></p>	Cell Lab
4.5.4	<p>Lift the shipper case lid.</p> <ul style="list-style-type: none"> <li>Verify that the pouch within the outer case contains the shipper kit pouch and consignee kit pouch—which are labeled.</li> </ul>  <ul style="list-style-type: none"> <li>Remove the shipper kit pouch and its materials. These materials will be used for packing the cryopreserved apheresis material.</li> </ul>  <p><b>NOTE: Leave the consignee kit pouch inside the pouch within the outer case.</b></p>	Cell Lab



### Instructions for Receipt of the Empty LN<sub>2</sub> Shipper

Step	Task	Responsibility
<b>4.5.5</b>	<p>Verify that the EVO-IS ID number (last 4 digits) on the AWB matches the EVO-IS ID number on the LN<sub>2</sub> shipper lid.</p> <div style="text-align: center; margin: 10px 0;"> <p><b>QuickSTAT AWB</b></p>  </div> <div style="text-align: center; margin: 10px 0;"> <p><b>World Courier AWB</b></p>  </div> <div style="text-align: center; margin: 10px 0;"> <p><b>Evo-IS ID number location</b></p>  </div>	Cell Lab

**4.5.6** Confirm if there is any temperature excursion:

Cell Lab

- 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. A steady light indicates that the temperature is within range. You can proceed to the next steps.
- A flashing light indicates a temperature excursion has occurred.
- If no light is present, scan QR code on DV-10 lid with a smart device. Scanning the QR code will direct the user to a web page that displays the last reported payload temperature with the last recorded temperature reading. This QR code should only be used as a BACK UP solution in case the light indicator fails.
- **NOTE:** The QR code label and the QR code displayed on the web page are correlated with the EVO-IS ID. Verify that the EVO-IS ID on the web page display exactly matches the QR code label ID and EVO-IS ID on the DV-10 lid. Confirm on the QR code temperature snapshot display that the time stamp is current.
- If any of the following occurs, notify CSOM via Central.Scheduling@ITS.JNJ.com and copy the SM:
  - A flashing light indicating a temperature excursion has occurred.
  - Temperature light indicator is not functioning (does not turn on).
  - There is any ID mismatch, concerns regarding the QR code, and/or an out-of-range temperature.

**Press Indicator**



**Light Indicator**


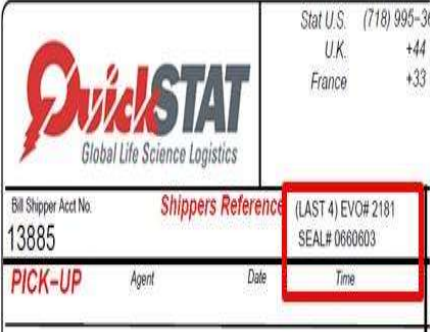


Example of QR code and web page display

The image shows three components related to the QR code verification process:

- Left:** A yellow EVO-IS label with a QR code. A yellow arrow points to the QR code. The label includes the ID: 862771041061543, SN: SC3012, and contact information for Biolife Solutions.
- Middle:** A web page display showing a green checkmark, indicating a successful scan. The displayed ID is 862771041061543 and the temperature is -191.9° C. The page also shows the last reported time and a LOGIN button.
- Right:** A web page display showing a red X, indicating a failed scan. The displayed ID is 862771041061543 and the temperature is 27.4° C. The page also shows the last reported time and a LOGIN button.

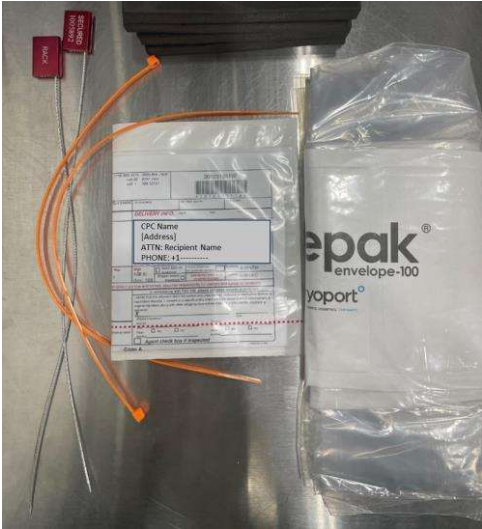
### Instructions for Receipt of the Empty LN<sub>2</sub> Shipper

Step	Task	Responsibility
4.5.7	<p>Inside the shipper kit pouch, there are 2 tamper evident seals</p> <ul style="list-style-type: none"> <li>Tamper evident seal with “SECURED” and serial number listed</li> <li>Tamper evident seal with “RACK” listed</li> </ul> <div style="text-align: center; margin: 10px 0;">  </div> <p>Verify the tamper evident seal number (SEAL#) listed on the AWB matches the tamper evident seal from the shipper kit pouch.</p> <div style="display: flex; justify-content: space-around; margin-top: 20px;"> <div style="text-align: center;"> <p><b>QuickSTAT</b></p>  </div> <div style="text-align: center;"> <p><b>World Courier</b></p> <p>TO (CONSIGNEE)</p> <p>Name Telephone Address</p> <p><b>FORMATION</b></p> <p>PICKUP: (Last 4) EVO#2181 Seal #0660603</p> </div> </div>	Cell Lab

## 4.6 Cryopreservation Shipping: Packing of cryopreserved apheresis material into the LN<sub>2</sub> Shipper

The following are step-by-step instructions for packing the cryopreserved apheresis material into the LN<sub>2</sub> shipper.



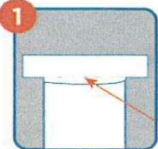



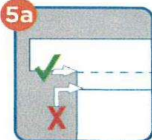



**REMINDER:** Ensure all necessary PPE is on before the next steps.

Packing of cryopreserved apheresis material into the LN <sub>2</sub> Shipper		
Step	Task	Responsibility
4.6.1	<p>Ensure that the following documents are available for reference and completion immediately after packing the shipper.</p> <ul style="list-style-type: none"> <li>SHIP_CRYO Site Shipment Form for Chain of Custody/Chain of Identity Form</li> <li>Copy of IRT notification with subject information</li> </ul>	Cell Lab
4.6.2	<p>Ensure all materials in the shipper kit pouch are removed and staged for the packing:</p> <ul style="list-style-type: none"> <li>- AWB</li> <li>- Cryogenic containment envelope pouches (2-4)</li> <li>- Foam dunnage (2-4)</li> <li>- Zip ties (x2)</li> <li>- 2 Tamper evident seals: "RACK" &amp; a numbered seal</li> </ul> 	Cell Lab



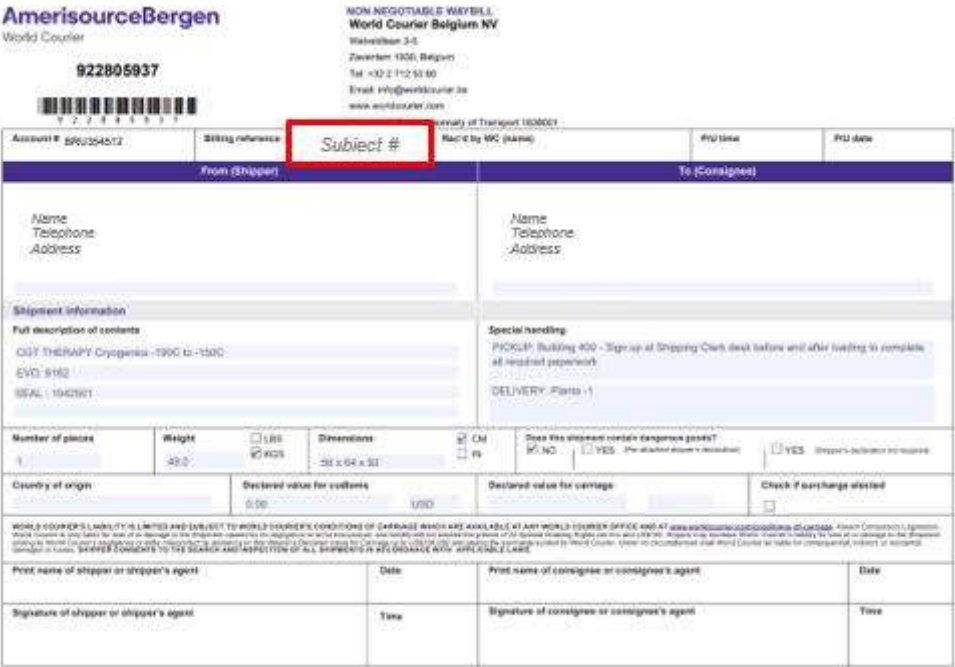


**IMPORTANT:** The next steps need to be performed as quickly as possible. It is critical to avoid thawing of the cryopreserved apheresis material as the cassette(s) are packed into the shipper. Place all packing materials and shipper as close as possible.

## Packing of cryopreserved apheresis material into the LN<sub>2</sub> Shipper

Step	Task	Responsibility
4.6.3	<p>Ensure the ports of the cryopreserved apheresis material bag are orientated towards the top of the cassette with the locking hinge.</p> <div style="display: flex; justify-content: space-around; align-items: center;">   </div> <p>Cryogenic containment envelope pouch:</p> <ol style="list-style-type: none"> <li>1) Pre-fold over the scored line shown by the arrow. The pre-fold may fold over the adhesive seal cover.</li> <li>2) Insert the cassette with the locking hinge toward the top and push completely down past the adhesive seal into the cryogenic containment envelope pouch. Ensure the cassette is not behind the adhesive seal.</li> <li>3) Peel off adhesive strip cover on top flap.</li> <li>4) Peel off adhesive strip cover on the envelope pouch.</li> </ol> <div style="display: flex; justify-content: space-around; align-items: center;">     </div> <ol style="list-style-type: none"> <li>5)             <ol style="list-style-type: none"> <li>a. Seal the cryogenic containment envelope pouch. Ensure to fold flap along pre-folded scored line.</li> <li>b. Start sealing from center of pre-fold and work out to the sides. Seal must not have any wrinkles or gaps.</li> </ol> </li> <li>6) Fold tabs around seal with pressure. Tabs must be sealed as close as possible to the envelope.</li> </ol> <div style="display: flex; justify-content: space-around; align-items: center;">    </div> <div style="text-align: center; margin-top: 20px;"> <p><b>Example of packed cassette</b></p>  </div>	Cell Lab





## Packing of cryopreserved apheresis material into the LN<sub>2</sub> Shipper

Step	Task	Responsibility
<b>4.6.4</b>  	<p><b>Remove the first cassette (with cryopreserved apheresis material) from LN<sub>2</sub> storage.</b></p> <ul style="list-style-type: none"> <li>Prior to packing the cassette, verify that the subject number on the cassette matches the Subject Number on the:               <ul style="list-style-type: none"> <li>• AWB</li> <li>• IRT notification</li> </ul> </li> <li>As a reminder, the AWB is inside the shipper kit pouch.</li> </ul> <p style="text-align: center;"><b>QuickSTAT AWB</b></p> <div style="border: 1px solid black; padding: 5px; margin: 10px auto; width: 80%;">  </div> <p style="text-align: center;"><b>World Courier AWB</b></p> <div style="margin: 10px auto; width: 90%;">  </div>	Cell Lab

### Packing of cryopreserved apheresis material into the LN<sub>2</sub> Shipper

Step	Task	Responsibility
4.6.5 	Begin completing <b>SHIP_CRYO Site Shipment Form for Chain of Custody/Chain of Identity Form.</b>	Cell Lab
4.6.6	Remove the shipper lid and lift the cassette rack.  	Cell Lab
4.6.7	<b>NOTE:</b> Proper placement of the DV10 Smart Cap when not seated in the dewar body is <b>PROBE SIDE UP</b> on a flat surface. Serious damage to the probe may occur if placed otherwise.  	Cell Lab

### Packing of cryopreserved apheresis material into the LN<sub>2</sub> Shipper



Step	Task	Responsibility
4.6.8	<ul style="list-style-type: none"> <li>Place sealed Cryogenic containment envelope 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.</li> </ul>  <ul style="list-style-type: none"> <li>Place one piece of the foam dunnage on top of the envelope within the cassette rack.</li> </ul> 	Cell Lab
4.6.9	<ul style="list-style-type: none"> <li>Return the rack into shipper to prevent warming and close the shipper lid.</li> </ul>  	Cell Lab







### Packing of cryopreserved apheresis material into the LN<sub>2</sub> Shipper

Step	Task	Responsibility
4.6.10	Repeat the packing process for any of the remaining cassettes to be shipped. <div style="text-align: center; margin-top: 10px;"> </div>	Cell Lab
4.6.11	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. <div style="text-align: center; margin-top: 10px;"> </div>	Cell Lab
4.6.12	Remove the shipper lid and place the cassette rack (with cryopreserved apheresis material) into the shipper. <div style="display: flex; justify-content: space-around; margin-top: 10px;"> </div>	Cell Lab
4.6.13	Close the shipper lid, secure the lid, and lower the shipper handle to allow for the closing of the shipper lid after tamper evident seal is attached. <div style="text-align: center; margin-top: 10px;"> </div>	Cell Lab

## Packing of cryopreserved apheresis material into the LN<sub>2</sub> Shipper


Step	Task	Responsibility
4.6.14	<ul style="list-style-type: none"> <li>Feed the tamper evident seal that contains the word “<b>SECURED</b>” 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.</li> <li>Wrap and secure a zip tie through the lid and around the handle located on the other side of the shipper.</li> </ul> 	Cell Lab
4.6.15	<p>Once the shipper lid is secured, place the verified shipper label inside the pouch within the shipper case.</p> <p><b>NOTE: Only the consignee kit pouch and the shipper label should remain inside the pouch within the shipper case.</b></p> 	Cell Lab

## Packing of cryopreserved apheresis material into the LN<sub>2</sub> Shipper

Step	Task	Responsibility
4.6.16	<ul style="list-style-type: none"> <li>Obtain the second zip tie provided in the shipper kit pouch.</li> <li>Zip the outer case lid closed and secure by passing the single zip tie through the zipper pulls.</li> <li>Fasten the lid of the outer corrugated case by fastening the buckle straps</li> </ul> <div style="display: flex; justify-content: space-around; margin-top: 10px;">   </div>	Cell Lab
4.6.17	<ul style="list-style-type: none"> <li>Remove the existing AWB and place the new AWB (from the shipper kit pouch) into the clear packing envelope.</li> <li>Place the additional shipper label with the new AWB into the clear packing envelope. Applicable to all sites <b>excluding USA</b>.</li> <li>Discard all leftover materials and packaging per site disposal procedures. Discard any remaining items and bags from shipper kit pouch.</li> </ul> <div style="display: flex; justify-content: space-around; margin-top: 10px;">   </div>	Cell Lab

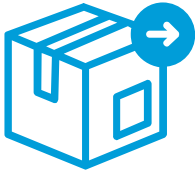


**REMINDER:** The sponsor will coordinate with the courier to pick up the LN<sub>2</sub> shipper packed with cryopreserved apheresis material from the site at agreed local time. Notify CSOM via email [Central.Scheduling@ITS.JNJ.com](mailto:Central.Scheduling@ITS.JNJ.com) and **copy the SM** immediately if there are any constraints for getting this shipment ready at agreed local time.

	MANUAL COC/COI ACTIONS:	Responsibility
	Complete the CAR-T Cryopreservation Chain of Custody/Chain of Identity Form (see SHIP_CRYO).	Cell Lab
	Upload a signed COC/COI form to the sponsor MBOX on the same day.	Cell Lab

# MODULE 4 COMPLETED

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0



## Module 5:

# Packaging and Shipment

**Version: 5.0**

**Date: 12-APR-2024**

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

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

## **Module 5: Table of Contents**

- 5.1 Communication Plan with Site, Courier & Sponsor**
- 5.2 Review of Packing Materials**
- 5.3 Packing of Apheresis Material into CREDO CUBE Shipper**
- 5.4 Courier Pickup of the Packed CREDO CUBE Shipper**

## 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
06-Mar-2023	5.1	Adjusted wording to refer to apheresis material, aligned wording of temperature monitoring device and courier arrangements
	5.2	Additional packing materials added for all regions
	5.3	Updated packing instructions, removed Vineti steps and added to secure the outer box of credo cube with tape
	5.4	Adjusted wording to refer to apheresis material, removed references to Vineti and added where applicable couriers will provide the AWB when pick up is completed while the courier waits on site.
12-APR-2024	5.1	Edited to provide more concise information: <ul style="list-style-type: none"> <li>- Couriers unspecified to accommodate for global flexibility.</li> <li>- Removed 5.1.2; 5.1.3, 5.1.4.</li> </ul>
	5.2.1, 5.3	Updated packing and shipment procedure for Japan with removal of SD Collabo courier
	5.2	Clarified that a Real Time Location Monitoring Device RTLM may be included by World Courier in Credo Cube, RTLM should not be removed.
	5.3	Removed references to obsolete videos
	5.2.1, 5.3	Updated wording for the polybag (previously referenced as poly bio bag or bio-pouch)
	5.3.1	Updated pictures for EEA, ISR, Canada, LATAM, AUS, KOR.


<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

	5.3.8	Added IDM procedure for the UK
	5.3.10	Updated steps to clarify IDM results packing for AUS
	5.4	Updated name of XX_SHIP_APH form Updated wording for MBOX system & responsibility

## 5.1 Communication Plan with Site, Courier & Sponsor

The apheresis material shipment procedure involves two steps:


1. Shipment of empty CREDO CUBE to the site (for packing of apheresis material)
2. Shipment of the apheresis material from the clinical site to the CPC

Communication Plan with Site, Courier & Sponsor		
Step	Task	Responsibility
5.1.1	<p>The sponsor will coordinate with the assigned shipping courier the pick-up of apheresis material on the day of apheresis.</p> <p>The courier will issue an automated pre-alert/order confirmation to the clinical site referencing:</p> <ul style="list-style-type: none"> <li>• Subject number reference with the AWB for the shipment</li> </ul> <p>The CREDO CUBE shipper will arrive at the site at <b>the agreed local time</b> for the packing of apheresis material.</p>	Sponsor
	<p><b>REMINDER: Notify CSOM email <a href="mailto:Central.Scheduling@ITS.JNJ.com">Central.Scheduling@ITS.JNJ.com</a> immediately if there are any constraints for getting this shipment ready at agreed local time.</b></p>	Clinical Site





## 5.2 Review of Packing Materials

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

Review of Packing Materials		
Step	Task	Responsibility
5.2.1	<p><b>Applicable for USA only</b> (For Canada, please see next table):</p> <p>Receipt of CREDO CUBE Shipper.</p> <p>Check that the CREDO CUBE shipment contains the following:</p> <ul style="list-style-type: none"> <li>• Outer corrugated box</li> <li>• Inside the corrugated box there is the CREDO CUBE shipper (do not remove it from the box)</li> <li>• Inside the CREDO CUBE there is a brown payload box (do not remove from the CREDO CUBE)</li> <li>• Inside the brown payload box there is:               <ul style="list-style-type: none"> <li>• Clinical site kit pouch</li> <li>• Cryopreservation kit pouch</li> </ul> </li> </ul>	Clinical Site
5.2.2	<p><b>Applicable for USA only</b> (For Canada, please see next table):</p> <p>The clinical site kit pouch contains the materials used for packing of apheresis material. The Clinical Site kit pouch includes:</p> <ul style="list-style-type: none"> <li>• Non activated temperature monitoring device (TempTale Ultra) - keep inside CREDO CUBE until it is time to activate.</li> <li>• Polybag</li> <li>• Absorbent pad</li> <li>• AWB for shipment to the CPC</li> </ul>	Clinical Site
5.2.3	<p><b>Applicable for USA only</b> (For Canada, please see next table):</p> <p>Keep the cryopreservation kit pouch inside the brown payload box. Do not remove as it is intended for future use at the CPC.</p>	Clinical Site
	<p><b>Notify CSOM via email <a href="mailto:Central.Scheduling@ITS.JNJ.com">Central.Scheduling@ITS.JNJ.com</a> and copy the SM if any contents are missing or temperature monitoring device activated prior to receipt at the site.</b></p>	Clinical Site







## Review of Packing Materials


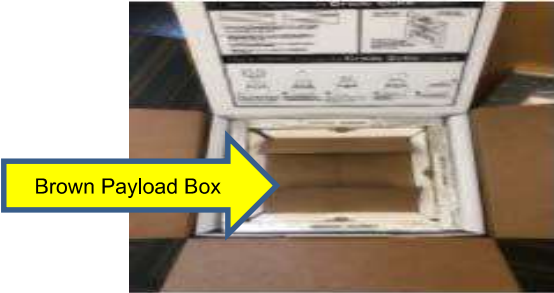

Step	Task	Responsibility
5.2.1	<p><b>Applicable for <span style="color: red;">Canada only</span>:</b></p> <p>Receipt of CREDO CUBE Shipper</p> <p>Check that the CREDO CUBE shipment contains the following:</p> <ul style="list-style-type: none"> <li>• CREDO CUBE shipper</li> <li>• Large Polythene Bag containing:               <ul style="list-style-type: none"> <li>• Polybag</li> <li>• Absorbent material</li> <li>• Non activated temperature monitoring device (TempTale Ultra)- keep inside CREDO CUBE until it is time to activate.</li> </ul> </li> </ul> <p>World Courier may include a Real Time Location Monitoring Device (RTLM) in the credo cube for tracking purposes (data will not be shared). The RTLM device will be positioned outside the box, ensuring there is no physical contact with the apheresis bag. Do NOT remove the RTLM device.</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p style="font-size: small;">Placement of the RTLM device inside credo cube</p> </div> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p style="color: blue; font-weight: bold; font-size: large;">AmerisourceBergen</p> <p style="font-size: small;">World Courier</p> <p style="font-weight: bold; font-size: large;">RTLM - Controlant GPS World Courier Property - Do Not Touch!</p> </div> </div> <p style="font-style: italic; font-size: small;">This information is included here only for reference.</p>	Clinical Site
	<p><b>Notify CSOM via email <a href="mailto:Central.Scheduling@ITS.JNJ.com">Central.Scheduling@ITS.JNJ.com</a> and copy the SM if any contents are missing or the temperature monitoring device was activated prior to receipt at the site.</b></p>	Clinical Site

## 5.3 Packing of Apheresis Material into the CREDO CUBE Shipper for USA only

This section provides step-by-step instructions for packing the apheresis material into the CREDO CUBE shipper.

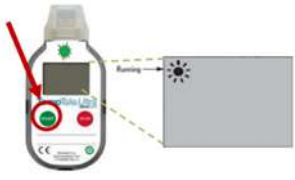
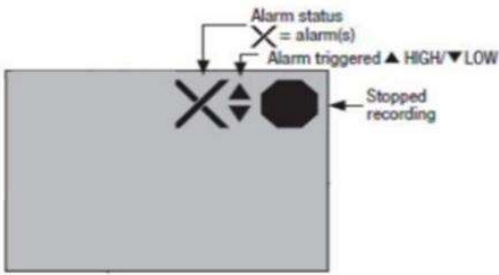

Applicable for USA only (**instructions for Canada**, please see pages XX-XX)

Packing of apheresis material into the CREDO CUBE Shipper		
Step	Task	Responsibility
5.3.1	Prior to starting packing: Verify that the subject number on the AWB matches the subject number listed on: <ul style="list-style-type: none"> <li>• Copy of the IRT notification which includes DIN /Apheresis ID. (If not available, contact site coordinator and request copy prior to continue to the next steps)</li> <li>• Sponsor apheresis label</li> <li>• Shipper label</li> </ul>	Clinical Site
5.3.2	<ul style="list-style-type: none"> <li>• Open outer corrugate box containing the empty CREDO CUBE shipper.</li> </ul> <div style="text-align: center;">   </div>	Clinical Site
5.3.3	<ul style="list-style-type: none"> <li>• Open the top panel and remove the VIP panel.</li> </ul> <div style="text-align: center;">   </div>	Clinical Site
5.3.4	<ul style="list-style-type: none"> <li>• Open the White TIC™ Panel and remove it.</li> </ul> <div style="text-align: center;">   </div>	





<p>5.3.5</p> 	<p>Brown payload box</p> <ul style="list-style-type: none"> <li>Open and remove the clinical site kit pouch and display its components on a flat surface. <b>NOTE: Leave TempTale inside the brown payload box until is time to activate.</b></li> </ul> <p><b>IMPORTANT:</b> Leave the cryopreservation kit pouch inside the brown payload box within the CREDO CUBE. This is for the CPC.</p> 	<p>Clinical Site</p>
<p>5.3.6</p>	<p>Once the subject information on the site apheresis label is verified:</p> <ul style="list-style-type: none"> <li>Place apheresis material into the polybag with the absorbent pad.</li> <li>Remove the adhesive backing and seal the polybag with the apheresis material inside.</li> </ul>  <p>Gently place the polybag containing the apheresis material inside the brown payload box within the CREDO CUBE.</p>	<p>Clinical Site</p>

Applicable for USA only

### Packing of apheresis material into the CREDO CUBE Shipper

Step	Task	Responsibility
5.3.7	<p>Temperature monitoring device (TempTale):</p> <ul style="list-style-type: none"> <li>Remove the TempTale from inside the brown payload box.</li> <li>Press on the Green Start button until the “SUN” icon appears.</li> </ul>  <p><b>IMPORTANT:</b> If any of these icons appears on the screen, notify CSOM via email <a href="mailto:Central.Scheduling@ITS.JNJ.com">Central.Scheduling@ITS.JNJ.com</a> and copy the SM immediately:</p>  <ul style="list-style-type: none"> <li>Once activated, place the TempTale into the brown payload box next to the apheresis material.</li> </ul> 	Clinical Site





Applicable for USA only

Packing of apheresis material into the CREDO CUBE Shipper		
Step	Task	Responsibility
5.3.8	<ul style="list-style-type: none"> <li>Close and secure the top White TIC™ panel of the shipper</li> </ul> 	Clinical Site
5.3.9	<ul style="list-style-type: none"> <li>Place the VIP Panel on the top and secure the outer corrugated box with tape.</li> </ul> 	Clinical Site
5.3.10	<p>Once the shipper is secured:</p> <ul style="list-style-type: none"> <li>Place the shipper label and AWB into the packing envelope.</li> <li>Ensure the existing AWB has been removed and the new shipping AWB replaces it.</li> <li>The shipper is now ready for pick-up by the courier.</li> </ul> 	Clinical Site
	<p><b>IMPORTANT!</b> In case of issues encountered during the packing process, notify CSOM via email <a href="mailto:Central.Scheduling@ITS.JNJ.com">Central.Scheduling@ITS.JNJ.com</a> and copy the SM.</p>	Clinical Site



### 5.3 Packing of Apheresis Material into the CREDO CUBE Shipper for Canada only

Applicable for Canada only (**instructions for USA**, please see pages XX-XX)

This section provides step-by-step instructions for packing the apheresis material into the CREDO CUBE shipper.

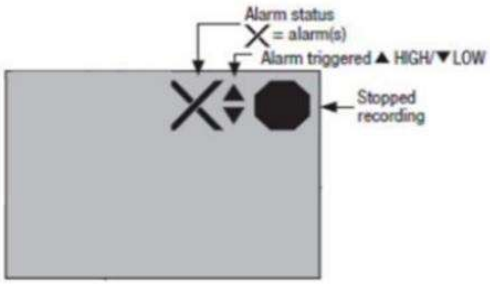
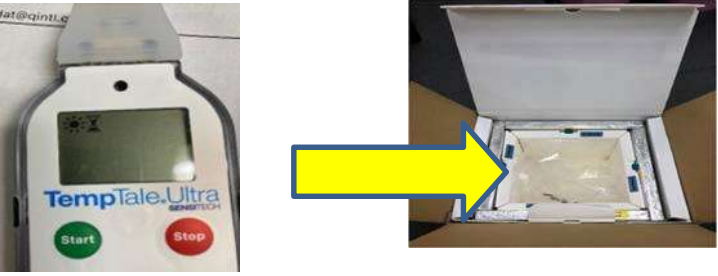
Packing of apheresis material into the CREDO CUBE Shipper		
Step	Task	Responsibility
5.3.1	<p>Prior to start packing:</p> <p>Remove the AWB from the outer pouch and verify that the Subject Number on the AWB matches the Subject Number listed on:</p> <ul style="list-style-type: none"> <li>Sponsor apheresis label</li> <li>Shipper label</li> </ul>  	Clinical Site
5.3.2	<p>Open outer corrugate of the empty CREDO CUBE shipper.</p> 	Clinical Site
5.3.3	<p>Open the top panel and remove the VIP panel.</p> 	Clinical Site

### Packing of apheresis material into the CREDO CUBE Shipper





Step	Task	Responsibility
5.3.4	Remove the White TIC™ Panel. <div style="text-align: center; margin-top: 20px;">  </div>	Clinical Site
5.3.5	Check contents inside the CREDO CUBE: <ul style="list-style-type: none"> <li>• Locate the Large Polythene, which contains the following:               <ul style="list-style-type: none"> <li>• Polybag</li> <li>• Absorbent pad</li> <li>• Non-activated temperature monitoring device (TempTale Ultra)- leave inside shipper until ready to activate</li> </ul> </li> </ul>	Clinical Site
5.3.6	Once the subject information is verified: <ul style="list-style-type: none"> <li>• Place the apheresis material bag into the polybag with the absorbent pad.</li> <li>• Remove the adhesive backing and seal the polybag with the apheresis material inside.</li> <li>• Gently place the polybag into the CREDO CUBE</li> </ul> <div style="text-align: center; margin-top: 20px;">  </div>	Clinical Site




### Packing of apheresis material into the CREDO CUBE Shipper




Step	Task	Responsibility
5.3.7	<p>Activate the TempTale:</p> <ul style="list-style-type: none"> <li>Remove the logger from inside the CREDO CUBE</li> <li>Press on the Green Start button until the "SUN" icon appears.</li> </ul> <p><b>IMPORTANT:</b> If any of these icons appears on the screen, immediately notify CSOM via email <a href="mailto:Central.Scheduling@ITS.JNJ.com">Central.Scheduling@ITS.JNJ.com</a> and copy SM:</p> 	Clinical Site
5.3.8	<p>Once activated:</p> <ul style="list-style-type: none"> <li>Place the TempTale into the CREDO CUBE next to the packed Polybag.</li> </ul> 	Clinical Site

### Packing of apheresis material into the CREDO CUBE Shipper

Step	Task	Responsibility
5.3.9	<ul style="list-style-type: none"> <li>Close &amp; secure the top White TIC™ panel of the shipper.</li> </ul>  <ul style="list-style-type: none"> <li>Place the VIP Panel on the top.</li> </ul> 	Clinical Site
5.3.10	Secure the outer corrugated box with tape.  	Clinical Site
5.3.11	Once the shipper is secured: <ul style="list-style-type: none"> <li>Place the completed sponsor shipper label and the existing AWB into the packing envelope.</li> </ul>  <p>The shipper is now ready for pick-up by the courier.</p>	Clinical Site

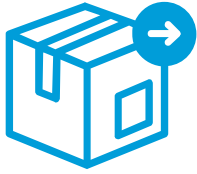
## 5.4 Courier Pick Up of the Packed CREDO CUBE Shipper

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 apheresis material at <b>agreed local time</b> for delivery to the CPC.	Sponsor
	<p><b>IMPORTANT</b> Notify CSOM via email <a href="mailto:Central.Scheduling@ITS.JNJ.com">Central.Scheduling@ITS.JNJ.com</a> if the packed Credo Cube will not be ready for pick-up by the courier by agreed local time.</p> <p>Should the pickup time be delayed, alternate plans may need to be implemented based on flight or ground transportation constraints.</p>	Clinical Site

	<b>COC/COI ACTIONS:</b>	Responsibility
	Complete the Site Shipment Form for Chain of Custody/Chain of Identity Form (see NA_SHIP_APH)	Clinical Site
	Upload a signed copy of this form to the MBOX on the same day.	Clinical Site

# MODULE 5 COMPLETED

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0



## Module 6:

# Receipt and Storage of the Investigational Product

**Version: 5.0**

**Date: 12-APR-2024**

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

## **Module 6: Table of Contents**

- 6.1 Communication Plan with Site, Courier & Sponsor**
- 6.2 Review of Packing Materials**
- 6.3 Receipt of the LN<sub>2</sub> shipper containing Investigational Product**
- 6.4 Unpacking and Storage of Investigational Product**
- 6.5 Prepare of Empty LN<sub>2</sub> Shipper for Shipment**
- 6.6 Storage and Monitoring of IP**
- 6.7 Problems and Special Situations**

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

## 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
06 Mar 2023	Module 6	Removed references to Vineti
	6.1.4	Deleted reference to courier phone call
	6.2.3	Added QR code to list to check prior opening box
	6.3.6	Added instruction for how and when to use QR code. Included pictures of QR code
	6.4.5	Added instructions for handling cassette and IP bag on receipt
12-APR-2024	6.1	Minor wording update to the type of shipments expected
	6.1.2	Further specified the courier companies per region
	6.1.6	Added courier responsibility
	6.2.2, 6.3.4, 6.4.1, 6.4.6	Updated wording to reflect that either certificate or compliance or CAR-T Final Release Form will be included with IP shipment documentation.
	6.2, 6.3	Removed references to obsolete videos

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

	6.3.5	Updated pictures
	6.4.2, 6.4.4, 6.4.7	Added instructions to unpack multiple cassettes
	6.4.5	Clarified the requirement to inspect both cassettes and IP bags
	6.4	Updated wording for MBOX system & COC/COI Actions table
	6.6	Consolidated IP warning and storage requirements Clarified documentation requirements for cryopreserved IP transport


<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

## 6.1 Communication Plan with Site, Courier & Sponsor

The IP shipment procedure involves two steps:

1. Shipment of IP from manufacturing facility to the site
2. Shipment of empty LN<sub>2</sub> shipper back to sponsor (for recharge/reuse).


If a situation falls outside of the shipments listed below, or the shipments related to the receipt of IP, notify CSOM via [Central.Scheduling@ITS.JNJ.com](mailto:Central.Scheduling@ITS.JNJ.com) and copy the SM for further instructions.

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 <a href="mailto:Central.Scheduling@its.jnj.com">Central.Scheduling@its.jnj.com</a> 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 delivery once the IP has been released from manufacturing quality.	Sponsor
6.1.3	The courier will issue an automated pre-alert/order confirmation to the site. <ul style="list-style-type: none"> <li>• The notification will reference the subject number and the AWB number to track and trace the shipment.</li> </ul> <p><b>NOTE: A print-out of the same AWB will be provided in the consignee kit pouch within the shipper.</b></p>	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: <ul style="list-style-type: none"> <li>• The day of delivery, within 1 hour prior to delivery. This is a geofence notification and will trigger when the shipment is within a 5-mile radius of the clinical site.</li> <li>• <b>NOTE:</b> The site or the sponsor local team does not have access to the EVO-IS system temperature data.</li> <li>• Any delays in shipment date will be communicated by the courier via e-mail to the designated site contact.</li> </ul>	Sponsor/ Courier
6.1.5	The shipper will arrive at the site at the agreed local time for the receipt of the IP.	Courier
6.1.6	The sponsor will coordinate with the courier to pick up the empty shipper at the agreed local time.	Sponsor/ Courier
	<b>IMPORTANT! Notify the CSOM via <a href="mailto:Central.Scheduling@ITS.JNJ.com">Central.Scheduling@ITS.JNJ.com</a> and copy the SM 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.</b>	Clinical Site




## 6.2 Review of Packing Materials

This section describes the materials required for unpacking IP.



Review of packing materials		
Step	Task	Responsibility
6.2.1	<p>Upon receipt of the IP, check to ensure all necessary contents and packaging materials are present.</p> <p>As a reminder, the following tools should be utilized in preparation for site unpacking of LN<sub>2</sub> shipper:</p> <ul style="list-style-type: none"> <li>• Cryogloves</li> <li>• Safety glasses</li> <li>• <b>Wire cutters (these are NOT included in the shipment).</b></li> </ul> <p> <b>NOTE: Adhere to any additional site requirements for PPE when handling cryopreserved products and equipment.</b></p> <p><b>Do not discard any contents or packaging materials until you have read these instructions.</b></p>	Clinical Site
6.2.2	<p>Upon the receipt of the shipper, you will find the following components inside the outer shipper case:</p> <ul style="list-style-type: none"> <li>• <b>LN<sub>2</sub> shipper</b> (Savsu DV-10)</li> <li>• <b>Consignee Kit pouch</b> (inside the pouch within the shipper case)</li> <li>• Certificate of Compliance or CAR-T Final Release Form</li> <li>• Cassette rack with IP: located inside of LN<sub>2</sub> shipper, secured with red tamper evident seal and wire (can be verified once LN<sub>2</sub> shipper is opened).</li> </ul> <p>The <b>consignee kit pouch</b> includes:</p> <ul style="list-style-type: none"> <li>• Materials used by the site when shipping the empty LN<sub>2</sub> shipper: <ul style="list-style-type: none"> <li>• 1 zip tie (for use on the outer shipper case). A back-up zip tie will be included.</li> <li>• AWB for return shipment of empty shipper</li> </ul> </li> </ul>	Clinical Site




## Review of packing materials

Step	Task	Responsibility
6.2.3	<p><b>NOTIFY CSOM via <a href="mailto:Central.Scheduling@ITS.JNJ.com">Central.Scheduling@ITS.JNJ.com</a> and cc the SM IF:</b></p> <ul style="list-style-type: none"> <li>The shipping container case is not secured.</li> <li>The zip tie is missing from the outer case lid.</li> <li>The subject number listed on the AWB does not match the intended subject.</li> <li>The EVO-IS ID (last 4 digits) listed on the AWB does not match the LN<sub>2</sub> shipper.</li> <li>The tamper evident seal number (SEAL#) listed on the AWB does not match the tamper seal on the shipper lid.</li> <li>Any contents are missing from the consignee kit pouch listed above.</li> <li>There is a flashing alarm indicating the temperature is out of range on the display.</li> <li>The temperature light indicator is not functioning.</li> <li>The temperature is unable to be confirmed using the QR code on the LN<sub>2</sub> shipper lid when the temperature light indicator is not functioning.</li> </ul> <p style="text-align: center;"><b>Shipping Container and Components</b></p> 	Clinical Site

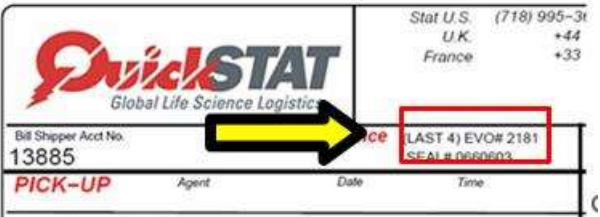


## 6.3 Receipt of the LN<sub>2</sub> Shipper Containing Investigational Product

This section outlines step-by-step instructions for receipt of the packed LN<sub>2</sub> shipper containing IP.

Receipt of the LN <sub>2</sub> shipper containing IP		
Step	Task	Responsibility
6.3.1	<p>The shipper will arrive inside an outer corrugated case. The outer corrugated case includes wheels and luggage handle for ease of transport.</p> <ul style="list-style-type: none"> <li>Prior to unpacking, make sure the confirmation of the IP lot number from IRT is available. If not available, contact site coordinator and request a copy before moving to the next steps.</li> <li>Once the shipper has been transported to the appropriate unpackaging location, set the shipper upright and lower the luggage handle.</li> <li>Remove the AWB and check the subject number matches the confirmation from IRT</li> </ul> 	Clinical Site
6.3.2	<p>The outer corrugated case is secured by buckle straps.</p> <ul style="list-style-type: none"> <li>Unclip the buckle straps. Open the outer corrugated case lid.</li> </ul> 	Clinical Site

Receipt of the LN <sub>2</sub> shipper containing IP		
Step	Task	Responsibility
6.3.3	<p>The outer case shipper lid is secured by a single zip tie through the zipper pulls.</p> <ul style="list-style-type: none"> <li>Cut and discard the zip tie then unzip the outer case lid.</li> </ul> <p><b>NOTE: The site will need to use wire cutters (these are NOT included in the shipment)</b></p> 	Clinical Site
6.3.4	<p>Lift the outer shipper case lid.</p> <ul style="list-style-type: none"> <li>Remove and verify that the pouch within the outer case contains the consignee kit pouch. The pouch contains: <ul style="list-style-type: none"> <li>Shipper label(s)</li> <li>One (1) zip-tie to secure the outer shipper lid prior to return.</li> <li>AWB use to return the empty LN<sub>2</sub> shipper.</li> <li>Certificate of Compliance or CAR-T Final Release Form</li> </ul> </li> <li>Take out materials from the consignee kit pouch.</li> </ul> <div style="display: flex; justify-content: space-around;"> <div style="text-align: center;"> <p><b>Pouch within outer case</b></p>  </div> <div style="text-align: center;"> <p><b>Consignee kit pouch</b></p>  </div> </div>	Clinical Site

## Receipt of the LN<sub>2</sub> shipper containing IP

Step	Task	Responsibility
<b>6.3.5</b>	<p>Verify that the EVO-IS ID number (last 4 digits) on the AWB matches the EVO-IS ID number on the LN<sub>2</sub> shipper lid. Examples below:</p> <p style="text-align: center;"><b>QuickSTAT AWB</b></p>  <p style="text-align: center;"><b>World Courier AWB</b></p>  <p style="text-align: center;"><b>EVO-IS ID number location</b></p> 	Clinical Site

**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. A **steady light** indicates that the temperature is within range. **You can proceed to the next steps.**
  - A **flashing light** indicates a temperature excursion has occurred. You can proceed to unpack the IP and follow the instructions outlined in Section 6.7 Problems and Special Situations for temperature excursion reporting guidance.
  - If **no light is present**, scan QR code on DV-10 lid with a smart device. Scanning the QR code will direct the user to a web page that displays the last reported payload temperature with the last recorded temperature reading. This QR code should only be used as a BACK UP solution in case the light indicator fails.
- NOTE:** The QR code label and the QR code displayed on the web page are correlated with the EVO-IS ID. Verify that the EVO-IS ID on the web page display exactly matches the QR code label ID and EVO-IS ID on the DV-10 lid. Confirm on the QR code temperature snapshot display that the time stamp is current.
- If any of the following occurs, remove the IP from the LN<sub>2</sub> shipper, place in the proper storage condition, and notify CSOM via [Central.Scheduling@ITS.JNJ.com](mailto:Central.Scheduling@ITS.JNJ.com) and copy the SM:
    - A flashing light indicating a temperature excursion has occurred.
    - Temperature light indicator is not functioning (does not turn on)
    - There is any ID mismatch, concerns regarding the QR code, and/or an out-of-range temperature

Clinical Site

**Press Indicator**



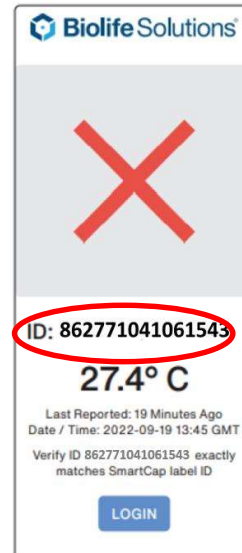
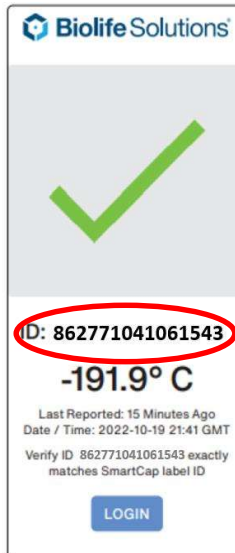
**Light Indicator**




Example of QR code and web page display:



Verify ID number matches the displayed ID number.





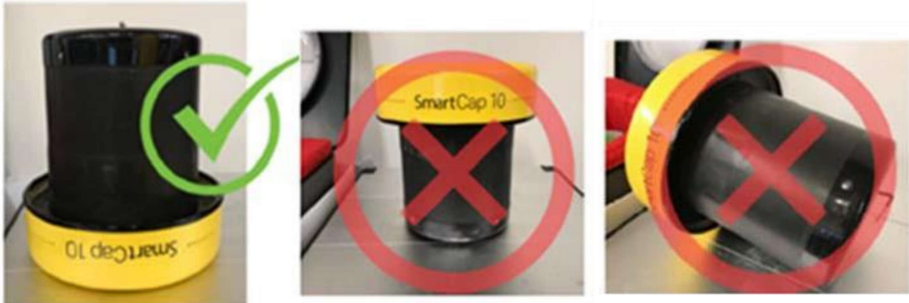

Receipt of the LN <sub>2</sub> shipper containing IP		
Step	Task	Responsibility
6.3.7	Verify the tamper evident seal number (SEAL#) listed on the AWB matches the tamper evident seal number located on the LN <sub>2</sub> shipper lid. <div style="text-align: center; margin: 10px 0;">  </div>	Clinical Site

## 6.4 Unpacking and Storage of Investigational Product

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



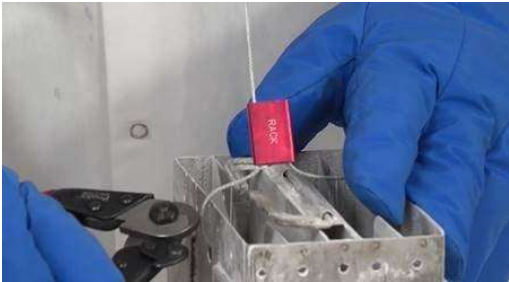

**REMINDER:** Ensure all necessary PPE is used before the next steps. Also, ensure that the COC/COI form is available for reference and completion.

**IMPORTANT:** IP must be placed into storage immediately following removal from the LN<sub>2</sub> and verification of COC/ COI.



Unpacking and Storage of IP		
Step	Task	Responsibility
6.4.1	<ul style="list-style-type: none"> <li>Make sure the following documents are available to conduct COC/COI checks:               <ul style="list-style-type: none"> <li>Certificate of Compliance or CAR-T Final Release Form</li> <li>Confirmation of the IP lot number from IRT</li> </ul> </li> <li>Cut and discard the zip tie and tamper seal on the shipper lid so it can be opened when necessary.</li> </ul> <p><b>NOTE:</b> The site will need to use wire cutters (these are NOT included in the shipment).</p> 	Clinical Site
	<p><b>NOTE:</b> Proper placement of the DV10 Smart Cap when not seated in the dewar body is <b>PROBE SIDE UP</b> on a flat surface. Serious damage to the probe may occur if placed otherwise.</p> 	Clinical Site
	<p><b>IMPORTANT:</b> Next steps below need to be performed as quickly as possible. It is critical to pack the cassette(s) into the LN<sub>2</sub> freezer quickly to avoid thawing of the IP.</p>	Clinical Site
6.4.2	<ul style="list-style-type: none"> <li>Remove the shipper lid and lift the cassette rack.</li> </ul>	Clinical Site





## Unpacking and Storage of IP

Step	Task	Responsibility
	<ul style="list-style-type: none"> <li>As soon the rack containing IP cassette(s) is pulled out of the shipper; start the timer to monitor IP exposure to room temperature for each cassette.</li> <li>Ensure the exposure time does not exceed 3 mins. The timer will be stopped when each cassette is placed in the vapor phase of LN<sub>2</sub>.</li> </ul> <div style="display: flex; justify-content: space-around; margin: 10px 0;">   </div> <p>Close the shipper lid once the rack is removed.</p>	
<b>6.4.3</b>	<p>Using a wire cutter:</p> <ul style="list-style-type: none"> <li>Cut and discard the tamper evident seal wire (labeled RACK) on the cassette rack.</li> </ul> <div style="text-align: center; margin: 10px 0;">  </div> <ul style="list-style-type: none"> <li>Remove dunnage located on top of the envelope within the cassette rack.</li> </ul> <div style="text-align: center; margin: 10px 0;">  </div>	Clinical Site




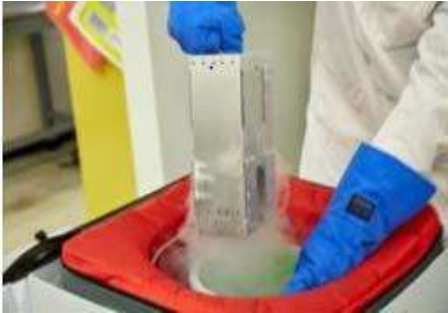

## Unpacking and Storage of IP




Step	Task	Responsibility
6.4.4	<ul style="list-style-type: none"> <li>Remove the cryogenic containment envelope pouch containing one IP cassette from the rack slots.</li> </ul>  <p><b>NOTE:</b> In case of multiple IP cassettes packed in the same shipper/rack: Immediately reinsert the rack with remaining cassettes back into the LN2 shipper and close the lid of the LN2 shipper.</p> <p>The lid of LN2 shipper uses a smart cap with built in thermocouple. When lid is removed the thermocouple warms up to ambient temperature. To avoid temperature excursions, secure lid back on shipper when multiple bags are being unpacked.</p> <ul style="list-style-type: none"> <li>Cut open the pouch and remove the cassette.</li> </ul> 	Clinical Site

Unpacking and Storage of IP		
Step	Task	Responsibility
6.4.5	<p><b>Prior to placing cassettes in LN<sub>2</sub> storage, each cassette and IP bag needs to be checked. Check the integrity &amp; label accuracy of each cassette and IP bag.</b></p> <ul style="list-style-type: none"> <li>When the cassette containing the IP bag is removed from vapor phase LN<sub>2</sub>, and is in the frozen state, the IP bag is brittle.</li> <li>It is very important to handle the cassette and IP bag with care to avoid damage.</li> <li>There are three (3) ports on the bag as shown below, which must be intact on receipt.</li> </ul> <div style="display: flex; justify-content: space-around; align-items: center;">   </div> <p><b>IMPORTANT: If there are any issues with the cassette or the IP bag notify the SM immediately and report a PQC.</b></p>	Clinical site

Unpacking and Storage of IP		
Step	Task	Responsibility
6.4.6	<p>Prior to placing the cassette into the site LN<sub>2</sub> storage, verify the following:</p> <p><b>Subject #</b> on <u>each bag and cassette label</u> matches the information on the:</p> <ul style="list-style-type: none"> <li>• AWB</li> <li>• IRT</li> <li>• Shipper label</li> <li>• Certificate of Compliance or CAR-T Final Release Form</li> </ul> <p><b>The unique identifier (DIN or Apheresis ID or SEC)</b> on <u>each bag and cassette label</u> matches the information on the:</p> <ul style="list-style-type: none"> <li>• IRT</li> <li>• Shipper label</li> <li>• Certificate of Compliance or CAR-T Final Release Form</li> </ul> <p><b>IP Lot #</b> on <u>each bag and cassette label</u> matches the information on the:</p> <ul style="list-style-type: none"> <li>• IRT</li> <li>• Shipper Label</li> <li>• Certificate of Compliance or CAR-T Final Release Form</li> </ul> <p><b>Note: IP cassette(s) should not be exposed to ambient temperature greater than 3 minutes.</b></p> <p><b>IMPORTANT: If 3 mins is exceeded, notify CSOM via Central.Scheduling@ITS.JNJ.com and copy the SM.</b></p> <p>Please refer to Module 6, section 6.7 for instructions on reporting Temperature Out-of-Range (TOR) Events &amp; Quarantining.</p> <p>Complete the required COI/ COC form.</p>	Clinical Site



## Unpacking and Storage of IP


Step	Task	Responsibility
6.4.7	<div style="text-align: center; margin-bottom: 10px;">    </div> <p>Repeat steps 6.4.2, 6.4.4, 6.4.5, 6.4.6 with each subsequent IP cassette.</p> <ul style="list-style-type: none"> <li>Place the empty cassette rack into the shipper.</li> </ul> <div style="text-align: center; margin: 10px 0;">  </div> <ul style="list-style-type: none"> <li>Lower the shipper handle to allow for the closing of the shipper lid.</li> <li>Close the LN<sub>2</sub> shipper lid.</li> </ul> <div style="text-align: center; margin-top: 10px;">  </div>	Clinical Site

	<b>COC/COI ACTIONS:</b>	<b>Responsibility</b>
	Complete the IP Shipment Receipt Checklist for Site (see NA_REC)	Clinical Site
	Upload a signed copy of this form to MBOX on the same day.	Clinical Site

## 6.5 Prepare of Empty LN<sub>2</sub> 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 <sub>2</sub> Shipper for Shipment		
Step	Task	Responsibility
6.5.1	<ul style="list-style-type: none"> <li>Obtain the zip tie provided in the consignee kit pouch.</li> <li>Zip the outer case lid closed and secure by passing the single zip tie through the zipper pulls.</li> </ul>  <ul style="list-style-type: none"> <li>Fasten the lid of the outer corrugated case by fastening the buckle straps.</li> </ul> 	Clinical Site

<b>6.5.2</b>	<ul style="list-style-type: none"> <li>Place the AWB into the clear packing envelope for courier pick-up.</li> </ul>  <ul style="list-style-type: none"> <li>Discard all leftover materials and packaging per site disposal procedures.</li> </ul>	Clinical Site
	<p><b>REMINDER:</b> The sponsor will coordinate with the courier to pick up the empty LN<sub>2</sub> shipper from the site at the agreed local time.</p> <p>Notify CSOM via <a href="mailto:Central.Scheduling@ITS.JNJ.com">Central.Scheduling@ITS.JNJ.com</a> and copy the SM immediately if there are any constraints for getting this shipment ready for agreed local time.</p>	Clinical Site



Johnson & Johnson	Cell Therapy Product Procedures Manual		
	Document No.:	TV-eFRM-13010	Version: 3.0

## 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.

### Warnings & Storage Requirements:

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

JNJ-68284528 (ciltacabtagene autoleucl) must be kept frozen at  $\leq -120^{\circ}\text{C}$  vapor phase of liquid nitrogen. For frozen IP, maintenance records for the liquid nitrogen storage system must be available for sponsor review.

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.

When the cassette containing the IP bag is removed from the vapor phase LN2 temperature and is in the frozen state, the IP bag can be brittle. It is very important to handle the cassette and IP bag with care to avoid damage.

**IP cassette(s) should not be exposed to ambient temperature greater than 3 minutes.**

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

### Storage

#### Storage Temperature Monitoring of IP

The use of a temperature monitoring device is required for the storage of all IP. Temperature conditions during on-site storage must be continuously monitored and recorded (e.g., temperature logs or data, charts or graphs from temperature monitoring equipment or devices). If not continuous (e.g., constant), the data recording interval of the temperature monitoring device should be less than or equal to 4 hours.

All temperature data and documentation must be retained in accordance with the records retention policy outlined in the Protocol and Clinical Trial Agreement, and applicable legal and regulatory requirements.

#### Transport Temperature Monitoring of IP

In addition to complying with all warnings and requirements outlined above during any transport of Cryopreserved IP; the following must be documented:

- Time of removal of IP from storage
- Temperature during transport of IP from the storage location to the administration site; or at the minimum temperature upon removal of cassette from transport equipment.

#### 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.

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 SM 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 LN<sub>2</sub> storage system.

Johnson & Johnson	Cell Therapy Product Procedures Manual		
	Document No.:	TV-eFRM-13010	Version: 3.0

### **Storage temperature monitoring with a site's own monitoring equipment**

In order 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. If the frequency of calibration is not specified, the device must be calibrated at least annually. Calibration and maintenance documentation for the LN<sub>2</sub> storage system must be filed and made available for review.

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 SM 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 & Relocation of IP**

When the equipment (LN<sub>2</sub> storage system) used to store or the equipment used to monitor the 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 SM 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) necessitating the temporary movement of IP.

### **Preparation, Dispensing and Administration of IP**

See the Protocol, Investigators Brochure, and 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 local guidelines and standard procedures for preparation of IP in alignment with sponsor instructions.

It is best practice for two qualified staff members to be involved whenever the IP is prepared; one to prepare the IP and the other staff member to verify. Guidance on the use of sponsor provided or site provided ancillary supplies in the IPPI.

Johnson&Johnson	Cell Therapy Product Procedures Manual		
	Document No.:	TV-eFRM-13010	Version: 3.0

## 6.7 Problems and Special Situations

This section applies to both LN<sub>2</sub> shipping container and site's LN<sub>2</sub> storage TORs.

### Problems and Special Situations

#### Temperature Out-of-Range (TOR) Events

Immediately upon discovery of a TOR 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<sub>2</sub> storage following the instructions provided in the Shipping section above.
- Immediately notify CSOM via [Central.Scheduling@ITS.JNJ.com](mailto:Central.Scheduling@ITS.JNJ.com) and copy the site manager of the TOR and discuss the potential impact, providing them with the last 4 digits of the EVO-IS # and the 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<sub>2</sub> 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 relevant section 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 no 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 the 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.

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	Document No.:	TV-eFRM-13010	Version: 3.0

## 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<sub>2</sub> 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<sub>2</sub> storage system and await instructions on return to sponsor.

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

## 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)**

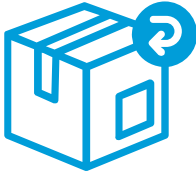
Do not dispense the IP to a subject if there is a concern about the quality of the product.

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 within 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

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0



## Module 7:

# Return and On-site Destruction of IP

**Version: 5.0**

**Date: 12-APR-2024**

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

# Module 7: Table of Contents

## Return

**7.1 Communication Plan with Site, Courier and Sponsor**

**7.2 Review of Packing Materials**

**7.3 Instructions for Receipt of Empty LN<sub>2</sub> Shipper**

**7.4 Packing of Investigational Product into LN<sub>2</sub> Shipper**

**7.5 Discontinuing or Withdrawing a Subject from Investigational Product**

## Destruction

**7.6 On-Site Destruction of Investigational Product**

## 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 IRT 'subject information'
10-Mar-2022	7.2.2, 7.3.4, 7.4.8, 7.4.10, 7.7	Updated step to include new packing materials Removed section as not applicable to BCMA CAR-T
28-Mar-2022	Module 7 7.6.1	Formatting and administrative changes Updated step to clarify CAR-T IP destruction process
06-Mar-2023	7.1.3 7.2.2, 7.3.4, 7.4.2, 7.4.5, 7.4.8 7.2.3 7.3.6 7.5	Change the geofence to 5 miles Removed 3-piece packing solution Added when to use QR code Added instructions for how and when to use QR code Moved to module 6 information about Discontinuing or Withdrawing a Subject from Investigational Product
12-APR-2024	7.3.4, 7.3.5, 7.3.7, 7.4.3 7.3.6 7.4.2 7.6.2 7.2, 7.3, 7.4 7.4, 7.6	Updated pictures Added recommendation to verify time stamp on web page when using QR code Added details on shipping materials expected Clarified documentation requirements prior to on-site destruction Removed references to obsolete videos Updated wording for MBOX system & responsibility




Johnson&Johnson	Cell Therapy Product Procedures Manual		
	Document No.:	TV-eFRM-13010	Version: 3.0


## 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<sub>2</sub> 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	<p>The courier will issue an automated pre-alert/order confirmation to the site.</p> <ul style="list-style-type: none"> <li>• The notification will reference the subject number to track and trace the shipment from clinical site to the sponsor.</li> <li>• The notification will also reference the AWB for the shipment. <b>NOTE:</b> a print-out of the same AWB will be provided in the shipper kit pouch within the shipper.</li> </ul>	Courier
7.1.3	<p>The courier will send one notification to the clinical site contact(s) prior to delivery of the empty charged shipper. The notification will be:</p> <ul style="list-style-type: none"> <li>• The day of delivery, within 1 hour prior to delivery. This geofence notification will trigger when the shipment is within a 5-mile radius of the clinical site.</li> <li>• <b>NOTE:</b> The site or the sponsor's local team do not have access to the EVO-IS system</li> <li>• Any delays in shipment date will be communicated by the courier via e- mail or phone call to the designated site contact.</li> </ul>	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
	<b>IMPORTANT:</b> Notify CSOM via <a href="mailto:Central.Scheduling@ITS.JNJ.com">Central.Scheduling@ITS.JNJ.com</a> and copy the SM if the packed shipper will not be ready for pick-up by the courier by agreed local time.	Clinical Site

## 7.2 Review of Packing Materials



Review of Packing Materials		
Step	Task	Responsibility
7.2.1	<p>The following tools should be utilized in preparation for site packing and unpacking of the LN<sub>2</sub> shipper:</p> <ul style="list-style-type: none"> <li>• Cryogloves</li> <li>• Safety glasses</li> <li>• Wire cutter</li> <li>• <b>NOTE: The site will need to use wire cutters (these are NOT included in the shipment).</b></li> </ul> <p> <b>NOTE: Adhere to any additional site requirements for PPE when handling cryopreserved apheresis products and equipment.</b></p> <p><b>Do not discard any contents or packaging materials until you have read these instructions.</b></p>	Clinical Site
7.2.2	<p>1-Piece Packing Solution: Cryogenic containment envelope pouch and foam dunnage</p> <p>Upon the receipt of shipper, you will find the following components inside the outer shipper case:</p> <ul style="list-style-type: none"> <li>• LN<sub>2</sub> shipper (Savsu DV-10)</li> <li>• shipper kit pouch (inside the pouch within the shipper case)</li> <li>• consignee kit pouch (inside the pouch within the shipper case)</li> </ul> <p>The shipper kit pouch is used when shipping IP back to the sponsor. The shipper kit pouch includes:</p> <ul style="list-style-type: none"> <li>• One (1) red tamper evident seal (for use on one side of the LN<sub>2</sub> shipper lid, number should match the AWB)</li> <li>• One (1) red tamper evident seal (for use on cassette rack)</li> <li>• One (1) zip tie (for use on the outer shipper case lid)</li> <li>• One (1) zip tie (for use on one side of the LN<sub>2</sub> shipper lid)</li> <li>• 1-Piece Packing Solution: Cryogenic containment envelope pouch and foam dunnage <ul style="list-style-type: none"> <li>• One (1) clear side packing envelope</li> <li>• AWB for the IP shipment</li> </ul> </li> </ul> <p>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.</p> <ul style="list-style-type: none"> <li>• One (1) zip tie (for use on the outer shipper case)</li> <li>• AWB for return shipment of empty shipper</li> </ul> <p><b>Inside the shipper</b>, there will be an empty cassette rack. This is used to store and secure the cassettes inside the shipper during transport.</p>	Clinical Site




## Review of Packing Materials

Step	Task	Responsibility
<b>7.2.3</b>  	<p><b>NOTIFY the CSOM via <a href="mailto:Central.Scheduling@ITS.JNJ.com">Central.Scheduling@ITS.JNJ.com</a> and copy the SM IF:</b></p> <ul style="list-style-type: none"> <li>The shipping container case is not secured.</li> <li>The zip tie is missing from the outer case lid.</li> <li>The subject number listed on the AWB does not match the intended subject.</li> <li>The EVO-IS ID (last 4 digits) listed on the AWB does not match the LN<sub>2</sub> shipper.</li> <li>Any contents are missing or incorrect from the shipper kit pouch listed above.</li> <li>There is a flashing alarm indicating the temperature is out of range on the display.</li> <li>The temperature light indicator is not functioning.</li> <li>The temperature is unable to be confirmed using the QR code on the LN<sub>2</sub> shipper lid when the temperature light indicator is not functioning.</li> </ul> <p style="text-align: center;"><b>Example of Shipping Container and Components</b></p> 	Sponsor/ Clinical Site

### 7.3 Instructions for Receipt of Empty LN<sub>2</sub> Shipper

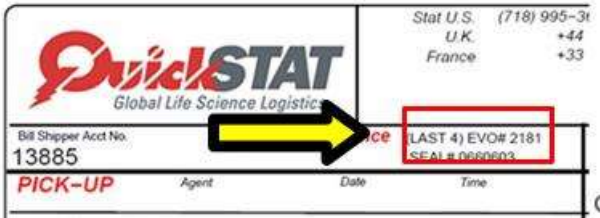
The following are step-by-step instructions for receipt of the empty LN<sub>2</sub> shipper in anticipation of packing of the IP.

Instructions for Receipt of the Empty LN <sub>2</sub> Shipper		
Step	Task	Responsibility
7.3.1	<p>The shipper will arrive inside an outer corrugated case. The outer corrugated case includes wheels and luggage handle for ease of transport.</p> <p>Once the shipper has been transported to the appropriate packaging location, set the shipper upright and lower the luggage handle.</p> 	Clinical Site
7.3.2	<p>The outer corrugated case is secured by buckle straps.</p> <ul style="list-style-type: none"> <li>• Unclip the buckle straps. Open the outer corrugated case lid.</li> <li>• The outer case shipper lid is secured by a single zip tie through the zipper pulls.</li> </ul> 	Clinical Site




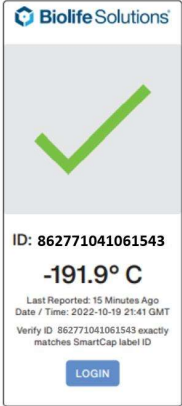
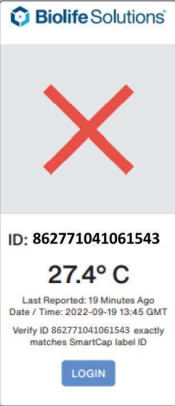
Instructions for Receipt of the Empty LN <sub>2</sub> Shipper		
Step	Task	Responsibility
7.3.3	<p>Cut and discard the zip tie then unzip the outer case lid.</p> <p><b>NOTE: The site will need to use wire cutters (these are NOT included in the shipment).</b></p> 	Clinical Site
7.3.4	<p>Lift the shipper case lid.</p> <ul style="list-style-type: none"> <li>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.</li> </ul> <p><b>Pouch within outer case:</b></p>  <ul style="list-style-type: none"> <li>Remove the shipper kit pouch and its materials including the foam dunnage. These materials will be used for packing the IP.</li> </ul>  <ul style="list-style-type: none"> <li>Leave the <u>consignee kit pouch</u> inside the pouch.</li> </ul>	Clinical Site

### Instructions for Receipt of the Empty LN<sub>2</sub> Shipper


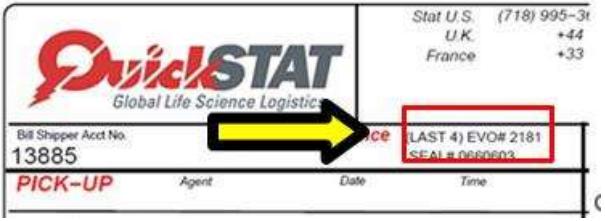

Step	Task	Responsibility
<b>7.3.5</b>	<p>Verify that the EVO-IS ID number (last 4 digits) on the AWB matches the EVO-IS ID number on the LN<sub>2</sub> shipper lid.</p> <p style="text-align: center;"><b>QuickSTAT AWB Example</b></p>  <p style="text-align: center;"><b>World Courier AWB Example</b></p>  <p style="text-align: center;"><b>EVO-IS ID number location</b></p> 	Clinical Site



## Instructions for Receipt of the Empty LN<sub>2</sub> Shipper

Step	Task	Responsibility
7.3.6	<p><b>Confirm if there is any temperature excursion:</b></p> <p>To determine if the temperature is within range, press the light indicator, release &amp; wait for 5 seconds on the DV-10 lid. The indicator will emit a light. A steady light indicates that the temperature is within range. You can proceed to the next steps.</p> <ul style="list-style-type: none"> <li>A flashing light indicates a temperature excursion has occurred.</li> <li>If no light is present, scan the QR code on DV-10 lid with a smart device. Scanning the QR code will direct the user to a web page that displays the last reported payload temperature with the last recorded temperature reading. This QR code should only be used as a BACK UP solution in case the light indicator fails.</li> </ul> <p><b>NOTE:</b> The QR code label and the QR code displayed on the web page are correlated with the EVO-IS ID. Verify that the EVO-IS ID on the web page display exactly matches the QR code label ID and EVO-IS ID on the DV-10 lid. Verify the time stamp on the web page display to confirm the temperature reading is recent.</p> <p>Notify CSOM via email <a href="mailto:Central.Scheduling@ITS.JNJ.com">Central.Scheduling@ITS.JNJ.com</a> and copy the SM immediately and do not continue if:</p> <ul style="list-style-type: none"> <li>A flashing light indicating a temperature excursion has occurred.</li> <li>Temperature light indicator is not functioning (does not turn on).</li> <li>There is any ID mismatch, concerns regarding the QR code, and/or an out-of-range temperature</li> </ul> <div style="display: flex; justify-content: space-around; margin-top: 10px;"> <div style="text-align: center;"> <p><b>Press Indicator</b></p>  </div> <div style="text-align: center;"> <p><b>Light Indicator</b></p>  </div> </div> <p style="margin-top: 10px;">Example of QR code and web page display:</p> <div style="display: flex; justify-content: space-around;"> <div style="text-align: center;">  <p style="font-size: 8px;">Verify ID number matches the displayed ID number.</p> </div> <div style="text-align: center;">  </div> <div style="text-align: center;">  </div> </div>	Clinical Site


### Instructions for Receipt of the Empty LN<sub>2</sub> Shipper


Step	Task	Responsibility
7.3.7	<p>Inside the shipper kit pouch, there are 2 tamper evident seals</p> <ul style="list-style-type: none"> <li>tamper evident seal with “SECURED” and serial number listed</li> <li>tamper evident seal with “RACK” listed</li> </ul> <div style="text-align: center; margin: 10px 0;">  </div> <p>Verify the tamper evident seal number (SEAL#) listed on the AWB matches the tamper evident seal from the shipper kit pouch.</p> <div style="text-align: center; margin: 10px 0;"> <p><b>QuickSTAT</b></p>  </div> <div style="text-align: center; margin: 10px 0;"> <p><b>World Courier</b></p>  </div>	Clinical Site



## 7.4 Packing of Investigational Product into LN<sub>2</sub> Shipper

In the following section there are step-by-step instructions for packing the IP into the LN<sub>2</sub> shipper. **REMINDER:** Ensure all necessary PPE is on before the next steps.




 The IP must be placed into the LN<sub>2</sub> shipper immediately following removal from the storage and verification of COC/COI.


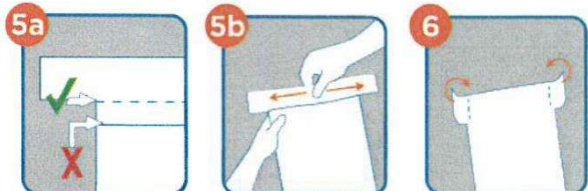
Packing of IP into LN <sub>2</sub> Shipper		
Step	Task	Responsibility
7.4.1	<p>Ensure that the following documents are available for reference and completion immediately after pack-out of the shipper.</p> <ol style="list-style-type: none"> <li>NA_RTN Site IP Return Shipment Form for Chain of Custody/ Chain of Identity</li> <li>Confirmation of the IP lot number from IRT</li> </ol>	Clinical Site
7.4.2	<p>Ensure all materials in the shipper kit pouch are removed and staged for the packing of the cassette:</p> <ul style="list-style-type: none"> <li>- AWB</li> <li>- Cryogenic containment envelope pouches (x3)</li> <li>- Foam dunnage (x3)</li> <li>- Zip ties (x2)</li> <li>- 2 Tamper evident seals: "RACK" &amp; a numbered seal</li> </ul> 	Clinical Site








**IMPORTANT:** The 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. Place all packing materials and shipper as close as possible.

## Packing of IP into LN<sub>2</sub> Shipper


Step	Task	Responsibility
7.4.3	<p>Remove the first cassette (with IP) from LN<sub>2</sub> storage.</p> <ul style="list-style-type: none"> <li>Prior to packing the cassette, verify that the subject number on the AWB and on the copy of the IRT matches the subject number on the cassette label.</li> <li>As a reminder, the AWB is inside the shipper kit pouch.</li> </ul> <p style="text-align: center;"><b>QuickSTAT AWB Example</b></p> <div style="text-align: center;">  <p>The image shows a QuickSTAT AWB form. At the top left is the QuickSTAT logo with the tagline 'Global Life Science Logistics'. To the right, it lists phone numbers for the U.S., U.K., and France. Below this, it includes 'Bill Shipper Acct No. 13885', 'Shippers Reference', and '(LAST 4) EVO# 2181'. A 'PICK-UP' section has columns for Agent, Date, and Time. The bottom section contains fields for Name, Address, and Subject #, with the Subject # field highlighted by a red box.</p> </div> <p style="text-align: center;"><b>World Courier AWB example</b></p> <div style="text-align: center;">  <p>The image shows a World Courier AWB form. It features the World Courier logo and 'AmerisourceBergen' branding. It includes 'ACCOUNT # 098765' and 'BILLING REFERENCE: Shipment Reference'. A 'FROM (SHIPPER)' section is present. The bottom section contains fields for Name, Address, and Subject #, with the Subject # field highlighted by a red box. At the very bottom, it says 'Finished Product UN3245 GMD 50mL'.</p> </div>	Clinical Site
7.4.4	<p>Complete Section 1 of the Site IP Return Shipment Form for Chain of Custody/Chain of Identity <b>NA_RTN</b>.</p> <p> This is completed prior to inserting the cassette (with IP) into the cassette rack and LN<sub>2</sub> shipper.</p>	Clinical Site

Packing of IP into LN <sub>2</sub> Shipper		
Step	Task	Responsibility
7.4.5	<p>1-piece packing (Cryogenic containment envelope pouch):</p> <ol style="list-style-type: none"> <li>Pre-fold over the scored line shown by the arrow. The pre-fold may fold over the adhesive seal cover.</li> <li>Insert the cassette with the locking hinge toward the top and push completely down past the adhesive seal into the cryogenic containment envelope pouch. Ensure the cassette is not behind the adhesive seal.</li> <li>Peel off adhesive strip cover on top flap.</li> <li>Peel off adhesive strip cover on the envelope pouch.</li> </ol>  <ol style="list-style-type: none"> <li> <ol style="list-style-type: none"> <li>Seal the cryogenic containment envelope pouch. Ensure to fold flap along pre-folded scored line.</li> <li>Start sealing from center of pre-fold and work out to the sides. Seal must not have any wrinkles or gaps.</li> </ol> </li> <li>Fold tabs around seal with pressure. Tabs must be sealed as close as possible to the envelope.</li> </ol> 	Clinical Site

7.4.6	<ul style="list-style-type: none"> <li>Remove the shipper lid and lift the cassette rack.</li> </ul> <div style="display: flex; justify-content: space-around;">   </div>	Clinical Site
7.4.7	<p><b>NOTE:</b> proper placement of the DV10 Smart Cap when not seated in the dewar body is <b>PROBE SIDE UP</b> on a flat surface. Serious damage to the probe may occur if placed otherwise.</p> <div style="display: flex; justify-content: space-around;">    </div>	Clinical Site

**7.4.8**

- Place sealed cryogenic containment envelope pouch with frozen bag inside the cassette into the cassette rack. Ensure proper orientation so the locking hinge of the cassette is at the top of the rack.



- Place one piece of the foam dunnage on top of the envelope within the cassette rack.






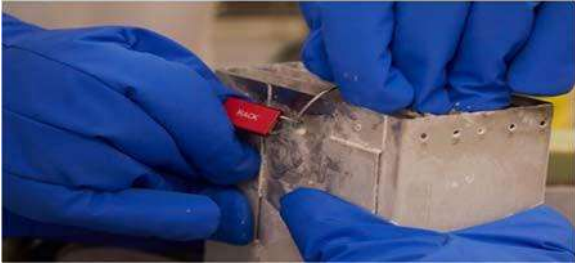



Clinical Site







**7.4.9**


- Return the rack into shipper to prevent warming and close the shipper lid.



Clinical Site




7.4.10	<div style="text-align: center;">    </div> <p>Repeat the packing process for any of the remaining cassettes to be shipped.</p>	Clinical Site
7.4.11	<p>After packing the final cassette:</p> <ul style="list-style-type: none"> <li>Secure the cassette rack with the tamper evident seal.</li> <li>Feed the tamper evident seal with “RACK” through the cassette holes and secure.</li> </ul> 	Clinical Site
7.4.12	<ul style="list-style-type: none"> <li>Remove the shipper lid and place the cassette rack (with IP) into the shipper.</li> <li>Close the shipper lid.</li> </ul>  	Clinical Site
7.4.13	<ul style="list-style-type: none"> <li>Secure the lid</li> <li>Lower the shipper handle</li> </ul> 	Clinical Site

<p><b>7.4.14</b></p> <ul style="list-style-type: none"> <li>• Feed the tamper evident seal that contains the word “<b>SECURED</b>” and seal number through the metal hook and lid.</li> </ul> <p>As a reminder, this seal number needs to match the seal number listed on the AWB.</p> <ul style="list-style-type: none"> <li>• On the other side of the shipper lid, wrap and secure a zip tie through the lid and around the handle.</li> </ul>	<div style="display: flex; justify-content: space-around;">   </div>	<p>Clinical Site</p>
<p><b>7.4.15</b></p> <p>Once the shipper lid is secured</p> <ul style="list-style-type: none"> <li>• Place the verified shipper label into the pouch.</li> </ul>	<div style="display: flex; justify-content: space-around;">   </div> <p><b>NOTE: Only the consignee kit pouch and the shipper label should remain inside the pouch within the shipper case.</b></p>	<p>Clinical Site</p>
<p><b>7.4.16</b></p> <ul style="list-style-type: none"> <li>• Close the outer shipper case lid and secure by passing the remaining zip tie through the zipper pulls.</li> <li>• Secure the outer corrugated case by clipping the buckle straps.</li> </ul>	<div style="display: flex; justify-content: space-around;">   </div>	<p>Clinical Site</p>

<b>7.4.17</b>	<ul style="list-style-type: none"> <li>Remove the existing AWB and place the new AWB (from the shipper kit pouch) into the clear packing envelope.</li> <li>If there is an additional shipper label place extra label with the new AWB into the clear packing envelope.</li> <li>Discard all leftover materials and packaging per site disposal procedures. Discard any remaining items and bags from shipper kit pouch.</li> </ul>	Clinical Site
		

**⚠️ REMINDER:** The sponsor will coordinate with the courier to pick up the LN<sub>2</sub> shipper packed with IP from the site at **agreed local time**.

Notify CSOM via email [Central.Scheduling@ITS.JNJ.com](mailto:Central.Scheduling@ITS.JNJ.com) and copy SM immediately if there are any constraints for getting this shipment ready by local agreed time.

	<b>COC/COI ACTIONS:</b>	Responsibility
	Complete the Return Chain of Custody/Chain of Identity Form (See NA_RTN)	<b>Clinical Site</b>
	On completion of the form, upload a signed copy of this form to MBOX on the same day.	<b>Clinical Site</b>



<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

## 7.5 Discontinuing or Withdrawing a Subject from Investigational Product

### Discontinuing or withdrawing a subject from study drug

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



See Protocol for information on retention of apheresis material 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  $\leq -120^{\circ}\text{C}$ . Contact the SM.

## 7.6 On-Site Destruction of Investigational Product

Any IP that is unused, assigned but not dispensed, expired, 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 <u>first IP destruction</u> at the site, the site must obtain approval from the sponsor. <ul style="list-style-type: none"> <li>Contact the SM and request approval for onsite CAR-T Investigational Product Destruction.</li> <li>If approval is obtained, proceed to step 7.6.2.</li> <li>If approval is denied proceed to section 7.1 for instructions on the return of IP.</li> </ul>	Sponsor/ Clinical Site
7.6.2	Ensure that the following documents are available for reference and completion before starting the destruction procedure. <ul style="list-style-type: none"> <li>Signed Investigational Product Destruction Questionnaire for Cell Therapy Products</li> <li>CAR-T IP On-Site Destruction Form</li> <li>Copy of the IRT notification containing the study subject number</li> </ul>	Clinical Site
7.6.3	Complete Page 1 of Form CAR-T IP On-Site Product Destruction Form. Obtain PI signature for destruction approval.	Clinical Site
7.6.4	Proceed to IP identification and destruction and complete page 2 of Form CAR-T IP On Site Product Destruction Form.  Follow institutional SOPs.  <b>NOTE:</b> Ensure all necessary PPE used before performing the procedure.	Clinical Site

	COC/COI ACTIONS:	Responsibility
	Complete the CAR-T IP On-Site Destruction Form.	Clinical Site
	Upload a signed COC/COI form to sponsor MBOX on the same day.	Clinical Site

# MODULE 7 COMPLETED

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0



# Module 8: COI/COC Maps & Forms

**Version: 5.0**

**Date: 12-APR-2024**

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

## **Module 8: Table of Contents**

- 8.1 Summary of Chain of Custody and Chain of Identity Documents**
- 8.2 Chain of Custody/Chain of Identity Forms**
- 8.3 Chain of Custody/Chain of Identity Cryo Forms**
- 8.4 Chain of Custody/Chain of Identity Maps**
- 8.5 Study/Region Specific Attachments**

## 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  <ul style="list-style-type: none"> <li>· USA and Vineti map updated to include the following regions North America/Latin America/Australia/Korea/Singapore</li> <li>· Additional Vineti maps added</li> <li>· New Saudi Arabia onsite cryopreservation map added</li> </ul>
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-FRM-57192
06-Mar-2023	8.6	Deleted this section related to Vineti maps
	8.1	Changes in wording to clarify instructions. Deleted mention of Vineti. Changed in wording to apheresis material
	8.2	Deleted description of the COC/COI form keeping form name. Deleted Vineti
	8.3	Deleted Central from the COC/COI forms description
	8.4	Deleted Local from the COC/COI forms description
	Module 8	Deleted maps for Vineti
12-APR-2024	8.1, 8.3	Replaced NA_APH and NA_TRN forms with new NA_APH-TRN form Updated name of NA_SHIP_APH form
	8.1, 8.2	Updated wording for MBOX system
	8.4	Revised to only specify the COC/COI forms used for on-site cryopreservation.
	8.5	Updated COC/COI maps
	8.6	Deleted previous section 8.6 Chain of Custody/Chain of Identity Central/Local Cryo TEMPLATE Section 8.7 became 8.6 as a result, with an updated attachment list

Johnson&Johnson	Cell Therapy Product Procedures Manual		
	Document No.:	TV-eFRM-13010	Version: 3.0

## 8.1 Summary of Chain of Custody and Chain of Identity Documents

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 IRT (refer to IRT manual): <ul style="list-style-type: none"> <li>Date of consent</li> </ul>	13-alphanumeric subject code is generated IRT notification email
Subject Randomized/enrolled	Site completes randomization/enrollment transaction per study design for the subject in IRT.	IRT notification email
Apheresis Collection	Site enters subject information into IRT on the day of apheresis, <b>as soon as unique identifier is assigned:</b> <ul style="list-style-type: none"> <li>Name</li> <li>DOB</li> <li>Unique identifier for apheresis (SEC-DIS or DIN or Apheresis ID)</li> <li>Weight in kg on day of apheresis (rounded to 1 decimal point)</li> </ul>	NA_APH-TRN
Transfer to shipment facility (for Shipment to CPC)	<ul style="list-style-type: none"> <li>If applicable: site transfers custody of the MNC, apheresis material to the cell lab or other department (referred to as "shipment facility") for packing and shipment to CPC.</li> <li>Site completes NA_APH-TRN and uploads the completed NA_APH-TRN form to MBOX on the same day.</li> </ul>	NA_APH-TRN
Shipment of cells: Site → CPC	<p>The site packs the apheresis material in CREDO CUBE shipper and sends to CPC:</p> <ul style="list-style-type: none"> <li>Site completes NA_SHIP_APH using the IRT notification and uploads the completed NA_SHIP_APH to the sponsor MBOX on the day of the shipment.</li> </ul> <p><b>NOTE: MNC, apheresis material must be stored at 2- 8 °C within 60 minutes of collection end time.</b></p>	NA_SHIP_APH
Receipt of IP: Manufacturing facility→site	<p>Site receives cryopreserved IP in LN<sub>2</sub> shipper from manufacturing facility and stores IP on-site in anticipation of dosing:</p> <ul style="list-style-type: none"> <li>Site completes NA_REC using the IRT notification and uploads to sponsor MBOX on the day of the receipt.</li> </ul>	NA_REC

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

## 8.2 Chain of Custody/Chain of Identity Forms

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

Sponsor COC/COI Form Number	Form Description	Form Name
TV-eFRM-10456	Apheresis Chain of Custody/Chain of Identity Form	NA_APH-TRN
TV-eFRM-10455	Site Shipment Form for Chain of Custody/Chain of Identity	NA_SHIP_APH
TV-eFRM-10449	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

<b>Johnson&amp;Johnson</b>	<b>Cell Therapy Product Procedures Manual</b>		
	Document No.:	TV-eFRM-13010	Version: 3.0

### 8.3 Chain of Custody/Chain of Identity Cryo Forms

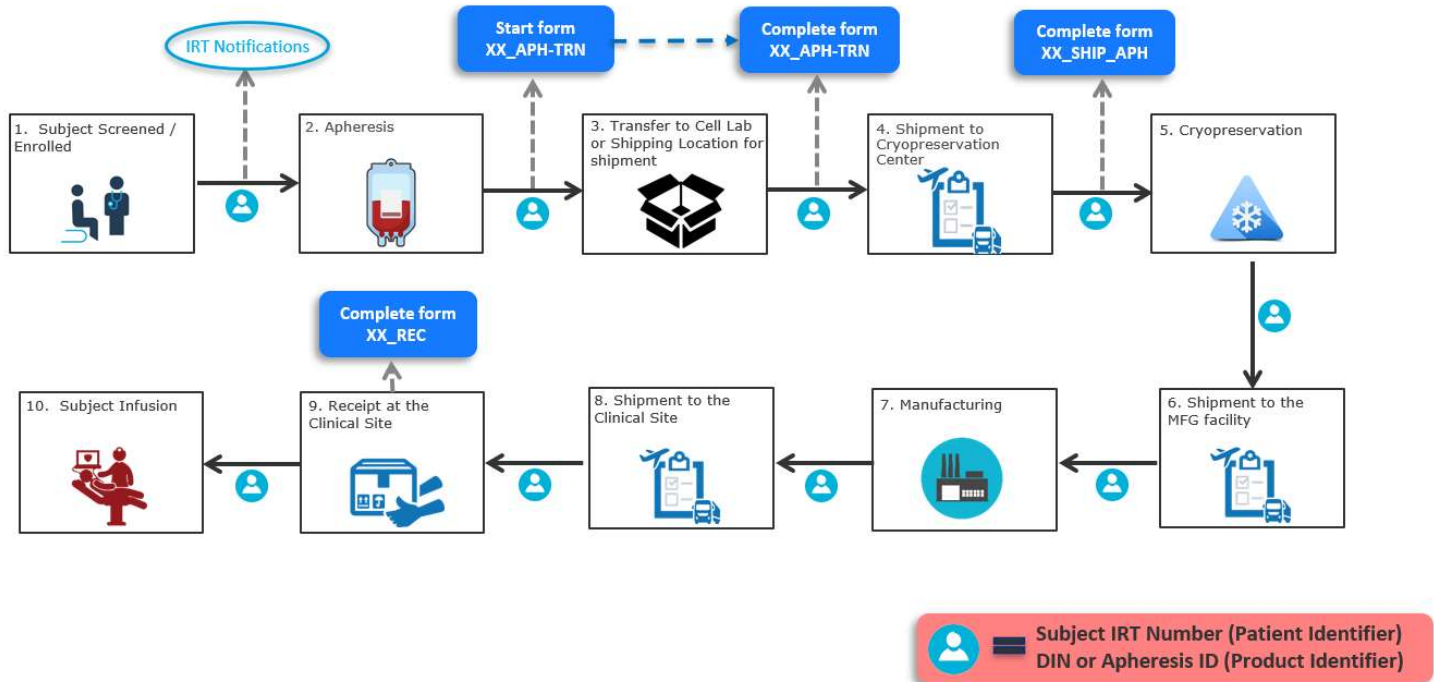
The table below provides an overview of the sponsor COC/COI form number, form description and CTPPM form name, for on-site cryopreservation. The COC/COI form naming convention will be used throughout the document to identify the COC/COI forms. COC/COI forms for your region can be found in your IP binder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

Sponsor COC/COI Form Number	Form Description	Form Name
TV-FRM-62994	Receipt of Apheresis Material (or MNC, Apheresis) and Cryopreservation at Cryopreservation Center	CRYO
TV-FRM-62995	Shipment of Cryopreserved Apheresis Material (or MNC, Apheresis Cryopreserved) at Cryopreservation Center	SHIP_CRYO

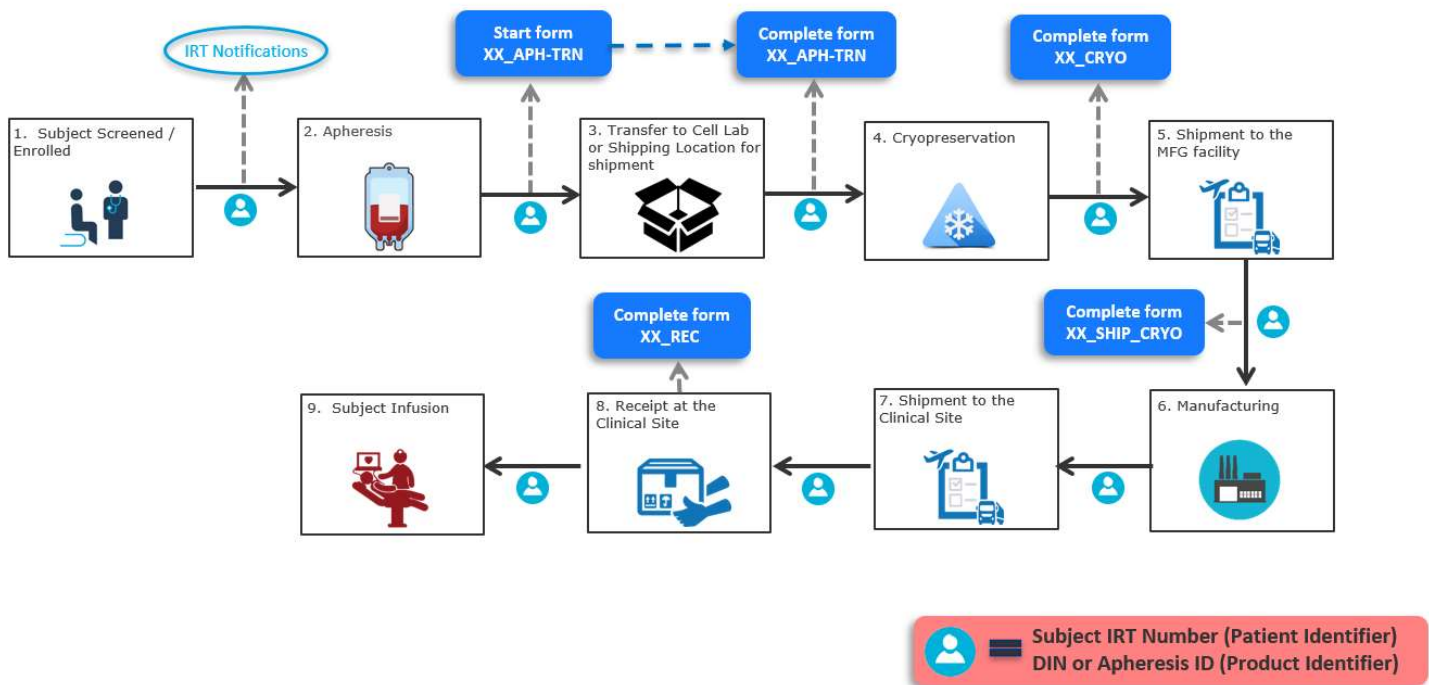


## 8.4 Chain of Custody/Chain of Identity Map – NA

**CENTRAL/External Cryopreservation: (see below)**



**On-site Cryopreservation: (see below)**



Johnson&Johnson	Cell Therapy Product Procedures Manual		
	Document No.:	TV-eFRM-13010	Version: 3.0

## 8.5 Study/Region Specific Attachments

Modified CTPPM procedures apply as outlined in the following memorandums:

- EMN28/68284528MMY3005 - Module 7
- 68284528SMM2001 Memorandum dated 21-APR-2023
- CLARIFICATION for J&J Innovative Medicine Cell Therapy Product Procedures Manual (CTPPM) Section 6.7 'Problems and Special Situations': Temperature Out of Range (TOR) Events.

**NOTE:** The above list is non-exhaustive as additional changes may be necessary prior to the next version update. The memorandums for your region/ study can be found in your IP binder and/ or the study portal. Contact your SM for a current complete list of memorandums.

# MODULE 8 COMPLETED