1. Purpose

1.1. The purpose of this document is to describe the process for handling of Kite commercial final product. This includes the receipt, storage and preparation for administration of Kite product at qualified treatment sites in the United States (US).

1.2. This document also includes the requirements for verifying and maintaining chain of custody and chain of identity while handling Kite final product.

2. Scope

2.1. The scope of this document is the Kite final product handling, including the receipt, handling, storage, chain of custody and chain of identity tracking and administration preparation of Kite product at the treatment site.

2.2. This SOP is to be used *internally* by Kite employees and *externally* by Treatment site staff at the Authorized Treatment Center.

2.3. Clinical investigational products are out of scope.

3. References

3.1. STD-00195- Global Requirements for Commercial Treatment Site Final Product Handling

4. Definitions

4.1. **Chain of Custody (COC):** Chain of custody is the historical record of movement or possession of an individual patient's cells as they traverse from the patient source at apheresis collection through shipping, manufacturing, and receipt of the finished product at the infusion site.

4.2. **Chain of Identity (COI):** Refers to the electronic and procedural controls that uniquely links and identifies patient cells and data to the correct individual at any point in time during the COC. This occurs at Kite with the link of the patient and their cells to the identifying information of Kite Patient ID number (PID), Cell Order number and the Lot number (also known as the COI number in Kite systems).

4.3. **DIN**: Donation Identification Number is a unique identifier that may be assigned to each collection by the apheresis center. Applicable to collections in the United States and Australia.

4.4. **Kite Konnect®:** A hospital portal built on the Salesforce platform, comprised of three main functions supported by their respective customer service team:

4.4.1. **Hospital Portal**: Website that will enable healthcare professionals the ability to register and enroll a patient, schedule leukapheresis, place a cell order, request reimbursement and other support, obtain order and manufacturing status.

4.4.2. **Case Management Tracking System (CMTS)**: A module that is used by Kite Konnect® Case Managers to track and manage patient cases from cell order submission through final product delivery. Site Qualification and QA teams will also have access to CMTS to support the Apheresis Collection Module.

4.4.3. **Apheresis Collection Module (ACM)**: An electronic web-based system used to record the shipper kit verification, apheresis collection, chain of custody handoffs, packing, and shipment preparation of apheresis material, with required verification steps in the process.

4.5. **Hospital Patient ID**: a unique identifier assigned by the hospital/medical center to an individual patient.

4.6. **Patient Label:** label on the final product bag and cassette containing COI and patient identifying information:

4.6.1. Product Lot Number

4.6.2. Kite Patient ID

4.6.3. Expiration Date

4.6.4. Patient's First Name, Middle Initial, Last Name

4.6.5. DOB (Date of Birth)

4.6.6. Hospital Patient ID

4.6.7. DIN

4.7. **Shipper Label:** label on the exterior of the shipper containing order identifying information:

4.7.1. Product Lot Number

4.7.2. Cell Order Number

4.8. **Qualified Treatment Site Staff:** Refers to personnel in the cell therapy laboratory/treatment site at a qualified Treatment Site that is trained to perform the steps in this procedure.

4.9. **Qualified Site:** a hospital institution comprised of an Apheresis Center and Treatment Site (ACTS) that has successfully completed the qualification requirements per the applicable Site Qualification procedure. The term "Qualified Site" is interchangeable with "Authorized Treatment Center"

4.10. **Treatment Site:** The Treatment Site may be made up of multiple area(s) of a hospital where any of the following activities occur:

4.10.1. Final product is delivered, inspected and stored

4.10.2. Final product is retrieved from storage and transported within the site

4.10.3. Final product is thawed and prepared for infusion

4.10.4. In Oracle EBS, the Treatment Site is known as "Infusion Center" and designated as the "Deliver To" location in Oracle EBS. Oracle EBS can only have one address associated with the Treatment Site, which is where the final product is delivered to.

5. Responsibilities

5.1. **Kite Quality Assurance - Site Qualification:**

5.1.1. Oversight of the regional Site Qualification and monitoring program of Qualified Apheresis Centers and Treatment Sites (ATCS).

5.1.2. Trains hospital staff on the regional procedure to become a Qualified Treatment Site Staff and perform steps in this procedure.

5.1.3. Forwards reports of product complaints related to the LN2 shipper and final product, as applicable.

5.2. **Kite Medical Affairs:**

5.2.1. Performs intake of non-study related suspected adverse events and/or product complaints.

5.2.2. Forwards reports of product complaints related to the LN2 shipper and final product, as applicable.

5.2.3. Responds to unsolicited medical inquiries.

5.3. **Kite Konnect® Team**

5.3.1. First point of contact for Treatment Sites to call for assistance or report issues that have occurred during the receipt, handling, storage or preparation of final product.

5.3.2. Forwards reports of product complaints related to the Apheresis Shipper Kit components, as applicable.

5.4. **Kite Supply Chain – Commercial Logistics:**

5.4.1. Tracks packaging and timely shipping of each patient's product between the manufacturing site and treatment site using specialty couriers.

5.5. **Qualified Treatment Site Staff:**

5.5.1. Hospital staff trained by Kite Quality Assurance.

5.5.2. Completes the Kite final product handling, to include receipt, handling, storage, chain of custody and chain of identity tracking and administration.

6. **Safety**

6.1. Per Institutional guidelines.

7. Equipment and Supplies

7.1. Liquid Nitrogen Shipper (used for final product shipped by Kite) – consisting of a rigid exterior shipper shell, vapor phase LN2 dewar, and foam cassette rack with the final product

7.2. Vapor Phase LN2 Freezer (final product storage at the site)

7.3. Vapor Phase LN2 transport vessel (to transport within the site, when applicable)

7.4. Dry ice container for final product inspection (when applicable)

7.5. Product thaw equipment (e.g. water bath, dry thaw, thermometer)

7.6. Personal Protective Equipment (PPE) as required per institutional procedures

8. Procedure

8.1. **<u>General Information About This Procedure</u>**

8.1.1. If there are any changes to the treatment site or cell therapy lab location, final product delivery, equipment used to store or thaw Kite product etc., report the change to Kite Quality or Kite account manager. Examples of changes that should be reported to Kite are listed in Attachment 1.

8.1.2. Report all complaints related to the LN2 shipper, temperature monitoring device and final product to Kite Konnect®.

8.1.3. Kite cryopreserved product is ***extremely fragile***, always handle the product with care.

8.2. **Product Receipt and Removal**

8.2.1. Ensure that there are at least two (2) Kite-trained staff available to receive and document the receipt, inspection and storage of the final product on the day of delivery.

8.2.2. Kite product arrives at the commercial treatment site via courier in a vapor phase LN2 shipper. There are two LN2 shippers qualified by Kite that may be used for the final product shipment. The LN2 shipper will be marked as either a **Cryoport**® or **Marken**® shipper:

Cryoport LN2 Shipper	Marken LN2 Shipper
	

8.2.3. Qualified Treatment Site Staff should follow the courier's instructions for documenting the delivery/receipt of final product on the accompanying shipping documentation.

8.2.3.1. The courier may ask a Qualified Treatment Site Staff document their name and sign and date the shipping documentation.

8.2.3.2. The time documented on the courier waybill is the official delivery time that the courier records in their tracking system and reports to Kite to document the change in custody of the final product.

8.2.4. Carefully transport the shipper to an unpacking location, preferably adjacent to the vapor phase LN2 freezer used for final product storage.

8.2.4.1. Due to the size and weight of the liquid nitrogen shipper, it is recommended that a dolly be used whenever transporting the shipper. **Do not tilt or lay the LN2 shipper on its side.**

8.2.5. Verify chain of identity by comparing the details on the LN2 shipper label against the Treatment site product order and/or apheresis report that was created during the apheresis collection for the product.

8.2.5.1. The information on the LN2 shipper label will include the **Kite Lot Number** and **Cell Order Number**.

8.2.5.2. **Note:** The cell order number may have changed since the apheresis collection and the institution should have received a notification of this change from Kite Konnect. If the cell order number does not match the apheresis report and you have not received a notification of this change, please contact Kite Konnect® at 1.844.454.KITE.

8.2.6. Inspect the shipping container for evidence of damage or tampering. Report any shipping container issues to Kite Konnect® immediately at 1.844.454.KITE.

8.2.7. Remove the two zip ties on the latches, unlatch and open the lid of the vapor phase LN2 shipping container.

8.2.8. Verify the vapor plug (Marken) or dewar lid (Cryoport) is affixed to the dewar using a blue serialized zip tie.

8.2.8.1. Verify the serial number on the blue zip tie matches the serial number documented on the waybill (this may be called the "shipper's reference number").

8.2.8.2. Document zip tie serial number according to institutional procedures.

8.2.8.3. Report any shipping container issues to Kite Konnect® immediately at 1.844.454.KITE.

8.3. **Reading and Verifying the Temperature Data**

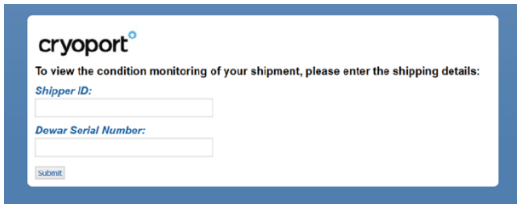
8.3.1. DO NOT open the dewar until the temperature of the shipper has been confirmed.

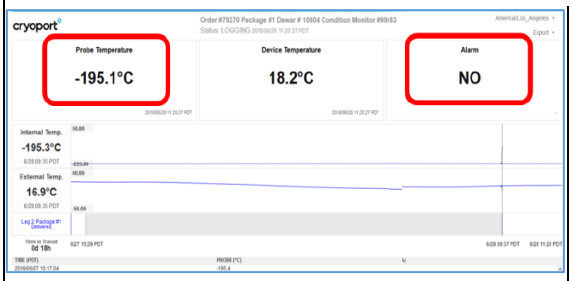
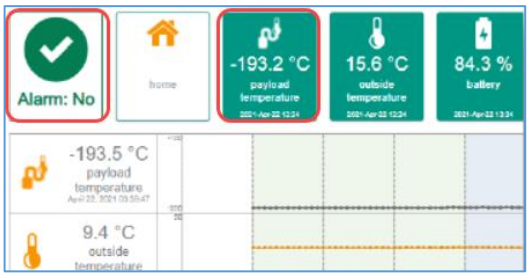
8.3.2. Verification of the final product temperature upon receipt is critical to ensure the validated storage temperature was maintained during the shipment from Kite to the Treatment Site.

8.3.3. The LN2 shipper is equipped with a temperature monitoring device that constantly monitors the temperature and sends periodic data updates to the web portal. If it appears that the temperature data is not current to the time of unpacking, it is likely that the device (and LN2 shipper with Kite product) is in an area that does not have network connection. **See section 8.9 for troubleshooting of the temperature monitoring device.**

8.3.3.1. **NOTE**: The monitoring device should **not** be removed, disconnected, or plugged into to any computer.

8.3.4. Based on the shipper received (refer to 8.2.2), follow the applicable instructions below for accessing and verifying the shipment temperature data.

Step	Cryoport LN2 Shipper	Marken LN2 Shipper
8.3.4.1 Log on to the LN2 Shipper website.	Go to: **https://www.cryoportal.com/livetemp** and enter in the ***Shipper ID*** and ***Dewar Serial Number*** 	Go to: **https://marken.sendum.com/visibility/public** and enter in the ***House Airway Bill (HAWB)*** number and ***Dewar Serial Number*** 

Step	Cryoport LN2 Shipper	Marken LN2 Shipper
The information needed to access the temperature data can be found on the shipper label.		
Note: It is recommended to access the URL in 'privacy' mode to ensure the user is directed to the correct website. If the web address asks for a "User Name and Password", recheck the web address that was entered, it may be incorrect.		
8.3.4.2	After entering in the required shipper label information, the website will re-direct and display the shipment temperature data.	
8.3.4.3	Verify that the temperature data is **current** and **constant** (Kite recommends time of data is +/- one (1) hour of opening the lid of the dewar). If it appears the temperature data isn't current, proceed with unpacking, inspecting, and storing the product. Then refer to section 8.9 for troubleshooting.	
8.3.4.4	Read the temperature of the probe/payload on the shipper's website, and document the temperature using institutional procedures. Verify that no alarm occurred ('NO').  	
8.3.4.5	If the alarm says 'YES', contact Kite Konnect® immediately to report the issue.	
8.3.4.6	Note: The temperature data displayed on the Cryport® website will ONLY be available until the dewar is returned to Cryoport®. If temperature monitoring data is required at a later date, please contact Kite Konnect®.	N/A

8.4 Opening the Dewar to Remove the Cassette Rack

8.4.1 Obtain appropriate Personal Protective Equipment (PPE) per institutional procedures.

8.4.2 Clear the unpacking location where the final product will be removed from the shipper to ensure final product is not mixed with other product lots or materials.

8.4.3 Prepare a container with dry ice or vapor phase LN2, in which to place and inspect the cassette and final product, at the unpacking station.

8.4.4 Remove the two zip ties on the latches, unlatch and open the lid of the vapor phase LN2 shipping container and follow the applicable instructions below to open the shipper based on the LN2 shipper received.

Step	Cryoport LN2 Shipper	Marken LN2 Shipper
8.4.5 Unlatch and open the lid of the LN2 shipper. Remove the thermal collar as applicable to remove the vapor plug. 8.4.5.1 For the ***Cryoport*** shipper, lift the hinged lid to reveal the vapor plug (dewar lid).		
8.4.6 Cut the serialized zip tie from the vapor plug.		

Step	Cryoport LN2 Shipper	Marken LN2 Shipper
8.4.7 Remove the vapor plug from the vapor phase LN2 dewar.		
8.4.8 Carefully remove the cassette rack from the LN2 dewar by pulling the cord straight up. Avoid pulling the cord at an angle as this may cause the foam rack to jam. 8.4.8.1 If there is any difficulty removing the rack in this manner, remove the lid from the white foam rack while it is still located inside the dewar. The finger slots in the sides of the lid may be used to help remove the rack.		
8.4.9 **IMPORTANT**: Do not carry the rack by the cord – always use two hands to support the rack when carrying.		

Step	Cryoport LN2 Shipper	Marken LN2 Shipper
8.4.10 Put the vapor plug (dewar lid) back on to keep the internal environment cold in the event that the cassette rack with the final product bag needs to be placed back inside the LN2 dewar.		
8.4.11 For the Cryoport shipper, close the hinged lid to cover the vapor plug.		N/A

8.5 <u>Removing the Cassette, Verification of Labels and Visual Inspection of the Product Bag</u>

8.5.1 Handle the product with extreme care, and treat like glass as the frozen product is fragile.

8.5.2 **Carefully** remove the cassette from the rack (do not bend the cassette) and immediately transfer the cassette to a container of dry ice or vapor phase LN2 to maintain temperature control of the product.

8.5.3 Verify that the patient information on the cassette matches the intended patient's records.

8.5.3.1 Do not remove the Final Product bag from the cassette if the information on the patient-specific cassette label does not match the intended patient.

8.5.3.2 If patient information ***does not match***, place the cassette back into the rack, place the rack back into the LN2 dewar (if removed). Place the vapor plug/dewar lid on the LN2 dewar and immediately contact Kite Konnect®.

8.5.4 **Carefully** open the cassette, leaving it within the dry ice or LN2 (vapor phase) container.

8.5.4.1 **NOTE:** To facilitate sliding up the side clasp, it may be helpful to apply **gentle pressure** to the very bottom corner of the cassette (as shown in the pictures below) to squeeze the cassette insert. DO NOT APPLY PRESSURE TO THE PRODUCT BAG WITHIN THE CASSETTE.

Opening the Final Product Cassette

8.5.5 Verify that information on the Patient Specific cassette label matches that on the final product bag.

8.5.6 Verify bag integrity, checking for cracks, tears, broken ports, etc. Close the cassette, turn the cassette over, open the cassette and verify the bag integrity on the other side of the bag. Report any issues observed to Kite Konnect® immediately.

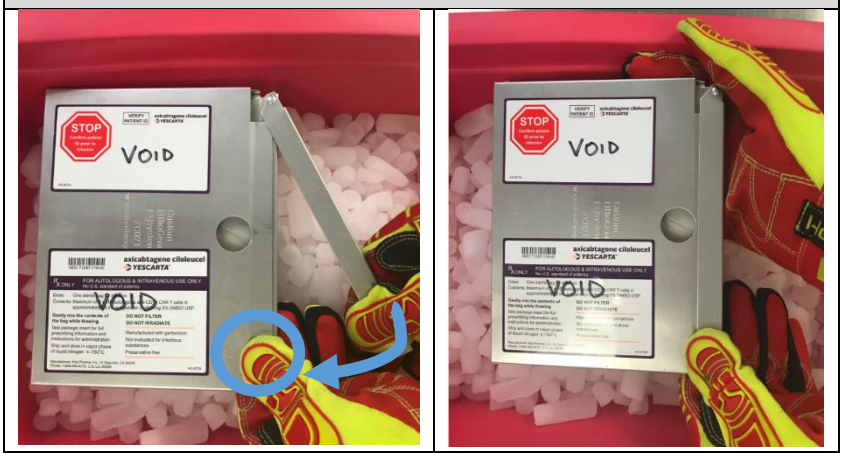
8.5.6.1 Prior to closing the cassette, ensure the product bag and the foam insert on the bag are fully seated within the cassette.

Final Product Bag Placement in Cassette

8.5.6.2 Close the cassette top and slide down the side clasp to close the cassette.

8.5.6.2.1 Note: To facilitate sliding down the side clasp, it may be helpful to apply gentle pressure to the very bottom corner of the cassette (as shown in the pictures below) to carefully squeeze the cassette insert. DO NOT APPLY PRESSURE TO THE PRODUCT BAG WITHIN THE CASSETTE.

Closing the Final Product Cassette



8.5.6.3 If any deviations are identified, notify Kite Konnect® to report a product complaint.

8.5.7 If the unpacking location is **not** adjacent to the vapor phase freezer used for final product storage:

8.5.7.1 Place the cassette back into the rack

8.5.7.2 Place the rack back into the LN2 dewar

8.5.7.3 Place the vapor plug (dewar lid) back on the dewar

8.5.7.4 Fasten the two latches on the shipper lid

8.5.7.5 Move the shipper to the vapor phase freezer location

8.6 Product Storage

8.6.1 Carefully transfer the final product to a vapor phase freezer:

8.6.1.1 Store product at a temperature of ≤ -150°C.

8.6.1.2 Ensure the cassette is stored in a designated location within the chosen vapor phase freezer to prevent product mix-up.

8.6.1.3 Confirm the temperature of the vapor phase freezer is ≤ -150°C at the time product is placed in the vapor phase freezer.

8.6.1.4 Temperature monitoring should follow institutional procedures.

8.6.1.5 Document storage location according to institutional procedures.

8.7 Preparation and verification of final product for Infusion

8.7.1 Confirm the designated location of the final product for the intended patient

8.7.1.1 Remove the cassette from the vapor phase freezer

8.7.1.2 Remember to handle the cassette with extreme care, and to treat like glass as the frozen product is fragile.

8.7.1.3 Verify the information on the patient specific label on the cassette matches the intended patient, following institutional procedures.

8.7.2 If final product will be ***thawed bedside***, the product shall be transported in the cassette in a dry shipper [transport vessel] to maintain a temperature of ≤ -150°C.

8.7.3 If the final product will be ***thawed in the lab***, the product shall be transported in a closed, rigid transport vessel that will maintain room temperature [20-25°C] during transport.

8.8 Thawing and Infusion (Administration Preparation)

8.8.1 Refer to package insert for thawing and infusion instructions.

8.8.2 The identity of the patient must be matched with the patient identifiers on the Final Product bag prior to thawing and documented per institutional procedures prior to thawing.

NOTE: Do not infuse the product if the information on the patient-specific label does not match the intended patient.

8.8.3 Remove the product bag from the metal cassette, inspect the bag for any damage (e.g. cracks, tears, broken ports, etc.) prior to thaw. Report any issues to Kite Konnect® immediately.

8.8.4 Remove the black foam insert below the product bag. Discard the foam insert.

8.8.5 Place the product bag in a second sealable overwrap bag, as applicable per local guidelines.

8.8.6 If any damage occurs to the final product bag during thaw, follow institutional procedures for recovery of the product.

8.8.7 Record the temperature of the water bath or dry thaw, just before start of thawing.

8.8.8 Record the thaw start and end times.

8.8.9 The identity of the patient must be matched with the patient identifiers on the Final Product bag prior to infusion and documented per institutional procedures prior to thawing.

8.8.10 Record the infusion start and stop times.

8.8.11 At the end of the infusion, complete post-infusion procedures per institutional guidelines.

8.8.12 Report a product complaint for any damage or quality issues to Kite Konnect, 1.844.454.KITE.

8.9 Troubleshooting the Temperature Monitoring Device

8.9.1 If the review of the temperature data for the LN2 shipper indicates that the temperature data is ***not current***, it is likely that the device (and LN2 shipper with Kite product) is in an area that does not have network connection.

8.9.1.1 **NOTE**: The monitoring device should **not** be removed, disconnected, or plugged into to any computer.

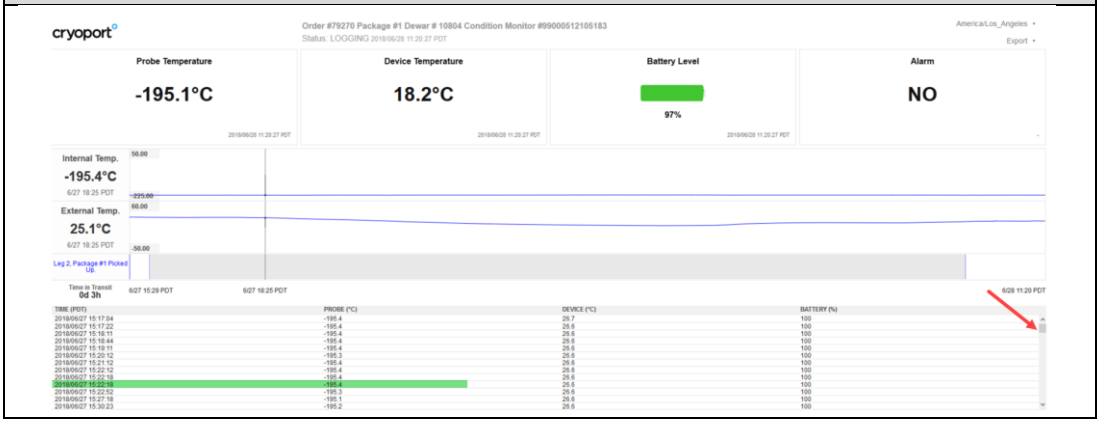
8.9.2 If you have observed that the temperature data is NOT current, move the LN2 shipper into an area that has cell service so the device can wirelessly transmit the temperature data to the web portal prior to opening the dewar.

8.9.3 Follow steps under section 8.3.3 for viewing the temperature data.

8.9.3.1 Once you are viewing the temperature data in the web portal, scroll down and identify the time the product was received (based on the time that the product receipt was recorded per institutional procedures).

8.9.3.2 Record the temperature that correlates to the time the product was received.

Cryoport Temperature Data Web Page



Marken Temperature Data Web Page

8.9.3.3 If there are still issues obtaining the temperature data, contact Kite Konnect®.

9 Attachments

9.4 Attachment 1, List of Changes to Report to Kite

9.5 Attachment 2, List of Approved Kite Products

Revision History Summary

Originator	Version	Summary of Changes	
K. Goss	8.0	1. Revision 7.0 was withdrawn and was not made effective. 2. Replaced 'Yescarta' with Kite Product 3. Created Attachment 1	1. SOP withdrawn to incorporate additional changes prior to release. 2. Process is not product-specific. 3. To provide sites with a list of potential changes that may be reported to Kite.
T. Hlucky	9.0	1. Created Attachment 2 2. Further clarification made to step 8.2.7 for reading the temperature data; updated information re: the Smartpak II device 3. Updated formatting throughout document 4. Step 8.2.6; added comment for hospital staff to document the serialized tie tag verification "per institutional procedures"	1. FDA approval of Tecartus™ 2. Additional instructions/notes added to assist hospital staff with reading the temperature data using the SENDUM Smartpak II 3. Ease of use 4. Was not specified in previous version
T. Hlucky	10.0	1. Updated entire document to align with Kite's global requirements for final product handling in STD-00195 (Global Requirements for Commercial Treatment Site Final Product Handling). 2. Removed instructions for the SmartPak II device and the Hobo Logger. 3. Updates to include the Marken LN2 shipper including additional instructions for use of this shipper. 4. Updated all photos of the Cryoport dry shipper and updated instructions for use of this shipper.	1. Global site qualification alignment. 2. Hobo logger no longer in use. SmartPak II is the temperature monitoring device for both LN2 shippers containing Kite products; SOP instructions were made specific to the ***courier***, not the temperature monitoring device. 3. Added Marken as a courier for the Kite final product. See AGILE-CC-01618- Implementation of Marken LN2 Shipper with Sendum Cap Condition Monitoring System. 4. Reconfiguration of the Cryoport shipper per AGILE-CC-02012- Implementation of the Cryoport CXHV2SPHU.

Examples of changes reasonably expected to be reported include anything that has a potential impact to the receipt of Kite materials, apheresis collection process, or pick-up of collected apheresis material. Examples of these changes include, but are not limited to:

- Physical move of all or part of the program to a new building or to a building that has not been audited by Kite.
- Change of equipment type used for collection, storage or thaw of products, changes to administration, and to facility/equipment monitoring systems.
- Change to Quality Systems, e.g. equipment validation requirements, document management.
- Reorganization of previously inspected physical space or annexation of additional contiguous space.
- Addition of new or additional clinical, collection, or processing partner.
- Changes in ownership or mergers between audited accredited organizations that impacts accreditation certification.
- Changes to accreditation and/or regulatory body certification status

Kite FDA approved products:

YESCARTA® (axicabtagene ciloleucel) Suspension for IV Infusion

TECARTUS™ (brexucabtagene autoleucel) Suspension for IV Infusion

Document Approval Information

Document No.: **SOP-00633** Document Version: **10.0**

Name: **SOP-00633 Commercial Treatment Site Final Product Handling - US**

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Approved By | Verdict	Capacity | Date Approved
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