KYV-101 Cell Collection and Product Handling Manual

Investigational Product: KYV-101 (mivocabtagene autoleucel)

Confidentiality Statement

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1.0 PURPOSE

The purpose of this manual is to establish and detail the procedures for cellular starting material apheresis and cryopreservation, and handling of the KYV-101 Investigational Product (KYV-101 IP). This includes Mononuclear Cell (MNC) collection, cryopreservation and shipment, KYV-101 IP receipt, storage, thawing, handling and disposal/destruction. These procedures are designed to ensure consistency and compliance, taking precedence over institutional standard operating procedures (SOPs) and policies.

2.0 SCOPE

This manual applies to Kyverna Therapeutics Inc. (Kyverna) sponsored trials as well as non-Kyverna sponsored trials. This manual outlines the procedures for collection of cellular starting material via apheresis, cryopreservation, shipping of the starting material, and handling of the KYV-101 IP for infusion. The KYV-101 IP handling for Kyverna Therapeutics Inc. procedures apply to the relevant departments at the clinical site and take precedence over institutional SOPs and policies.

Out Of Scope: This manual is not intended to describe all steps that may be covered in local SOPs. Clinical decisions, patient eligibility, and medical management are governed by the clinical protocol and are outside the scope of this manual.

3.0 PRODUCT DESCRIPTION AND COMPOSITION

The Investigational Product (IP), KYV-101 (mivocabtagene autoleucel), is an autologous anti-CD19 Chimeric Antigen Receptor (CAR) T-cell immunotherapy. The anti-CD19 CAR in KYV-101 is composed of a human single-chain variable fragment (scFv) domain specific for CD19 antigen, CD8α hinge and transmembrane domain (CD8α hinge + TM), a CD28 co-stimulatory domain, and CD3-zeta intracellular signaling domains.

The KYV-101 IP is manufactured from autologous cryopreserved Total Nucleated Cells (TNC) that are obtained from the subjects via standard apheresis collection procedures. The finished product is filled into a CryoMACS freezing bag and stored at ≤ -150 °C, in the vapor phase of liquid nitrogen (LN_2). KYV-101 IP is provided in a single-dose unit containing anti-CD19 CAR+ viable T cells and is administered intravenously (IV) as a single infusion.

4.0 ABBREVIATIONS

Abbreviation	Definition
ALC	Absolute Lymphocyte Count
CAR	Chimeric Antigen Receptor
COC	Chain of Custody
COI	Chain of Identity
COS	Cell Orchestration System
DIN	Donor Identification Number
IDM	Infectious Disease Marker
IMP	Investigational Medicinal Product
IP	Investigational Product
ISBT	International Society of Blood Transfusion
ISF	Investigator Site File
IV	Intravenously
LN_2	Liquid Nitrogen
MNC	Mononuclear Cell
PI	Principal Investigator
QP	Qualified Person
SEC	Single European Code
SOP	Standard Operating Procedure
TNC	Total Nucleated Cell

5.0 DEFINITIONS

Term/Acronym	Definition/Meaning
Adverse Event	Any undesirable experience associated with the use of a medicine in a patient. Adverse events can range from mild to severe.

Term/Acronym	Definition/Meaning
Cell Center	A facility (or facilities) that participate in the collection, cryopreservation, and packing of the starting material. It may be part of the Clinical Site executing the clinical trial or a contracted vendor. This includes the Apheresis Facility and Cell Processing Laboratory.
Cell Orchestration System (COS)	A validated, web-based platform, used to track and manage the chain of identity (COI) and chain of custody (COC) for autologous cell therapies.
Clinical Site	A healthcare facility or location where clinical trials are conducted to evaluate the safety, efficacy, and overall performance of investigational drugs or medical treatments.
Chain of Custody (COC)	Permanent and auditable data capture of the custody of the cells at each hand-off, from the origin of cell collection through product administration. The data identifies the staff who handled the product, actions performed by those staff, and the location/date/time of those actions (i.e., who, what, when, where, and how).
Chain of Identity (COI)	The systematic process of maintaining accurate and continuous identification of a patient's biological material throughout the entire lifecycle of the drug product.
Donor Identification Number (DIN)	A 13-character code, compliant with International Society of Blood Transfusion (ISBT) 128 standards, which uniquely identifies a donation of blood or cellular therapy products.
Investigational (Medicinal) Product (IP/IMP)	A pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products with marketing authorization used in a way different from their approved form or indication.
Medical Monitor	The Sponsor medical physician representative responsible for the medical oversight of the drug product study.
Serious Adverse Event (SAE)	An untoward medical occurrence that, at any dose, results in death, is life-threatening, results in hospitalization (initial or prolonged), results in permanent disability or permanent damage, results in a congenital anomaly/birth defect, or is an important medical event.
Single European Code (SEC)	A 40-digit, alphanumeric, unique identifier applied to tissues and cells collected from and distributed in the European Union. This identifier consists of a Donation Identification sequence (SEC-DI), essentially indicating the origin of the tissue or cells, and a Product Identification sequence (SEC-PI), essentially classifying the type of tissue or cells.

Term/Acronym	Definition/Meaning
Sponsor	Kyverna Therapeutics, Inc. or outside institution conducting the trial.
Subject ID Number	A unique identifier assigned to each trial subject to protect the subject's identity.

6.0 CONTACTS

6.1 Reference Appendix 1 for a list of contacts for assistance with where to send documents, logistics, or general assistance.

7.0 MATERIALS AND EQUIPMENT

The following materials and equipment are provided by the Cell Center:

7.1 Anticoagulants per institutional SOP(s)

7.2 Apheresis Collection Instruments: Spectra Optia, Fresenius Kabi Amicus

NOTE: Other collection devices must have approval prior to use.

7.3 Apheresis Collection Kit per institutional SOP(s)

7.4 Apheresis Labels: International Society of Blood Transfusion (ISTB) 128 or Single European Code (SEC – for European Union (EU) only)

7.5 Cassettes

7.6 Controlled Rate Freezer

7.7 Cryobags

7.8 Cryobag/Cryovial/Cassette labels

7.9 Liquid Nitrogen (LN2) Dry Shipper (used for KYV-101 IP shipped by Kyverna)

7.10 Vapor Phase (LN2) Freezer (used for KYV-101 IP storage on-site)

7.11 Vapor phase LN2 shipper container or equivalent (used for transport of the KYV101 IP)

7.12 Cassette storage rack(s) that can hold cassette sizes of 19.2 cm x 15.3 cm x 1.2 cm (Cassette Model # CS250) or 16.0 cm x 9.2 cm x 1.2cm (Cassette Model # CS50)

7.13 KYV-101 IP thawing equipment (example: water bath or dry thaw)

8.0 DOCUMENTS AND FORMS

Name	Document Number	Description
Subject Identification Form	FOR-0000183	The primary source document used to capture the Subject ID. NOTE: This document is not applicable for non-Kyverna sponsored trials.
Kyverna Temperature Excursion Form	FOR-0000065	A form used to document any temperature excursion of the product during KYV-101 IP receipt or storage at the Clinical Site.
Kyverna Product Complaint Form	FOR-0000064	A form used to document product complaints regarding any inquiry about the product quality, strength, or identity of the IP.
KYV-101 Investigational Product (IP) Accountability Form	FOR-0000228	A form that is used to record thaw, infusion and disposition information of the investigational product at the Clinical Site. This form is not used in non-Kyverna sponsored trials.
Certificate of Compliance	FOR-0000085	A document accompanying the shipment confirming that the batch meets all GMP requirements and approved specifications for release.
Chain of Identity/Chain of Custody Form – Starting Material (Back-up form to be used in the event COS is not used or available)	FOR-0000113	A back-up form, in the event COS is not used or available, that accompanies the shipment that is used at the Clinical Site to document the inspection of the shipper after receipt through final processing and shipping of the cryopreserved starting material.
KYV-101 General Kyverna Apheresis Site Shipment Form (Back-up form to be used in the	FOR-0000119	A back-up form for non-Kyverna sponsored studies, in the event COS is not used or available, used to document any requested testing

Name	Document Number	Description
event COS is not used or available)		results and the quantity of cryobags and cryovials in the shipment.
Kyverna Apheresis Site Shipment Form (Back-up form to be used in the event COS is not used or available)	FOR-0000075	A back-up form, for Kyverna sponsored studies in the event COS is not used or available, used to document any requested testing results and the quantity of cryobags and cryovials in the shipment.
Chain of Identity/Chain of Custody Depot Investigational Product Record (Back-up form to be used in the event COS is not used or available)	FOR-0000112	Backup form in the event COS is not used or available that accompanies the shipment which is used at the Clinical Site to document the inspection of the shipper after receipt
Chain of Identity/Chain of Custody Standard Investigational Product Form (Back-up form to be used in the event COS is not used or available)	FOR-0000265	Backup form in the event COS is not used or available that accompanies the shipment which is used at the Clinical Site to document the inspection of the shipper after receipt

9.0 MNC APHERESIS, CRYOPRESERVATION, STORAGE AND SHIPMENT

NOTE: In the event COS is unavailable or not yet implemented at a cell center, complete documentation using FOR-0000113 (COI/COC Form – Starting Material) and FOR-0000075 (Apheresis Site Shipment Form) as alternate documentation methods/as a backup option.

9.1 Pre-Collection Activities

9.1.1 Upon patient consent, the site study coordinator schedules the apheresis MNC(A) collection date in coordination with apheresis personnel.

9.1.2 The site study coordinator submits FOR-0000183 (pre-filled and signed by Investigator) to apheresis personnel, as applicable.

NOTE: For non-Kyverna sponsored trials completion of FOR-0000183 is not required.

9.1.3 The study coordinator registers the patient and provides apheresis scheduling information in COS.

9.1.4 Schedule/coordinate the following subject testing activities prior to the MNC(A) collection:

9.1.4.1 If the timeframe of the collection is < 24 hours, then perform a Complete Blood Count (CBC) with automated differential and Absolute Lymphocyte Count (ALC).

NOTE: These results are "For Information Only."

9.1.4.2 **INFECTIOUS DISEASE MARKERS FOR US:** Per FDA 21 CFR 1271, Infectious Disease Markers (IDMs) are not required for autologous use.

9.1.4.3 **INFECTIOUS DISEASE MARKERS FOR Ex-US:** Adhere to all institutional and regional/national Infectious Disease Testing requirements as required.

9.1.5 All infectious disease testing, if performed, must be negative/non-reactive. If any screening test was reactive, verify that confirmatory testing was performed and is negative/non-reactive.

9.1.6 **For Ex-US**, record Infectious Disease Marker testing results in the Cell Orchestration System (COS), as applicable.

NOTE: Store all test results in the patient record at the Clinical Site.

9.1.7 Notify Kyverna Patient Operations of any test results or changes that have an impact on the already scheduled dates associated with these patient activities.

9.1.8 The Kyverna Logistics Coordinator sends confirmation of scheduled shipment dates to the Clinical Site and relevant parties. This information is typically sent 2-6 days prior to any collection.

9.2 MNC(A) Procedure

9.2.1 Confirm the subject identity following institutional procedures.

9.2.2 Confirm the subject meets all safety criteria according to the applicable study protocol requirements and institutional procedures.

9.2.2.1 If the subject meets all acceptance criteria, then proceed to next step.

9.2.2.2 If the subject does not meet all acceptance criteria, then **STOP** – Contact Kyverna Patient Operations immediately with details of the incident (refer to contact list in Appendix 1).

9.2.3 Obtain printed collection DIN/SEC labels and affix labels to the following:

- Subject Identification Form (FOR-0000183)
- Apheresis Collection Bag(s)
- Any required organizational procedure records

9.2.4 Perform vein assessment according to institutional procedures.

9.2.4.1 If collection will use peripheral venous access (preferred method), then prepare venipuncture site following institutional procedures and manage venipuncture process according to institutional procedures.

9.2.4.2 If central venous catheter is used, then prepare catheter according to institutional procedures.

9.2.5 Utilize the apheresis instrument's operating manual and institutional SOP(s) for guidance on initiating and monitoring the MNC(A) collection procedure. Observe the following Kyverna guidelines:

- Collection parameters should be set to focus on mononuclear cells and minimizing platelets, red blood cells, and other multi-nucleic cells.
- Do not add concurrent plasma to the starting material during the apheresis procedure.
- The total number of cells needed is $1 \times 10^9 – 2 \times 10^9$ TNC. Generally achieved with 2-3x Total Blood Volume or 10-15 Liters.
- Anticoagulant(s) must be added in sufficient quantities to prevent clumping per institutional SOP(s).
- Any Adverse Events (AE)/Serious Adverse Events (SAE) during the collection procedure must be reported in accordance with the associated study protocol.

9.3 Internal MNC(A) Transport and Storage

9.3.1 Complete the apheresis section information in COS and transport the cellular starting material, as soon as possible, to the Cell Processing Lab in accordance with Institutional SOP(s) for transport.

9.3.2 Receive the cellular starting material in accordance with institutional SOP(s).

9.3.3 Complete the COC for the cellular starting material in the COS.

9.3.4 Verify the Subject ID on the bag label matches the Subject ID in COS.

9.3.5 Visually inspect the product bag and seals for integrity.

9.3.6 Determine storage requirements for the cellular starting material:

- If cryopreservation is initiated < 4 hours from collection end time, then product may remain at room temperature.
- If cryopreservation is initiated > 4 hours from collection end time, then store product in monitored refrigerator at 2-8 °C.

  NOTE: Maximum refrigerated storage time is 24 hours from the end of collection.

9.4 Labeling

9.4.1 The cryopreserved, formulated product cryobags and cryovials must meet the following Kyverna requirements:

- The cryopreserved, formulated cryobags and cryovials must be labeled in compliance with ISBT 128 standards and/or Single European Code (SEC) standards, as well as any relevant center accreditation requirements.
- The entire SEC number is not required on the cryobag label; the SEC-DI is sufficient. If institutional procedure requires using entire SEC on labels, that is acceptable (EU only).
- Electronically printed labels are required. No handwritten labels are accepted.
- If printing capability is not available, then contact Kyverna Patient Operations for instructions (refer to contact list in Appendix 1).
- Labels must be directly affixed to cryobags and cryovials. Attached labels and/or partial labels require approval by Kyverna prior to use.
- Do not include subject name, initials, medical record number (MRN) or date of birth across any product labels or attached shipping/collection documentation shared with manufacturer, unless approved in advance by Kyverna.

  NOTE: If cassette labels are used, they need to be affixed to the cassette.

9.4.2 The cryovial label must include the following at minimum:

- Subject ID number (in the Recipient ID field, if using ISBT label template)

9.4.3 The cryobag label must include the following, at minimum (if size of label allows), additional requirements as listed below:

- Unique apheresis donation identification number (SEC-DI or DIN). DIN is only used if using ISBT compliant label, otherwise include SEC-DI.

- Subject ID number (in the Recipient ID field, if using ISBT label template)

9.4.4 If the cryobag labels are limited in size or text value, then supplementary attached shipping/collection documentation or affixed cassette labels must include:

- Unique apheresis donation identification number (SEC-DI or DIN). DIN is only used if using ISBT compliant label, otherwise include SEC-DI.
- Date of collection and end time
- Subject ID number (in the Recipient ID field, if using ISBT label template)
- Expiration date assigned according to institutional standard procedures
- Include the statements:
  - "For autologous use only"
  - "Not Evaluated for Infectious Substances" (for US only)
  - "For further processing"
  - "Do Not Irradiate"
  - "Do Not Use Leukoreduction Filters"

9.5 Testing

9.5.1 After formulation, obtain a sample for cell viability testing and process per institutional SOP(s). Formulated cell viability (after cryomedia addition) is preferred but pre-formulation viability is acceptable.

9.5.2 Utilizing the same sample, perform product total cell count per institutional SOP(s). For total cell count, use cells/mL x total volume in mL.

9.5.3 Obtain sterility samples and run sterility tests on formulated product (post-processed apheresis product with cryomedia added) per institutional SOP(s).

9.5.4 If the preliminary results indicate any growth, then **STOP** – Contact Kyverna Patient Operations immediately with details of the incident and submit the final report (along with any subculture results) to Kyverna Patient Operations immediately (refer to contact list in Appendix 1).

9.6 Processing and Cryopreservation

9.6.1 Utilize the institutional SOP(s) for guidance for the preparation, processing, and cryopreservation of the cellular starting material. Observe Kyverna guidelines as indicated in the following steps.

9.6.2 The target cell count for the post-processed formulated cell product is 1×10^9 – 2×10^9 TNC.

- If fewer than 1 x 10^9 total cells are collected, then fill the cells into one cryobag and contact Kyverna Patient Operations as a notification that there are fewer than 1 x 10^9 total cells that will be shipped.
- If more than 2 x 10^9 total cells are collected, then fill cells into two cryobags for cryopreservation and subsequent shipment to the manufacturer.

  NOTE: It is allowed to cryopreserve more than the target range per cryobag so fill all cells into two cryobags.

  NOTE: If any excess material remains, dispose per institutional SOP(s).

9.6.3 Split the collection into two (2) cryobags of near equal volume with a target range between 5 x 10^8 – 1 x 10^9 TNC in each cryobag and the maximum volume for each cryobag is ≤ 200 mL.

9.6.4 In total, fill three (3) cryovials (1.5 - 2.0 mL size) with 1 mL of formulated product in each cryovial. All three cryovials must be of the same size. No cell count target is required for the cryovials.

9.6.5 Ensure that all samples for product testing are obtained at the requested timepoints.

9.6.6 Use control rate freezing for the cryopreservation of the formulated product. **No dump freezing is allowed.**

9.6.7 After cryobags have been filled, seal the tubing so that the end of the tubing is as close as possible to the cryobag port.

9.6.8 Affix labels directly to the cryobags and cryovials prior to the start of freezing.

9.6.9 Complete any documentation per institutional SOP(s) and in the cryopreservation section of COS to capture the testing, processing, and cryopreservation steps.

9.7 Cryopreserved Starting Material Storage

9.7.1 Store cryopreserved material at ≤ -150 °C in vapor phase LN_2 per site institutional SOP(s).

9.7.2 Complete any documentation per institutional SOP(s).

9.8 Receipt of Dry Shipper

9.8.1 The empty dry shipper delivery arrives at the pick-up location at minimum one business day prior to the scheduled pick-up of the cryopreserved product.

NOTE: The dry shipper will arrive charged and will maintain an internal transport temperature of ≤ -150 °C for up to 10 days.

9.8.2 Notification emails are sent to designated Site Personnel to provide scheduled delivery date for dry shipper and includes a complete list of the accompanying dry shipper accessories and documentation.

9.8.3 Site Personnel will receive additional documentation for international shipments.

NOTE: Contact Kyverna for any country specific documentation required for shipments.

9.8.4 Inspect the dry shipper immediately upon receipt for any damage and or issues and verify all listed accessories are present:

- Do Not X-Ray Label
- 2 Cryovial Boxes w/insert
- ZIP Ties
- Cryostrap
- Safepak bag
- Serialized Tag

NOTE: Notify the Logistics Coordinator immediately of any found damage/issues or missing listed accessories.

9.9 **Packaging of the Dry Shipper**

9.9.1 Gather all dry shipper accessories. This will include (refer to Figure 1):

- Two (2) cryovial boxes
- One (1) Cryostrap
- One (1) Safepak bag
- One (1) Serialized Tag

9.9.2 Retrieve cryobags and cryovials following institutional procedures to verify Chain of Identity and minimize exposure to ambient conditions.

9.9.3 Complete the outgoing shipment COC in the COS once the process is executed.

9.9.4 Place all cryovials into one of the cryovial boxes. One box will remain empty.

9.9.5 Wrap the cassettes together with the provided cryostrap (refer to Figure 1).

NOTE: If only one bag was processed and is being shipped, the individual cassette must still be wrapped with the provided cryostrap.

Figure 1. Cassettes wrapped with cryostrap and placed in the Safepak

9.9.6 Place the wrapped cassette(s) vertically into the Safepak bag (refer to Figure1)

9.9.7 Place the cryovial boxes next to the cassette(s) so that the cassette(s) and cryovial boxes are all touching the bottom of the Safepak bag (refer to Figure 1).

NOTE: If Cryoport shipper is not used (e.g., DV10 is used), the cryovial boxes should be stacked, one on top of the other, in the Safepak. Only one box may be used if there are any space limitations.

9.9.8 Seal the Safepak bag and place into the dry shipper.

9.9.9 Close the dry shipper inner lid and use the Serialized Tag to secure and seal the inner lid.

9.9.10 Place the following document in the designated document retention location inside the shipper.

- Packing List (EU and UK only)

NOTE: In the event COS is unavailable or not yet implemented at a cell center, completed FOR-0000113 and FOR-0000075 must be included in the designated document retention location inside the shipper.

9.9.11 Close the outer lid and secure the latch with a zip tie.

9.10 Shipping of the Dry Shipper

9.10.1 Ensure all applicable sections in COS are completed prior to shipping of the cellular starting material.

9.10.2 For international shipments place applicable transport and customs documents into the external shipper pouch and provide electronic copies to the Logistics Coordinator.

NOTE: Contact Kyverna for any country specific documentation required for shipments.

9.10.3 Place the Shipper Label on the outer lid of the shipper, if applicable.

9.10.4 For all shipments, secure the external shipper lid and place the dry shipper in the facility's designated secure pick-up area.

9.10.5 Notify the Logistics Coordinator immediately if the dry shipper is not picked up on the designated date.

10.0 KYV-101 INVESTIGATIONAL PRODUCT RECEIPT AND STORAGE

NOTE: In the event COS is unavailable or not yet implemented at a cell center, complete documentation using FOR-0000112 (Chain of Identity/Chain of Custody Depot Investigational Product Record) or FOR-0000265 (Chain of Identity/Chain of Custody Standard Investigational Product Form) as alternate documentation methods/as a backup option.

10.1 General Considerations

10.1.1 Staff members participating in the clinical study and executing any steps in handling KYV-101 IP are required to be trained by Kyverna or appropriately trained staff at the Clinical Site prior to performing any study-related procedures.

10.1.2 Complete and submit FOR-0000064 for product complaints regarding any inquiry about the product quality, strength, or identity of KYV-101 IP. (Reference Appendix 1: Kyverna Contact List)

10.1.3 Always wear cryogenic gloves and other personal protective equipment per institutional procedure(s) while handling frozen KYV-101 IP.

10.1.4 KYV-101 IP can be manufactured and shipped in the following cassette sizes. If your Cell Center requires a cassette rack(s) to store the KYV-101 IP with these specific dimensions in your Vapor Phase (LN2) Freezer, contact Kyverna Patient Operations (Reference Appendix 1: Kyverna Contact List).

i. 19.2 cm x 15.3 cm x 1.2 cm (cassette model # CS250)

ii. 16.0 cm x 9.2 cm x 1.2 cm (cassette model # CS50)

10.2 Pre-shipment Activities

10.2.1 Kyverna Patient Operations informs the Clinical Site on successful product manufacturing and KYV-101 IP release and delivery date.

10.2.2 The Clinical Site (Investigator, Study Coordinator) schedules infusion for study subject and confirms delivery date in COS.

10.2.3 The Logistics Coordinator provides shipment details and the temperature tracking link to Cell Processing Laboratory via email.

10.3 Receipt of KYV-101 IP at the Site

10.3.1 Before receiving the LN2 Dry Shipper, obtain the following documents from the Study Coordinator and complete the execution of the process steps:

- Kyverna Temperature Excursion Form (FOR-0000065) (when applicable)
- Kyverna Product Complaint Form (FOR-0000064) (when applicable)

10.3.2 Receive LN2 Dry Shipper with KYV-101 IP from courier. Inspect the LN2 Dry Shipper for evidence of damage and ensure the serialized tag is present and intact and sign the waybill per the courier's instructions.

- If integrity issues are detected, then do not unload the LN2 Dry Shipper. Store the shipper in quarantine per institutional SOP and immediately contact the Logistics Coordinator (Reference Appendix 1: Kyverna Contact List)

10.3.3 Document the receipt, storage, and transfer of KYV-101 IP in the corresponding sections of the Cell Orchestration System (COS) during the execution of the process steps.

NOTE: For reporting temperature excursions, use Kyverna Temperature Excursion Form (FOR-0000065)

10.3.4 Remove the serialized tag and open the lid of the LN2 Dry Shipper

10.3.5 Remove the associated documents from the LN2 Dry Shipper:

- Certificate of Compliance (FOR-0000085)
- Certificate of Analysis
- IMP Certificate of Conformance (QP certification, as applicable)

NOTE: DO NOT open the LN2 Dry Shipper until the inspection of the shipper and temperature data have been reviewed.

10.3.6 Complete the incoming COC in the COS during the execution of the process steps.

10.3.7 Verify the temperature via the LN2 Dry Shipper temperature monitoring system to ensure the temperature was maintained at ≤-150°C during the shipment of KYV-101 IP.

- If temperature deviations are detected (warmer than ≤ -150°C), then complete the Temperature Excursion Form and send it to Kyverna Patient Operations immediately with the applicable supporting documentation (Reference Appendix 1: Kyverna Contact List) and wait for next steps from Kyverna Patient Operations.

NOTE: The Clinical Site must download a copy of the temperature report from the temperature monitoring system and file in the Investigator Site File (ISF)

10.4 Transfer and Intermediate Storage of KYV-101 IP at the Site

10.4.1 Cut the serialized tag from the LN2 Dry Shipper lid, open the LN2 Dry Shipper, and remove the KYV-101 IP.

10.4.2 Immediately verify the KYV-101 IP identifiers (Subject ID number and DIN/SEC-DI) on the cassette, KYV-101 IP bag label and across all other documentation against the Certificate of Compliance (FOR-0000085) over the Vapor Phase LN2 Freezer (if applicable) to maintain temperature of the KYV-101 IP.

NOTE: This inspection may expose the cryopreserved KYV-101 IP to ambient temperature for an extended period if the cassette and KYV-101 IP bag inspection is not performed at LN2 temperature levels; this may be detrimental to the KYV-101 IP. Unloading the KYV-101 IP from the LN2 Dry Shipper must be performed quickly to limit exposure to ambient temperatures.

NOTE: If mismatches in the Subject ID or Donor Identification are detected, place the KYV-101 IP into on-site LN2 freezer, quarantine per institutional procedures and contact Kyverna Patient Operations (Reference Appendix 1: Kyverna Contact List) and wait for next steps from Kyverna Patient Operations

10.4.3 Verify KYV-101 IP bag integrity, check for cracks, tears, broken ports and verify the KYV-101 IP is frozen.

- If KYV-101 IP is damaged or compromised (e.g. cracks, leaks, etc.), place the KYV-101 IP into on-site LN2 freezer and quarantine per institutional procedures and contact Kyverna Patient Operations (Reference Appendix 1: Kyverna Contact List) and wait for next steps from Kyverna Patient Operations.

10.4.4 Transfer and store the KYV-101 IP at temperature of ≤-150°C into the designated storage location. KYV-101 IP must be stored in an on-site LN2 Vapor Phase Freezer until day of infusion.

- If storing the KYV-101 IP in a Vapor phase LN2 freezer, then store the cassette in a freezer rack in a designated location within the chosen vapor phase freezer per institutional policies and monitor the temperature per institutional monitoring system.
- If storing the KYV-101 IP in a LN2 Dry Shipper (exception only for pre-approved Clinical Sites, EU only), then return the KYV-101 IP back into the dry shipper and attach the new serialized tag (provided with shipment) and ensure to monitor LN2 Dry Shipper temperature daily via the LN2 Dry Shipper temperature monitoring system.

  NOTE: Each LN2 Dry Shipper delivery comprises a certificate (packing list) indicating shipper shelf life (+10d from filling of LN2 Dry Shipper). Confirm with the Logistics Coordinator for longer periods that there is sufficient LN2 and time remaining. Otherwise, the supply of a new shipper can be coordinated.

10.4.5 The KYV-101 IP is stored at the Clinical Site during the subject's lymphodepletion period and until product administration (typically 5 days).

10.4.6 If the product experiences a storage temperature excursion, then quarantine per institutional procedures, complete the Temperature Excursion Form and send it to Kyverna Patient Operations immediately with the applicable supporting documentation (Reference Appendix 1: List of Investigational Product (KYV-101 IP) Contacts) and wait for next steps from Kyverna Patient Operations.

10.5 Return of Dry Shipper

10.5.1 Ensure the "empty" LN2 Dry Shipper is ready for collection no later than one day after receipt of the KYV-101 IP.

10.5.2 Remove the old label on the outside of the LN2 Dry Shipper.

10.5.3 Peel the backing from the EMPTY label and affix it to the outside of the shipper.

10.5.4 Return the "empty" LN2 Dry Shipper per the instructions provided by the Logistics Coordinator.

11.0 KYV-101 INVESTIGATIONAL PRODUCT THAW AND HANDLING

11.1 General Considerations

11.1.1 Follow universal precautions and local biosafety guidelines applicable for handling and disposal to avoid potential transmission of infectious diseases.

11.1.2 The preparation of KYV-101 IP must only be performed by qualified and trained study staff in a setting equipped for the safe administration of cellular products.

11.1.3 A dedicated patient IV line must be available for KYV-101 IP administration. No other fluids or medications may be administered through this dedicated line during administration.

11.1.4 Do NOT use a leukodepleting or cell filter. No inline filters are permitted in the administration of KYV-101 IP.

11.1.5 The volume in the KYV-101 IP bag may range from 10 mL to 70 mL. Please refer to the Certificate of Compliance (FOR-0000085) for the manufactured dose level of KYV-101 CAR+T cells available for administration and volume in the KYV-101 IP bag.

11.1.6 Thawing of the KYV-101 IP must occur with consideration to the expiration time of the KYV-101 IP which is two (2) hours from start of thaw. Bedside thaw is preferred.

11.2 Removal of KYV-101 IP from Intermediate Storge and Transport to Unit for Infusion

11.2.1 Once the subject has been confirmed for infusion, gather the following documents in preparation to remove the KYV-101 IP from the storage location to thaw the KYV-101 IP.

- Certificate of Compliance (FOR-0000085)
- IMP Certificate of Conformance (QP certification, as applicable)
- KYV-101 Investigational Product (IP) Accountability Form (FOR-0000228), applicable for Kyverna sponsored trials only
- Additional documentation per institutional SOP(s)

11.2.2 Confirm the designated location of the KYV-101 IP for the intended subject and remove the cassette from the storage location.

11.2.3 Verify the KYV-101 IP identifiers (Subject ID number and DIN/SEC-DI) on the KYV-101 IP cassette label and KYV-101 IP bag label against the Certificate of Compliance (FOR-0000085) over the Vapor Phase LN2 Freezer (if applicable) to maintain temperature of the KYV-101 IP.

NOTE: Verification of the cassette and bag label is required which may expose the cryopreserved KYV-101 IP to ambient temperature for extended period if not done quickly. Loading and unloading of the LN2 transport system or equivalent must include this label verification as “one action” to minimize exposure of the KYV-101 IP to ambient temperatures and prevent any thawing or refreezing.

11.2.4 Document the removal of the KYV-101 IP to the infusion area in the COS.

11.2.5 Transport the KYV-101 IP to the thawing equipment in the vapor phase of a suitable vapor phase LN2 shipper container or equivalent to maintain a temperature ≤-150°C.

11.3 KYV 101 IP Thaw

11.3.1 Document the thaw of the KYV-101 IP on the KYV-101 Investigational Product (IP) Accountability Form (FOR-0000228) during the execution of the process steps.

NOTE: For non-Kyverna sponsored trials completion of IP Accountability Form (FOR-0000228) is not required.

11.3.2 Prepare the KYV-101 IP thawing equipment (example: calibrated/validated water bath or dry thaw) at 37°C per institutional SOP(s).

11.3.3 Record the thawing device temperature prior to the start of the thaw on the KYV-101 IP Accountability Form.

11.3.4 Start thaw only after subject eligibility is confirmed and premedication has been given. Reference clinical study protocol for premedication, dosing and administration.

11.3.5 Remove the KYV-101 IP from the vapor phase LN2 shipper container or equivalent.

11.3.6 Verify the KYV-101 IP identifiers (Subject ID number and DIN/SEC-DI) on the cassette, KYV-101 IP bag label and subject's medical record documentation prior to thaw against FOR-0000085. Inspect the cassette and KYV-101 IP bag integrity, check for cracks, tears, broken ports and verify the KYV-101 IP is frozen.

11.3.7 Remove the KYV101 IP from overwrap bag, if present, and place the KYV-101 IP bag in a secondary sealable over pouch.

- If the identifiers do not match between the documentation and the label or If KYV-101 IP is damaged or compromised, then do not proceed with thawing. Return the KYV-101 IP bag to the Vapor phase LN2 shipper container or equivalent and troubleshoot to resolve the issue. If the issue cannot be resolved, contact Kyverna Patient Operations (Reference Appendix 1: Kyverna Contact List) and wait for next steps from Kyverna Patient Operations.

11.3.8 Place the KYV-101 IP bag into thawing device and start thawing.

11.3.9 Record the start time along with the temperature of the bath on the KYV-101 IP Accountability Form. The thaw start time is the time the KYV-101 IP bag is placed in the thawing device.

- Complete thawing within 10 minutes. If the thaw is longer than 10 minutes, then proceed with the process and notify Kyverna Patient Operations (Reference Appendix 1: Kyverna Contact List)

NOTE: KYV-101 IP shall be mostly thawed (some residual ice remains and cool to the touch). Gently mix KYV-101 IP bag contents to disperse clumps of cells. Small clumps of cellular material will disperse with gentle manual mixing.

11.3.10 Remove the KYV-101 IP bag from thawing device.

11.3.11 Record the stop time on FOR-0000228. The thaw stop time is the time the KYV-101 IP bag is removed from thawing device.

11.3.12 Remove the over pouch bag without compromising the integrity of the KYV-101 IP bag and remove the KYV-101 IP bag.

11.3.13 Inspect the thawed KYV-101 IP bag for any leaks or damage.

- If KYV-101 IP is damaged or compromised (e.g. cracks, leaks, etc.), contact Kyverna Patient Operations (Reference Appendix 1: List of Investigational Product (KYV-101 IP) Contacts) and wait for next steps from Kyverna Patient Operations.

  NOTE: KYV-101 must be administered within 2 hours from the start of thaw.

11.3.14 Where transportation is required for the administration after a thaw, the KYV-101 IP bag must be transported at room temperature. A protective barrier pad must be placed inside of a closed leakproof container.

11.4 KYV-101 Infusion

11.4.1 Follow institutional CAR-T product administration procedures for administration of KYV-101 IP. Subjects must be monitored for infusion reactions throughout the administration of the KYV-101 IP per institutional policies and according to study protocol. In the event of an infusion reaction, contact the PI. Also contact Kyverna Patient Operations.

11.4.2 Once KYV-101 IP thaw has completed, start administration as soon as possible. The total time from the start of the thaw to subject administration must not exceed 2 hrs.

11.4.3 Prior to the infusion, verify the COI identifiers (Subject ID number and DIN) on the KYV-101 IP vial label, the subject's medical record documentation and against FOR-0000085.

- If there is a mismatch between the Subject and the KYV-101 IP identifiers, then DO NOT administer KYV-101 IP. Contact Kyverna Patient Operations immediately (Refer to Appendix 1 and complete FOR-0000064).

11.4.4 Flush the tubing with IV normal saline prior to and after KYV-101 IP administration. The KYV-101 IP will be administered by gravity via IV as a single administration.

1.1.1 Document the infusion start and stop time on FOR-0000228 and subject's medical record.
NOTE: The infusion stop time is the time at which the entire KYV-101 IP is administered, and the tubing has been flushed with IV normal saline.

11.5 KYV-101 IP Disposal and Destruction

11.5.1 Dispose of any unused or expired KYV-101 IP in accordance with the institution's biohazard disposal policy applicable for cellular products. All infusion supplies, including the KYV-101 IP bag and tubing, must be destroyed according to the site's biohazard disposal policy for blood-borne pathogens.

- If the dose is not fully administered, then return the infusion bag to the Cell Processing Laboratory immediately. The Cell Processing Laboratory will perform a volume measurement (according to institutional SOPs) to determine how much of the dose was administered.
- If the dose is not fully administered and there are no SOPs regarding volume measurement, then the un-administered volume will be determined by removing all remaining contents via syringe (the IV-line volume must NOT be included). Record the reason for incomplete administration and the volume administered on FOR-0000228 and Kyverna Patient Operations.
- If the Clinical Site wishes to destroy the unadministered KYV-101 IP, then a formal written request must be sent to Kyverna Patient Operations.
- If Kyverna wishes to recover the remaining KYV-101 IP for investigational purposes, then Kyverna will notify the PI of the request and forward instructions for returning the material.
- **NOTE:** Do NOT use any of the KYV-101 IP supplies for any other purpose other than directed by the clinical study protocol and this manual.

11.5.2 File KYV-101 IP Accountability Form and all other KYV-101 IP related records in ISF / subject's site file. Document accordingly in the subject's medical record.

NOTE: For non-Kyverna sponsored trials completion of IP Accountability Form (FOR-0000228) is not required.

12.0 APPENDICES

12.1 Appendix 1: Kyverna Contact List

12.2 Appendix 2: Document Description and Responsibilities Charts

Appendix 1: Kyverna Contact List

Contact Name	Email/Phone	When to Contact
Kyverna Therapeutics Patient Operations and Logistics Coordinator	KYV-PtOps@kyvernatx.com Emergency Phone: +1-888-700-5361 OR +1-510-626-8708	• Urgent issues/questions during Apheresis, Cryopreservation, IP and Infusion • COS or form questions. • Scheduling or changes to schedule (pick-up, delivery, infusion) • Temperature excursions • **USA only:** Questions related to scheduling of shipper and shipment delivery and pick-up, apheresis packaging equipment, missing apheresis shipment supplies or documentation, courier transport, apheresis packaging and pick-up, issues during the packaging and loading of the shipper, product integrity issues during transport.
Kyverna Therapeutics QA	Complaints@kyvernatx.com	• Product complaints regarding any inquiry about the product quality, strength, or identity of the cellular starting material or associated processes.
Logistics Coordinator (EU and UK)	coordination4cellLogistics@cellex.me info@cellex-transports.me Emergency Phone (after hours): Coordination: +49 173 4974322 Transport: +49 173 7968630	• Questions related to shipper delivery and pick-up, apheresis packaging equipment and documentation, missing apheresis shipment supplies or documentation.

Appendix 2: KYV-101 IP Document Description and Responsibilities Chart

Please refer to the ISF (Study Binder) for the latest approved version of the following documents.

Document	Accompanies Investigational Product	Provided to site by	To be completed by
Certificate of Compliance (FOR-0000085)	Yes	Accompanies KYV-101 IP Shipment	To be filed in ISF only.
Certificate of Analysis	Yes	Accompanies KYV-101 IP Shipment	To be filed in ISF only.
IMP Certificate of conformance (QP Certification) [EU only]	Yes	Accompanies KYV-101 IP Shipment	To be filed in ISF only
KYV-101 Investigational Product (IP) Accountability Form (FOR-0000228)	No	Kyverna Patient Operations	Site staff trained according to this manual, for Kyverna sponsored trials only.
Kyverna Temperature Excursion Form (FOR-0000065)	No	Kyverna Patient Operations	Site staff trained according to this manual
Kyverna Product Complaint Form (FOR-0000064)	No	Kyverna Patient Operations	Site staff trained according to this manual

REVISION HISTORY		
Version	**Description of Change(s)**	**Justification**
1.0	New Document	1. This manual consolidates the previously separate Apheresis (MAN-0000124), Product Handling (MAN-0000266), and IIT (MAN-0000125) manuals into a single, comprehensive document to ensure alignment with current procedures and change controls. 2. To capture and complete Action Items (AI-0000507, AI-0000508, AI-0000509) from Change Control (CC-0000108) 3. To capture and complete Action Item (AI-0000537) from Change Control (CC-0000106)

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Signatory Table

Action Name	User Name	Title	Signature Date
Send for Review (Written By)	Bryan Prentice	Director, Patient Operations	20-Feb-2026 14:54
Review	Roy Thomas	Associate Director, Patient Operations	24-Feb-2026 14:33
Review	Bryan Silvey	Sr Dir Quality Compliance, GCP & Risk Management	25-Feb-2026 18:08
Review	Nick Enderle	Associate Director, Supply Chain Logistics	04-Mar-2026 16:33
Review	Aida Kaplan	Sr. Director, Clinical Operations	08-Mar-2026 22:08
Review	Katherine Wachmann	Director	09-Mar-2026 10:32
Review	Joanna Hellmuth	Senior Medical Director, Clinical Development	09-Mar-2026 10:55
Review	Charvee Tandel	Sr Manager, QA Patient Operations Management & Supply Chai	12-Mar-2026 09:44
Send for Approval	Bryan Prentice	Director, Patient Operations	24-Mar-2026 09:27
Approve	Bryan Prentice	Director, Patient Operations	24-Mar-2026 09:28
Approve	Katherine Wachmann	Director	24-Mar-2026 20:34
Approve	Charvee Tandel	Sr Manager, QA Patient Operations Management & Supply Chai	25-Mar-2026 13:27
QA Approval	Marissa Gustafson	Sr. Manager, Quality Systems	26-Mar-2026 16:22
Scheduled Release	Marissa Gustafson	Sr. Manager, Quality Systems	26-Mar-2026 18:45

* Dates are displayed according to the system time zone: (GMT-07:00) Pacific Daylight Time (America/Los_Angeles)