# AUCATZYL® Apheresis Manual (US)

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# Introduction

This **Manual** provides guidance on the steps involved in procurement of leukapheresis material, management, traceability, packaging, and shipping of a patient's cells to an Autolus manufacturing facility. It is essential that patient cells are handled correctly at each stage of the process to ensure integrity of the leukapheresis material, the AUCATZYL® (obecabtagene autoleucel) product and, ultimately, patient safety.

Guidance on Receipt and handling of the AUCATZYL® final drug product at the Treatment Center, Drug product preparation and administration is provided in the **Autolus AUCATZYL® Product Handling Manual (US)** and the **Release for Infusion Certificate**.

It is necessary to follow the steps outlined in this Apheresis manual to avoid delay in AUCATZYL® product manufacturing. Compliance with local quality standards and the Autolus Apheresis Quality Agreement must be maintained.

It is vital that the Center provides Autolus with current correct contact details and addresses to ensure safe handling of leukapheresis material and AUCATZYL® product. These details will be collected during onboarding.

Transport of leukapheresis material and AUCATZYL® product, including import and export are managed by Autolus using the designated courier.

# Chain of Identity

Autolus uses a Cell Orchestration Platform, known as the **AutolusAssist™ Scheduling Portal**, to manage the Patient Cell Journey and act as a system of record for Chain of Identity (COI) and Chain of Custody (COC).

To ensure traceability of a patient's cells Autolus uses a unique identifier, the **Chain of Identity Identifier (COI ID)**. The COI ID is generated following patient registration in the AutolusAssist™ Scheduling Portal.

Patient Full Name, Date of Birth, Patient Hospital ID and an apheresis identifier (ISBT128 DIN or locally defined identifier) are additional identifiers to ensure maintenance of the vein-to-vein Chain of Identity. The COI ID and additional patient identifiers are applied to the leukapheresis collection bag and will be present on the final drug product label.

Full patient identifiers are maintained securely in the AutolusAssist™ Scheduling Portal and are only present on the leukapheresis label and final drug product labels. In the event of any potential, suspected or actual data breach, please notify AutolusAssist™ (scheduling@autolus.com **Tel. 1-855-288-5227**) as soon as possible and in any event within 24 hours.

# Responsibilities

Instructions in this manual are designed to enable compliance with legal and regulatory requirements and seamless operation of the Autolus supply chain.

The prescribing physician is responsible for determining patient readiness for leukapheresis and treatment with AUCATZYL® and obtaining appropriate consent.

The Apheresis Collection Center or Authorized Treatment Center must adhere to the Compliance Requirements detailed in the Autolus Apheresis Quality Agreement and notify Autolus without delay of any changes/events/issues that may impact that agreement.

Autolus will ensure that suitable training is provided prior to Apheresis Collection or Treatment Center activation. A requirement for follow-up or additional training may be identified by Autolus or the Center to ensure compliance and quality requirements are met.

## AutolusAssist™

Autolus has a dedicated team of experts providing support 24/7 all year round.

**For assistance please call:**
**AutolusAssist™: Tel. 1-855-288-5227**

AutolusAssist™ Case Managers are the primary point of contact and will be able to assist with most enquiries or put you in direct contact with functional specialists where required.

AutolusAssist™ Patient Scheduling and Logistics team arrange, coordinate and track collection of leukapheresis material from the Apheresis Collection Center, delivery to Autolus manufacturing and return of the AUCATZYL® product back to the Authorized Treatment Center for infusion .

Logistics arrangements and milestone updates will be provided by email.

The Autolus Patient Scheduling and Logistics team can be contacted at scheduling@autolus.com.

## Autolus Apheresis and Infusion Operations

Autolus has a team of field-based experts with experience across apheresis, infusion and quality assurance. The team will work with you to establish the Autolus autologous cell therapy supply chain and provide technical training and assistance where required. Apheresis and Infusion Managers may be contacted directly or AutolusAssist™.

## AutolusAssist™ Scheduling Portal

To manage the pateint cell journey, a web-based Cell Orchestration Platform, also known as the AutolusAssist™ Scheduling Portal, is used. Upon registration of a patient in the AutolusAssist™ Scheduling Portal the center user will be able to view availability and select a suitable leukapheresis collection date. Refer to the AutolusAssist™ Scheduling Portal User Guide for detail.

The AutolusAssist™ Scheduling Portal (Apheresis) is required for the following tasks:


*Figure 1: Scope of the Apheresis Manual and associated AutolusAssist™ Scheduling Portal tasks.*

The requirements for Drug Product will be described in the AUCATZYL® product handling manual.

# Pre-Registration Considerations

Determining patient readiness for leukapheresis and treatment with AUCATZYL® should be carefully coordinated with the prescribing physician in accordance with local institutional procedures and information in the AUCATZYL® US Prescribing Information. Please contact Autolus (AutolusAssist™ on 1-855-288-5227, or your local representatives) with any questions specific to patient treatment.

**Infectious Disease Testing**
Patients must be tested for infectious diseases as detailed in the relevant section (Page 6).

**No Active or Uncontrolled Infection**
In the event of infection or signs of infection, presence of active or uncontrolled fungal, bacterial, viral (including COVID-19), or other infection requiring systemic antimicrobials for management, leukapheresis should be delayed until resolution of the event.

# Patient Registration

Upon identification a patient must be consented by the center and then registered in the AutolusAssist™ Scheduling Portal. Refer to AutolusAssist™ Scheduling Portal User Guide Task: Register Patient.

Completion of the Patient Registration step will generate a COI ID for the patient. The COI ID must be used throughout the patient cell journey and referenced on all communications with respect to the patient, their cells or drug product.

The Authorized Treatment Center must complete the Coverage & Support requirements for the patient in the AutolusAssist™ Scheduling Portal prior to scheduling a leukapheresis collection. All Autolus Patient support programs are subject to eligibility. In order for a patient to be screened by an Autolus Case Manager for Patient Support Programs, Free Goods, or to request assistance with a benefit verification a completed and signed enrollment form must be submitted to Autolus by the patient and HCP.

# Therapy Schedule

Following confirmation of patient registration, the clinical site user will schedule the patient in the AutolusAssist™ Scheduling Portal. The user can select a leukapheresis date, review the estimated therapy schedule milestones, and proceed to complete the CAR T-cell order. Refer to AutolusAssist™ Scheduling Portal User Guide Task: Continue Registration.

The Center team will receive an email notification confirming the booking.

A leukapheresis date is aligned to a specific manufacturing slot at Autolus. Manufacturing of AUCATZYL® requires a dedicated team, equipment, and time allocation at the manufacturing facility. It is essential that Autolus are kept informed of any events and status changes relating to patients booked for AUCATZYL® manufacture.

If it is not possible to proceed with leukapheresis on the scheduled date, please contact AutolusAssist™ to discuss and make any adjustments required. Please contact us by telephone for any urgent issues.

The clinical site must not schedule or reschedule a leukapheresis procedure to a date different to the one booked in the AutolusAssist™ Scheduling Portal and confirmed on the Booking Confirmation Notification without prior agreement from AutolusAssist™ Patient Scheduling and Logistics.

# Infectious Disease Marker (IDM) Screening

Two IDM screens are required for patients registered for AUCATZYL® manufacturing to meet obligations for donor testing of cells for use in human application and UK Human Tissue Authority requirements.

The IDM screening results from a sample obtained within 30 days prior to the leukapheresis date must be submitted in the Scheduling Portal before to leukapheresis, ideally 72 hours prior. A second IDM screening must be performed on a sample obtained on the day of leukapheresis (or within 7 days following leukapheresis). ***Delays to the provision of IDM results may risk leukapheresis reschedule (screening sample) and may postpone the release and delivery of AUCATZYL® (day-of-collection sample)***.

**Infectious Disease Marker (Eligibility Screen)**
Leukapheresis can only occur after negative screening IDM results are submitted and confirmed.

Results from Table 1 tests need to be submitted and verified in the AutolusAssist™ Scheduling Portal. Refer to the AutolusAssist™ Scheduling Portal User Guide Task: Record Screening IDM.

| **Infectious Agent** | **Test** | |
|---|---|---|
| HIV 1 & 2 | HIV 1 and 2 antibodies | anti-HIV I/II |
| Hepatitis C | Hepatitis C virus antibody | anti-HCV |
| Hepatitis B | Hepatitis B surface antigen | HBsAg |
| Hepatitis B | Hepatitis B core antibody | anti-HBc |
| *Treponema pallidum* | *Treponema pallidum* | Syphilis Serology |
| Human T-lymphotropic virus 1 &2 | HTLV I and II antibodies | anti-HTLV I/II |

*Table 1 - Mandatory Infectious Disease Screening for Autolus CAR T production*

A negative IDM screen is needed for AUCATZYL® product manufacture and to proceed with pre-collection checks and leukapheresis in the Scheduling Portal. The Patient Overview screen shows the "Screening IDM Results Status," and the Center team will receive updates from Autolus until the results are submitted.

If any test results are marked as 'Reactive or Ambiguous', you must fill in the 'Additional Information' field with relevant details, including results of any confirmatory tests like Nucleic Acid Testing (NAT). An Autolus Medical representative may contact the Center to request additional information and discuss eligibility.

| HBsAg HepB Surface Antigen | HBcAb HepB Core Antibody | HBsAb HepB Surface Antibody | Eligibility & Interpretation |
|---|---|---|---|
| **Positive** | Any | Any | **Not Eligible**<br>Infected. Hep B virus is present. |
| Negative | **Positive** | Negative | **Not Eligible**<br>Interpretation unclear, possible past or current Hep B infection. |
| Negative | **Positive** | **Positive** | **Eligible**<br>Surface antibodies due to prior natural infection. Cannot infect others. |
| Negative | Negative | **Positive** | **Eligible**<br>Immune due to Hep B vaccination. |
| Negative | Negative | Negative | **Eligible**<br>Not immune, not protected. |

*Table 2 - Hepatitis B Blood Test results, Eligibility & Interpretation*

**Please note: leukapheresis must not proceed without confirmation of a negative Infectious disease screen as without this leukapheresis material cannot be accepted at an Autolus manufacturing facility.**

# Courier Arrangements

The Autolus Patient Scheduling and Logistics team will book a courier to deliver a temperature-controlled shipment box and accessories on the day of leukapheresis for packaging and shipment of the leukapheresis material. Leukapheresis material must be packed into the temperature-controlled shipment box immediately upon completion of the leukapheresis procedure.

Collection of the packed shipment box will be arranged for a pick-up time previously agreed with the center, this is usually 2pm. If delay to Leukapheresis prevents pick up of material past 2PM please contact AutolusAssist™: **Tel. 1-855-288-5227**

Please contact AutolusAssist™ scheduling@autolus.com if the temperature-controlled shipment box and accessories have not been received by the agreed time on the day of leukapheresis.

# Leukapheresis

**Infectious Disease Screening - Procurement Testing**

A second IDM Screen must be performed on a sample obtained on the day of leukapheresis. The Center team will receive periodic notifications until the day of procurement IDM results have been submitted. A Center user should submit the IDM results to the AutolusAssist™ Scheduling Portal as soon as they are available. Refer to AutolusAssist™ Scheduling Portal User Guide Task: Record Aph-Day IDM. Any missing data or delays may impact patient treatment as AUCATZYL® drug product cannot be released for shipment until the 2nd infectious disease screen results are received.

If any of the required serological test results are reactive or inconclusive, it is essential that confirmatory testing (preferably including Nucleic Acid Testing (NAT)) is performed to demonstrate that the patient does not have an active infection.

**Please note: Autolus has a UK legal obligation to ensure that a "Day of Collection" IDM panel is performed on a sample obtained on the day of collection or within 7 days after the collection. A delay in or failure to provide results may impact product release.**

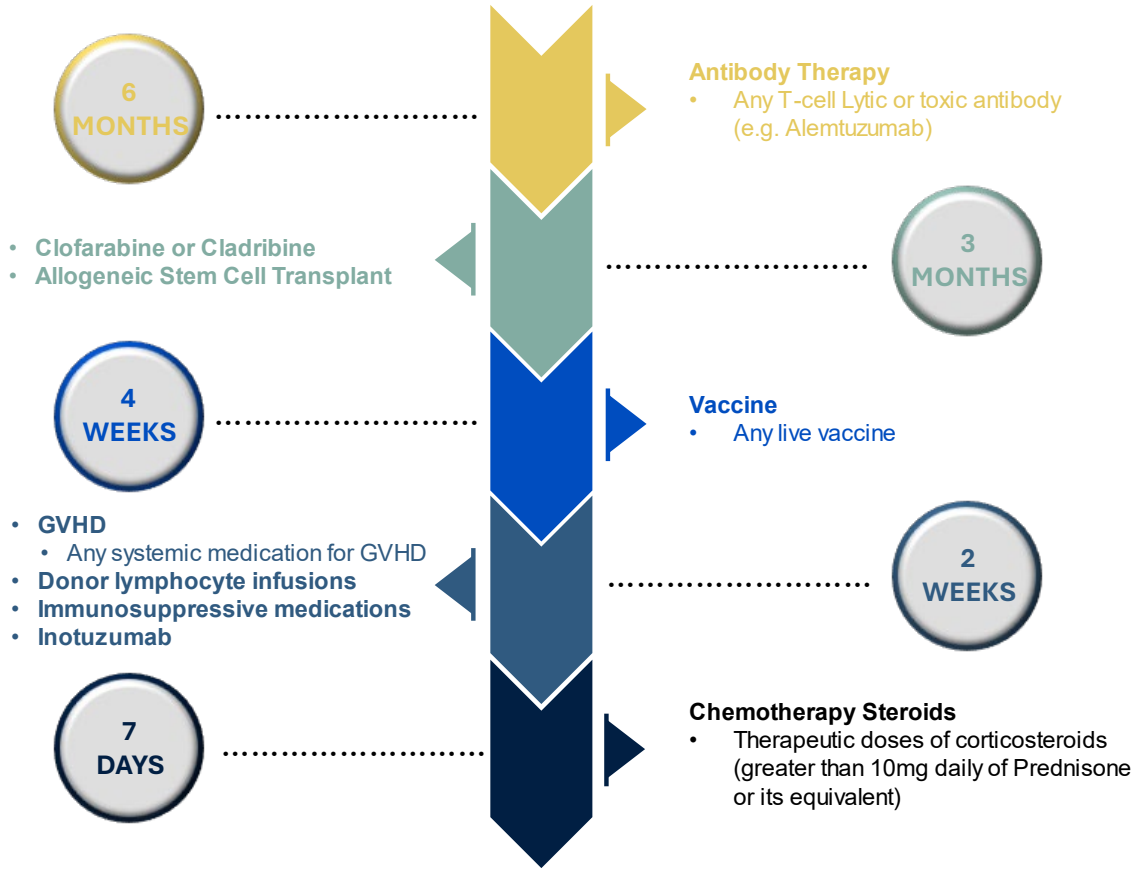
**Treatment Center may be subject to additional local or health authority donor eligibility and infectious disease testing requirements and must also comply with these.**

### Therapeutic Washout

The following medications would exclude a patient from collection, adequate washout of medications should be observed. Table 3 also provides recommendations for stopping therapies prior to a scheduled leukapheresis procedure.

| | |
|---|---|
| **Steroids** | Therapeutic doses of corticosteroids (greater than 10 mg daily of prednisone or its equivalent) within 7 days of leukapheresis or 72 hours prior to AUCATZYL® administration. However, physiological replacement, topical, and inhaled steroids are permitted. |
| **Allogeneic Stem Cell Transplant** | Allogeneic Stem Cell Transplant must be completed >3 months prior to leukapheresis. |
| **Immunosuppression** | Immunosuppressive medication must be stopped ≥2 weeks prior to leukapheresis and AUCATZYL® infusion. |
| **Inotuzumab** | Inotuzumab ozogamicin treatment must be stopped ≥2 weeks prior to leukapheresis |
| **Donor lymphocyte infusions** | Any donor lymphocyte infusions must be completed >2 weeks prior to leukapheresis and not repeated thereafter. |
| **Graft versus host disease therapies** | Any systemic drug used for the treatment GVHD must be stopped >2 weeks prior to leukapheresis and not repeated thereafter. |
| **Chemotherapy** | Chemotherapy should be stopped 7 days prior to leukapheresis and starting pre-conditioning chemotherapy. TKIs for Ph+ ALL should be stopped >72 hours prior to pre-conditioning chemotherapy. |
| **Antibody Therapy** | Treatment with any T cell lytic or toxic antibody (e.g., alemtuzumab) within 6 months prior to leukapheresis, or treatment with clofarabine or cladribine within 3 months prior to leukapheresis. |
| **Vaccine** | Live vaccine ≤4 weeks prior to leukapheresis. |

*Table 3 - Therapeutic Washout of agents prior to Leukapheresis*



**Leukapheresis Procedure**

Leukapheresis must be conducted by trained apheresis personnel at an Autolus Authorized Apheresis Collection Center according to local institutional guidelines, and the Autolus AUCATZYL® Apheresis Manual.

Unstimulated leukapheresis should be conducted in the morning on the date confirmed by Autolus Patient Scheduling to allow for same-day shipping. Leukapheresis material should be collected using an FDA approved sterile collection kit. Use only Anticoagulant Citrate Dextrose, Solution A (ACD-A) as anticoagulant.

Apheresis Collection Center personnel must complete the collection checklist in the AutolusAssist™ Scheduling Portal to confirm that the appropriate pre-collection checks have been completed prior to initiating the leukapheresis collection. Refer to AutolusAssist™ Scheduling Portal User Guide Task: Pre-Collection Checks.

Apheresis Collection Center personnel will verify Patient Identity to ensure that the correct patient is present for leukapheresis collection and will record the Apheresis ID to be used for the collection in the Scheduling Portal so that it can be linked with other key identifiers. A second user must attest that the pre collection checks, patient identity and Apheresis ID are accurate and consistent.

A Center can use either their ISBT-128 label or one from the AutolusAssist™ Scheduling Portal. When using the portal, they can preview the Leukapheresis Collection Label after confirming patient identifiers. The Apheresis Collection Center should verify all details on the label for accuracy before downloading and printing it. Refer to the AutolusAssist™ Scheduling Portal User Guide Task: Print Collection Label.

Regardless of how the Apheresis Label was generated the Centre is required to provide an attestation in the AutolusAssist™ Scheduling portal that the label contains accurate COI information. Refer to AutolusAssist™ Scheduling Portal User Guide Task: Attest Collection Label. Following confirmation of patient identity, the ISBT-128 leukapheresis label must be affixed to the leukapheresis collection bag following Centre procedures.

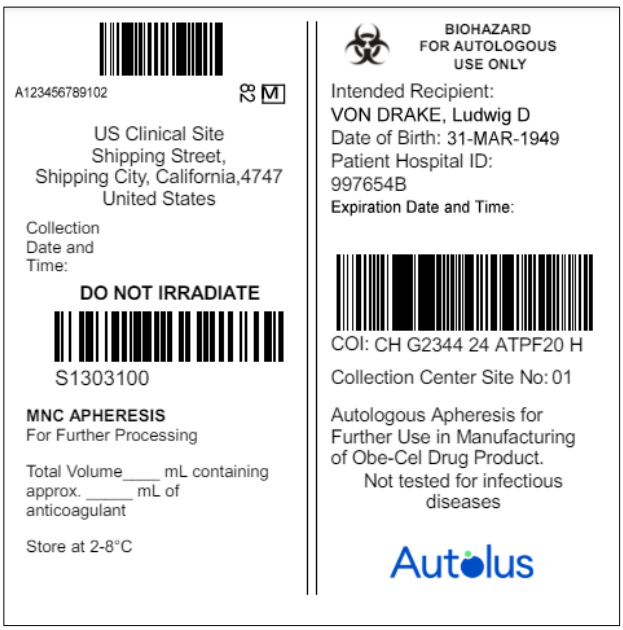



*Figure 2 - Example of ISBT-128(ST-018) leukapheresis bag label*

The ISBT-128 leukapheresis label must be affixed to the collection bag and must (as a minimum) contain the following information:

- Donation Identifier / Apheresis ID
- Autolus Chain of Identity ID
- Patient Name (First Name, Surname)
- Date of Birth
- Collection date and time.
- Local time zone

Use only alcohol-resistant indelible ink if any label information is completed by hand.

The label must be affixed to the base label of the collection bag, to ensure one face of the bag remains clear for inspection.

**Leukapheresis Collection Targets**

The target for collection is 1.5x$10^9$ CD3+ cells. Target a cell separation which minimizes the number of RBCs, granulocytes, and platelets in the collection product.

**Collection Optimization:**

Typically, processing two total blood volumes (TBV) should be sufficient to obtain the required cell yield, but in some ALL patients, particularly those with peripheral blasts, processing of up to three total blood volumes may be required. For patients with a high body mass index, it is recommended that ideal body weight rather than actual body weight is used to calculate patient total blood volume. Please contact Autolus to discuss prior to collection if required.

**General Leukapheresis Cell Collection Targets are as follows:**

- Two total blood volumes processed (final volume will typically vary between 50-200 ml of leukapheresis material collected)
- Target yield of least 1.5 x$10^9$ CD3+ cells

**High Peripheral Blasts:**

In some Acute Lymphoblastic Leukaemia (ALL) patients with peripheral blasts >50%, processing of up to three total blood volumes may be required. This would typically generate 50-400 mL of leukapheresis product to obtain at least 1.5 x$10^9$ CD3+ cells.

**Leukapheresis Collection Bag Tubing Tail and Product Sampling**

A tubing tail length of at least 4" (10cm) (ideally 6" (15cm)) must be left on the leukapheresis collection bag Tubing does not need to be stripped. Aseptic sampling is permitted using the sample collection bulbs only.

**Documenting Leukapheresis Collection**

Enter the details of the leukapheresis collection into the Scheduling Portal. Refer to the AutolusAssist™ Scheduling Portal User Guide Task: Record Collection.

Ensure that the patient identifiers match the values in the patient record, and complete all mandatory fields related to the collected material.

Record:

- The start and finish date
- Final volume of the collection
- Total volume of blood processed
- Collection end time (start of rinseback) and time zone*
- Volume of anticoagulant
- Batch details for the anticoagulant and collection kit used

Review and verify the entered details carefully to ensure all data provided is accurate and consistent.

* Local time zone may be prepopulated based on your location and will be used to calculate leukapheresis material expiry for manufacturing (96 hours for Autolus AUCATZYL® collections).

**Important note:** The Donation Identifier recorded in the AutolusAssist™ Scheduling Portal must correspond with the Donation Identifier used on the leukapheresis collection bag. The Donation Identifier documented in the Scheduling Portal will be printed on the final drug product label.

A second user must review the information entered for the leukapheresis collection in the AutolusAssist™ Scheduling Portal and attest that the details are correct before the leukapheresis material is packed for shipment to Autolus.

Refer to the AutolusAssist™ Scheduling Portal User Guide for detailed instructions.

# Shipping of Leukapheresis Material

**Preparation of leukapheresis material for shipping to Autolus**

Autolus will arrange for a courier to deliver a preconditioned shipping container on the day of Leukapheresis. The shipper will be delivered on the morning of collection and will contain all required shipping materials.

Please contact Autolus immediately if there are any changes in scheduled leukapheresis timings or the shipper does not arrived or is damaged on receipt.


*Figure 3 – Representative Transport Box and accessories*

The preconditioned shipment box will include:

- Transparent Specimen Transport Bag
- Absorbent Material
- Temperature monitoring device
- Tamper evident seals
- Self-adhesive document pouch

**Leukapheresis material Shipping Documentation**

A copy of the air waybill is required for shipment of the leukapheresis material. The required shipping documents will be provided in advance by Autolus via email and via the Scheduling Portal.

**Autolus will provide:**

- An air waybill (also provided by the courier with the shipper)
- Shipper preparation form (which must remain with the shipper)
- Customs Invoice (provided in the Scheduling Portal).
- Do not Xray instruction (provided in the Scheduling Portal).

The Apheresis Collection Center will need to print 3 copies each of the **Customs Invoice** and **Do Not Xray Instruction** in advance of the shipment.

Autolus uses multiple couriers and the packaging shown in the images may differ from those received.

**Temperature Controlled Shipper Contingency Plan**

NanoCool™ Temperature-controlled shippers will be supplied to Autolus Approved Centers as a contingency.

The NanoCool™ shippers are intended as a back-up and should only be used after agreement with Autolus Patient Scheduling and Logistics.

If you need to use a NanoCool™ shipper, please refer to the instructions in **Appendix 3 Shipping Leukapheresis Material using a NanoCool™ Shipper** prior to proceeding with **Packaging the leukapheresis material for shipment (below).**

**Packaging the leukapheresis material for shipment**

The corrugated plastic box can be removed from the external cardboard box prior to packaging leukapheresis material for shipment.

When the leukapheresis procedure has completed and associated data is entered in the Scheduling Portal, remove the transparent specimen transport bag, absorbent material, temperature monitoring device, and inner cardboard box from the temperature-controlled shipment box and replace the lid to maintain the internal temperature.

Packaging of the leukapheresis material for shipment to Autolus manufacturing must be documented in the Scheduling Portal. Refer to AutolusAssist™ Scheduling Portal User Guide Task: Pack Collection.

*Figure 4 – Leukapheresis Bag in transparent specimen transport bag packed into inner cardboard box*

The labelled leukapheresis collection bag should be placed inside the transparent specimen transport bag provided along with the absorbent material.

Gently expel any excess air from the specimen bag, ensuring that the leukapheresis bag is placed with the label facing towards the clear side of the specimen bag.

Before sealing the bag, it is important to ensure that the attached tubing set and absorbent material are not obscuring the leukapheresis label.

Place the transparent specimen transport bag into the cardboard box.

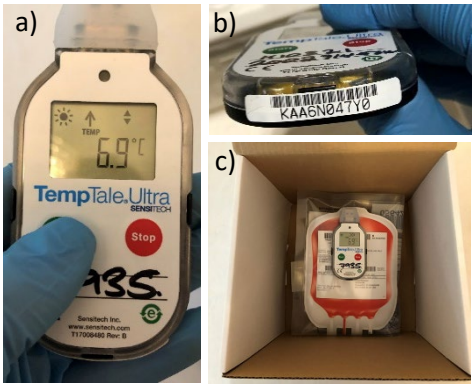



*Figure 5 – Temperature Monitoring Device*

Inspect the temperature monitoring device to ensure it is displaying a temperature reading. The sun icon in the upper left corner indicates that the device is active. (see Figure 7a)

Record the serial number for the tamper evident seal used in the Scheduling Portal. (see Figure 7b)

Remove the adhesive strip from the back of the temperature monitoring device

Place the device face up on top of the specimen bag and close the cardboard box. (see Figure 7c)

Affix one tamper evident seal to the closure of the cardboard box. **Record the serial number for the tamper evident seal used in the Scheduling Portal.**

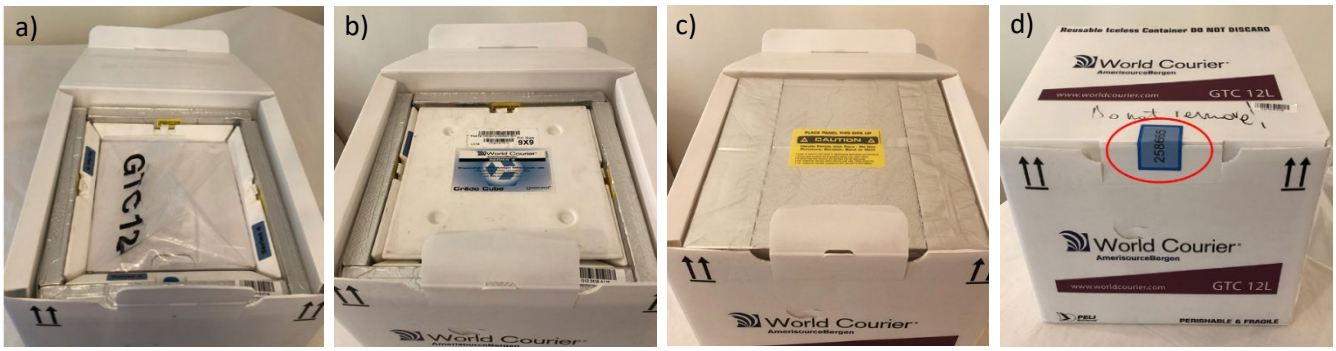



*Figure 6 – Replacement of a) inner cardboard box, b) cooling panel, c) insulated lid, and d) closure of corrugated plastic box with serialized seal (circled in image)*

Place the cardboard box into the temperature-controlled shipment box (see Figure 8a). Replace the cooling panel (see Figure 8b) followed by the insulated lid (see Figure 8c), then close the outer panel of corrugated plastic (see Figure 8d). Affix one tamper evident seal directly to the closure of the corrugated plastic box (see Figure 8d). **Record the serial number for the tamper evident seal used in the Scheduling Portal.**


*Figure 7 – Outer cardboard box with tamper evident seals*

Place the corrugated plastic box into the outer cardboard box. Apply 2 tamper evident seals to the outer cardboard box on completion of packaging. **Record the serial numbers of the seals used in the Scheduling Portal.**

Seal the cardboard box with adhesive tape.

Complete the leukapheresis packing details in the Scheduling Portal. A second user must attest.

**Dispatch Leukapheresis Material for Shipment**

On arrival to pick up the collection the courier will confirm the Autolus Chain of Identity ID of the shipment they are scheduled to collect. The leukapheresis material must not be handed over until the COI ID has been verified. The COI ID will be referenced on the air waybill for the shipment. It is the responsibility of the Apheresis Collection Center to ensure they are handing over the correct package to the courier.

The Apheresis Collection Center user must record handover of the leukapheresis shipper to the courier in the Scheduling Portal to establish chain of custody. Refer to AutolusAssist™ Scheduling Portal User Guide Task: Dispatch Collection Shipper.

The air waybill document maintains chain of custody. The air waybill **must be** signed by **both** the member of staff handing over the shipment box and the courier when the shipment is handed over to the courier. One copy of the signed air waybill must be retained by the Center for their records in accordance with local procedures.


*Figure 8 – Transport box with air waybill and shipping docs*

The remaining copies of the air waybill must be placed in the document pouch to travel with shipment along with 3 copies of both a Customs Invoice and a Do Not Xray instruction.

The document pouch should then be sealed.

## Apheresis related Adverse events and reactions

Notify AutolusAssist™ immediately of any deviations, non-conformances, or data integrity breaches this includes but not limited to, issues relating to the apheresis collection, storage, labelling, packing, shipment, chain of custody and chain of identity

Inform Autolus without delay, and within 24 hours at the latest, of discovery of any untoward occurrence which may be associated with the collection, testing, processing, storage, or distribution of tissue or cells intended for human application and which, in relation to a patient of tissues or cells intended for human application or a recipient of tissue or cells:

i. Might lead to the transmission of a communicable disease, to death or life-threatening, disabling or incapacitating conditions; or
ii. Might result in, or prolong, hospitalization or morbidity.

Contact Autolus AutolusAssist™ by telephone if there are any issues, delays, or questions.

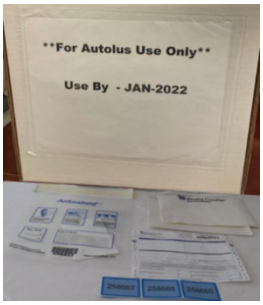
## Autolus Manufacturing Milestones

Periodic notifications regarding the progress of manufacturing and preparation for product delivery will be provided to the Apheresis Collection and Authorized Treatment Center by email and via the AutolusAssist™ Scheduling Portal. The estimated date for product delivery will be based on the manufacturing timeline, expected Quality release date, and shipping time to the Treatment Center.

Please refer to the **Autolus AUCATZYL® Product Handling Manual (US)** for guidance on communications and the process for distribution of AUCATZYL® product to the Authorized Treatment Center.

# Appendix 1 Shipping Leukapheresis Material using a NanoCool™ Shipper

NanoCool™ Temperature-controlled shippers will be supplied as a contingency. Always check the expiry dates of both the temperature monitoring device **and** the NanoCool™ box prior to use, and check that the activation buttons on the underside of the lid have not been depressed.




**Preparation for Shipping using a NanoCool™ shipper**

If advised by Autolus to use a back-up NanoCool™ shipper for a leukapheresis shipment, please ensure the kit contains:

- Transparent Specimen Transport Bag and Absorbent Material
- Tamper evident seals
- Temperature monitoring device
- Additional packaging (bubble wrap)

Activate the temperature monitoring device. The monitor has a start-up delay of 30 minutes. To turn the device on press and hold the green 'Start' button for 3 seconds. A sun icon will appear in the upper left corner of the display screen indicating that the device is active.

**Leukapheresis material Shipping Documentation (NanoCool™ use)**

To package the leukapheresis material, you will need three printouts of each of the shipping documents including the **air waybill** for shipment, the **Customs Invoice**, and the **Do not Xray instruction**.

## Instructions for Activation

Adapted from PELI Biothermal™

NanoCool® technology does not require refrigeration of the package or of the cooler prior to use.

To start the cooling process:

1) Open the package, remove the item with the silver foil (the cooler!), and place it, foil side down, on a hard, flat, surface. The white actuator button should be pointing upward.

2) In one motion, press straight down on each of the actuator buttons with a thumb (not a sharp object). Only a moderate amount of force is necessary to depress the actuator.

3) Depending on the ambient temperature, the NanoCool Logo should turn blue between 30 seconds and 3 minutes after activation. The blue indicates that the cooling action has begun which can be confirmed by touching the surface of the cooler near the button. Note: Storage of the NanoCool in cold environment (below 15°C/59°F) can cause the NanoCool Logo to turn blue before activation. Placing NanoCool at room temperature (21°C/70°C) for 15 minutes will revert the color (make the logo clear again).

4) Proceed with packaging the leukapheresis material as described in **Preparation of leukapheresis material for shipping to Autolus (Page 11)****. Use the additional packaging (bubble wrap) to wrap the leukapheresis material and ensure separation from the cooler.

5) **Please note that the NanoCool™ does not have a cardboard insert and all documentation should be completed prior to application of any of the tamper evident seals.

6) Complete the leukapheresis packing details in the Scheduling Portal. A second user must attest.

7) Replace the cooler in its original position. Press firmly and evenly to ensure a snug fit.


8) Close the package, insert the flaps, and apply 3 tamper evident seals where indicated. Additional clear packaging tape can be used to secure the box if necessary.

9) Attach the document pouch to the box ensuring the 'THIS SIDE UP' instruction is not obscured. Refer to the **Dispatch Leukapheresis Material for Shipment** instructions on **Page 13** ensuring that the shipping documents are sealed into the document pouch.

Your package is now ready for shipment!

# Appendix 2 Leukapheresis Collection Requirements Summary

| Topic | Summary guidance | Page |
|---|---|---|
| Therapeutic Washout | Please refer to Prescribing Information for study-specific washout requirements | 9 |
| Lab requirements | Repeat blood draw for IDM screening panel on day of collection (see page 7 for panel)<br>Complete Blood Count on day of collection | 6 |
| Label | An ISBT-128 Apheresis label affixed to base label of collection bag. Including as a minimum:<br>• DIN or Apheresis ID<br>• Collection Date<br>• Patient Name (Frist Name, Last Name)<br>• Date of Birth<br>• Autolus Chain of Identity number | 10 |
| Anti-coagulant | ACD-A only | 10 |
| Target yield | 1.5 x$10^9$ CD3+ cells | 11 |
| Target blood processing volume | ➢ 2 x Total blood volume (TBV)<br>• For patients with peripheral blasts a collection of up to 3 x TBV may be required<br>➢ For patients with high body mass index, we recommend using ideal body weight to calculate TBV | 11 |
| Other collection settings | Target a cell separation which minimizes the number of RBCs, granulocytes, and platelets in the collection product.<br>Other Parameters per institutional policy | 11 |
| Collection volume | Expected range: 50 – 400 mL.<br>• No required minimum or maximum<br>No added plasma required | 11 |
| Collection End Time | The time at the start of rinse back should be recorded as the Collection End Time. | 11 |
| Collection kit tubing | Tail: Minimum 10 cm (4 inches); ideally 15 cm (6 inches). Tubing does not need to be stripped.<br>Sampling bulbs may be sealed and removed before packaging | 11 |