INVESTIGATIONAL PRODUCT MANUAL
SBT777101

Investigational Product	SBT777101
Sponsor Name	Sonoma Biotherapeutics, Inc.
Legal Registered Address	201 Haskins Way, Suite 203 South San Francisco, CA 94080
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SONOMA BIOTHERAPEUTICS

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GLOSSARY OF TERMS

Autologous	Cells or tissues intended for the same recipient they were obtained from
Apheresis	The process of collecting whole blood, separating specific components by density via an external centrifugation apparatus, and returning the remaining components to the donor
Certificate of Release (CoR) for Infusion	Externally facing document issued by Sonoma Biotherapeutics and used to communicate the release of Investigational Product with associated product information
Chain of Identity (COI)	The permanent and transparent association of subject identifiers assigned at subject onboarding and used to identify their cellular therapy starting materials and Investigational Products
Chain of Identity (COI) Number	A Sonoma Biotherapeutics managed and controlled unique identifier that is generated and assigned to each autologous order. The Chain of Identity Number is directly associated to the subject identifiers and is used for traceability and verification throughout the entire cellular therapy process, from subject onboarding to Investigational Product infusion and post-infusion monitoring.
Clinical Trial Protocol	A carefully designed plan to safeguard the subjects' health and answer specific research questions
Clinical Site	Location where subjects are seen by study staff for study purposes, where study procedures are performed, where study product or materials are maintained, and where data and regulatory records are stored
Courier	An external group or supplier that manages the transport of Sonoma Biotherapeutics cellular therapy products, including but not limited to: starting material, in-process samples, finished product and Investigational Product
Exterior Shipper	The corrugated plastic container that makes up the external shell of the liquid nitrogen shipper where shipping documents are adhered via document pouch for easy access in-transit
Expiration Time	The time at which IP is considered expired. The time is calculated 3-hours from 'End of Thaw Time'

Investigator's Brochure (IB)	A compilation of the clinical and nonclinical data on the Investigational Product(s) that are relevant to the study of the product(s) in human subjects
Investigational Product (IP)	A drug or biological product that has not been approved for general use by the US Food and Drug Administration (FDA). It is used in a clinical trial to investigate the drug or biological product's safety and efficacy. The Investigational Product (eg, SBT777101) is released by Sonoma Biotherapeutics per product specifications and testing requirements.
Investigational Product Manual	Instructions/procedures for the clinical site that includes details on the administration of Investigational Product (eg, SBT777101)
Liquid nitrogen (LN2) Shipper	Package intended for transporting advanced therapies in vapor-phase liquid nitrogen composed of an exterior box made of corrugated plastic and an inner metal container containing liquid nitrogen and the payload
ModPak	Inner package containing Investigational Product cassettes with a handle for easy retrieval from liquid nitrogen shipper container
Screening	Procedures for clinical trial protocol eligibility that are considered part of the subject selection and recruitment process
Soft Pack	Foam insert between the exterior shipper and the inner liquid nitrogen-filled vessel of the liquid nitrogen shipper which is zipped closed in-transit
Subject	A person who is enrolled in the clinical trial, and who meets all eligibility criteria for enrollment into the clinical trial set out in the clinical trial protocol or otherwise
Subject ID	Clinical trial unique numbering scheme generated to identify a subject participating in the clinical trial
Waybill	A document that summarizes the details of and instructions relating to goods that are being transported and must accompany the Investigational Product from shipment to delivery

1. INTRODUCTION

The purpose of this manual is to document the processes and procedures associated with the receipt, handling, and administration of SBT777101 investigational product. Other study specific procedures and eligibility criteria will be described within the clinical trial protocol.

Read and acknowledgment of this Investigational Product (IP) Manual is required. The signed IP Manual Signature Page should be maintained within your investigator site file.

SBT777101 will be referred to as the IP in this manual.

1.1 Study Contacts

Table 1. Study Contacts

Sonoma SBT777101 Clinical Team	ClinicalOperations@Sonomabio.com
Sonoma Patient Operations	PatientOps@Sonomabio.com

2. INVESTIGATIONAL PRODUCT OVERVIEW

SBT777101 is a suspension of autologous human regulatory T cells (T_{regs}) expressing a chimeric antigen receptor (CAR) transmembrane protein which targets citrullinated proteins in the extracellular domain of subjects with inflammatory diseases. The starting material used in the manufacturing of the cell therapy product is obtained through apheresis collection.

Refer to the current Investigator's Brochure (IB) for more information about SBT777101.

2.1 Manufacturing Process

Peripheral blood cells are removed from a subject through apheresis collection. The apheresis material is enriched for $CD25^+$ cells and sorted for Treg cells, which are subsequently activated. The Treg cells are transduced with the SBT777101 lentiviral vector. Culture medium is added, cells are reseeded and subsequently expanded and the transduced Treg cells are restimulated. At Day 14, cells are harvested, filled into cryobags and cryopreserved. The IP is then stored in liquid nitrogen.

Upon completion of the manufacturing and release testing, the IP is shipped under qualified conditions to the clinical site and thawed prior to administration to the subject. Shipment to the clinical site will occur following the completion of required quality control testing.

3. INVESTIGATIONAL PRODUCT DELIVERY AND RECEIPT VERIFICATION

Once a subject's infusion date has been confirmed and the subject is deemed eligible for infusion, Sonoma will prepare to have the IP shipped and delivered to the infusion delivery location in advance of the scheduled infusion. Standard delivery is one business day prior to the scheduled infusion date, barring no shipping or manufacturing delays. Should the delivery or infusion date need to be rescheduled, contact Sonoma Patient Operations as soon as possible (Refer to Section 1.1).

3.1 Shipment Tracking and Delivery Notifications

In advance of the investigational product (IP) delivery, Sonoma Patient Operations will notify the clinical site with the confirmed delivery details. This email notification may include:

- Confirmation of appropriate staff to receive the IP
    - Delivery contact name
    - Delivery address
- Scheduled delivery date and time
- Subject's Sonoma Chain of Identity (COI) Number
- Web link access to the shipper's temperature monitoring and GPS device (can be provided upon request)

It is important to review these details for accuracy and notify Sonoma Patient Operations immediately if any updates or corrections are required.

Once the shipper is in transit, Sonoma Patient Operations will notify the delivery contact listed on the order if there are any delays to the scheduled delivery date or time. Every attempt will be made to deliver as planned but there are rare circumstances when unintended manufacturing or logistical anomalies, (i.e., airline delays from weather, manufacturing delay, etc.) may have an impact on the originally scheduled delivery time. If the infusion date is affected, Sonoma Patient Operations will notify the scheduling coordinator at the clinical site.

Sonoma Patient Operations will email the **IP Shipping and Receipt Form**, with electronic fillable fields and signature capabilities, prior to or during shipper transit. This form will be needed to receive and inspect the shipper. The recipient will have the option to complete the form electronically or manually.

3.2 Liquid Nitrogen Shipper and Logistics Overview

The IP is shipped to the clinical site in a liquid nitrogen (LN2) shipper, with continuous temperature and GPS monitoring, that is validated to maintain the temperature below -135°C. The scheduling process is designed to ensure adequate charge beyond the scheduled infusion date to ensure sufficient and continuous temperature storage conditions through the day of infusion. Should the infusion date change -post shipment, Sonoma Patient Operations will evaluate the shipper and determine if a fully charged replacement LN2 shipper needs to be sent and IP transferred for replacement storage.

The IP must never be removed from the LN2 shipper for on-site storage in freezers.

The LN2 shipping unit consists of an exterior shipper box with interior cushioning that houses the LN2 shipper for transit and storage. The outer box measures 23 in. x 23 in. x 35 in. The unit has wheels and an easy-to-use handle that can be used for easy maneuvering and transfer. The LN2 shipper itself does not get removed from the exterior shipper box and should always remain in the exterior shipper box.

Sonoma partners with qualified specialty couriers who are experienced in the transportation of cold chain cell therapy products. The courier supports the management of handling, storing and security of the IP during transit.

Below is an example of an LN2 shipper used by Sonoma for transporting IP:

3.3 Liquid Nitrogen Shipper Receipt and Inspection

Upon arrival at the delivery location, the receipt and inspection of the shipper will require immediate action by the approved delivery contact. The clinical site must follow institutional guidelines for receipt and handling of products in liquid nitrogen, human samples, and/or cell therapy products.

3.3.1 Receipt/Delivery of Shipment

1. Obtain the **IP Shipping and Receipt Form**. This form will be sent electronically in advance and as a hardcopy in the document pouch on the outside of the exterior shipper box. <u>This will be required to complete shipper receipt.</u>
    i. Complete the **IP Shipping and Receipt Form: Section 3**, either manually or electronically, concurrently with the following steps.
2. Review the accompanying waybill, located in the document pouch on the outside of the exterior shipper box, outlining the shipment details. Ensure the Subject's Sonoma COI listed on the waybill is as expected.
3. Check the exterior shipper box to ensure no visible damage and that the zip tie holding the box lid is secure.

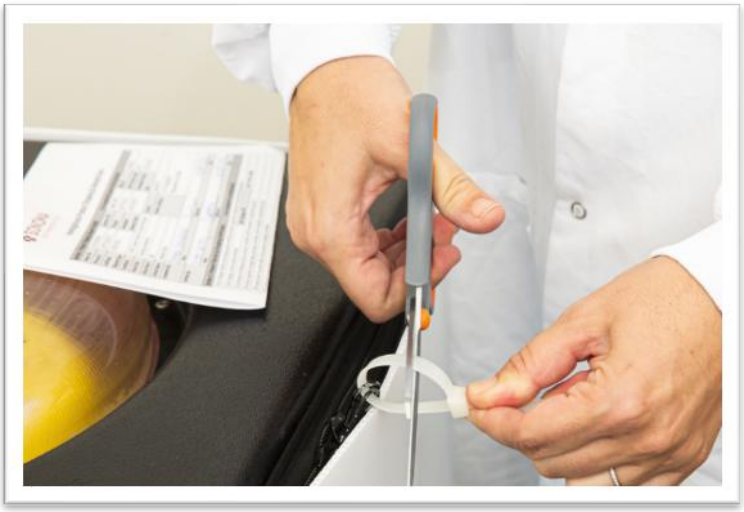
4. As the consignee, sign, date and document the time of delivery on the waybill, accepting control of the shipment from the courier. Retain a copy for your records.

3.3.2 LN2 Shipper Inspection

1. Cut the clear zip tie of the exterior shipper box and carefully lift the lid to expose the interior Soft Pack shipping layer housing the LN2 shipper.

2. Verify the zippers to the Soft Pack are secured with a zip tie and have not been cut or tampered with.

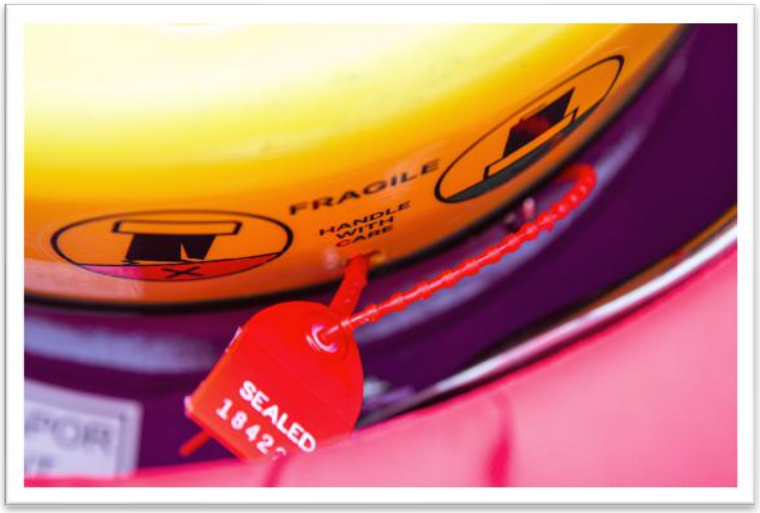
3. Cut the zip tie on the zipper of the Soft Pack.



4. Unzip the lid of the Soft Pack and carefully lift the Soft Pack lid, exposing the cap/lid of the LN2 shipper.
5. Access the document pouch, located within the Soft Pack of the shipper, and confirm the following is included:
    - **Certificate of Release (CoR) for Infusion**
    - Syringe Labels, used at time of infusion
    - Additional zip ties for use *set one aside to re-secure Soft Pack in later step*

6. Verify the serialized zip tie (eg, colored tag), securing the LN2 shipper cap/lid to the shipper, is intact and the cap zip tie serial number matches what is documented on the **IP Shipping and Receipt Form: Section 2.** Any discrepancies, contact Sonoma Patient Operations immediately.

   DO NOT cut the serialized zip tie. Only confirm it is intact and verify it matches what is documented. This zip tie will not be cut until time of infusion unless local site procedures require inspection upon receipt (see Step 0 below).



7. Verify the LN2 shipper ID, located on the LN2 shipper cap/lid, matches what is documented in the **IP Shipping and Receipt Form: Section 2.** Any discrepancies, contact Sonoma Patient Operations immediately.

8. Verify the shipper temperature is within range (≤ -135°C) by following either of the steps below:
    a. Use your phone or device to scan the QR code located on the left side of the shipper lid, then click on the link to take you to the current temperate reading on your phone/device.

Or

    b. Use the Temperature Indicator Button:
        1. Locate the Temperature Indicator Button (TIB) on the shipper lid and press the button to its fullest extent, then release.
        2. Wait approximately 5 seconds for the internal poll of the temperature to occur.
        3. If the LED light is **SOLID** and does not blink, then the temperature is **WITHIN** temperature range.
        4. If the LED light is **BLINKING**, then the temperature is **OUTSIDE** of temperature range.

NOTE: If the temperature is indicating as outside of the required range (≤ -135°C), please notify Sonoma Patient Operations immediately for next steps and/or troubleshooting.

9. In the event local site procedures require confirmation of IP integrity and/or identity inspection upon receipt, proceed with IP inspection per local procedures with the following considerations:
    - Cut and discard serial zip tie. Remove shipper cap and remove ModPak from LN2 shipper. Remove IP cassette from ModPak. See Section 4.4.
    - Complete inspection per local site procedures.

    Note – to minimize temperature fluctuation within the shipper (during and after inspection) please replace shipper lid (yellow SmartCap) to the cylinder promptly to close opening

    - **Do not expose the IP to ambient temperature (20 - 25°C) for more than 2 minutes during inspection.** Minimize contact or manipulation (i.e. massaging, wiping, rubbing, clearing ice) to the IP cassette and/or IP bag to prevent inadvertent thawing or damage.
    - Upon completion of inspection, return the IP cassettes immediately back into the LN2 shipper.
    - Record inspection times on the **IP Shipping and Receipt Form.**
    - Secure LN2 shipper with zip tie.

10. Return remaining materials and documents to the document pouch, on the Soft Pack, for storage until time of infusion.
11. Close the Soft Pack lid and re-secure with provided zip tie.
12. Close the exterior shipper box lid.
13. Move the shipping unit into a secure area with controlled access and cellular service to ensure continuous temperature monitoring, in alignment with institutional policy.
14. Complete, sign, and submit the **IP Shipping and Receipt Form**. If completed manually instead of electronically, please:
    i. Send a scanned PDF file to PatientOps@sonomabio.com as soon as possible.
    ii. Return completed form back to the document pouch on the outside of the exterior shipper box to be accessed on the day of infusion.
    iii. Retain a copy in the subject's file.

4. INVESTIGATIONAL PRODUCT HANDLING, PREPARATION, AND ADMINISTRATION

The IP may only be administered in a healthcare facility approved by Sonoma. SBT777101 is an investigational therapy and is not approved for any indication at this time.

The inner chamber of LN2 shipper contains the SBT777101 IP.

Do not open the LN2 shipper until the time of thaw, following subject eligibility confirmation and pre-medication administration, and just prior to the administration of SBT777101 to the subject.

Once fully thawed, SBT777101 infusion must be completed within 3 hours.

4.1 Supplies/Equipment

Assemble the following supplies prior to opening the inner chamber of the LN2 shipper to retrieve the IP bag. Ensure the following equipment is readily available and in validated conditions.

Supplies:

- Disposable absorbent protective barrier pads
- O-Wrap overwrap pouch
- Cryogloves and relevant PPE
- Luer-Lok sterile syringes – volume capacity guided by dosage volume on the **CoR for Infusion**
- Sterile needle free bag spikes (chemospike)
- 0.9% NaCl (normal saline)
- 70% IPA alcohol swabs
- Infusion tubing
- Supplies for blood sample collection in the event of an infusion related adverse event (Refer to Section 4.6.1)

Equipment:

- Water bath warmed to 37°C or Commercial Dry Automated Thawer set to 35°C.

4.2 Pre-Medications

Once the subject has completed the clinical trial protocol required assessments and the study site staff have verified the subject's identity, the subject should receive pre-medications with an antipyretic (eg, acetaminophen 650 mg PO) and/or an antihistamine (eg, diphenhydramine 25-50 mg PO or IV, or other H1-histamine blocker) as required per clinical trial protocol.

Pre-medications should be administered 30-60 minutes prior to IP infusion administration.

Place peripheral intravenous (IV) or peripherally inserted central catheter (PICC) as clinically indicated if the subject does not already have a central line. Subject will be prepared by starting an IV infusion of 0.9% NaCl (normal saline) to keep the infusion line open during IP administration and used in the event of an acute anaphylactic or infusion reaction.

Ensure tocilizumab is readily available if signs or symptoms of cytokine release syndrome (CRS) develop as defined in the clinical trial protocol.

4.3 Day of Infusion Criteria

Prior to thawing the IP on the day of infusion (Day 1):

- Subject must be confirmed as eligible per clinical trial protocol
- Subject identity must be confirmed by the study site staff per institutional policy
- Subject must complete all pre-medications as per clinical trial protocol as described above
- Subject IV access must be confirmed: peripheral IV (18-20 gauge), peripherally inserted central catheter (PICC), or central line as clinically indicated for access

In addition, clinical assessments, as described in the clinical trial protocol, may include but are not limited to:

- Vital signs (including blood pressure, temperature, respiratory rate, heartrate, and oxygen saturation)
- Directed physical exam
- Review of concomitant medications

IMPORTANT: Preparation and administration of the IP **MUST** be delayed and the Sponsor Medical Monitor contacted if the subject has any signs and/or symptoms of a clinically significant medical finding that was not present at screening or during the Pre-Treatment eligibility checks or if there is evidence of an infection requiring systemic treatment.

4.4 Investigational Product Handling and Preparation

4.4.1 Shipper Verification

1. Carefully transport the shipper to its unpacking location.
2. Retrieve the **IP Shipping and Receipt Form** from the document pouch on the outside of the exterior shipper box.
3. Obtain the **IP Preparation and Administration Form.** This form will be sent electronically in advance.
    i. Complete the **IP Preparation and Administration Form**, either manually or electronically, concurrently with the following steps.

4. The work area should be an empty counter space (other sturdy flat surface) for laying out the cassette containing the IP bag flat and for completing the applicable forms. Place disposable absorbent barrier pad and have all supplies readily available.

5. Carefully lift the lid of the exterior shipper box to expose the interior Soft Pack shipping layer housing the LN2 shipper.
6. Cut the zip tie on the zipper of the Soft Pack.
7. Unzip the lid of the Soft Pack and carefully lift the Soft Pack lid, exposing the cap/lid of the LN2 shipper.

8. Verify the shipper temperature is within range (≤ -135°C) by following either of the steps below:

   i. Use your phone or device to scan the QR code located on the left side of the shipper lid, then click on the link to take you to the current temperate reading on your phone/device.

Or

   ii. Use the Temperature Indicator Button:

      1. Locate the Temperature Indicator Button (TIB) on the LN2 shipper lid and press the button to its fullest extent, then release.
      2. Wait approximately 5 seconds for the internal poll of the temperature to occur.
      3. If the LED light is **SOLID** and does not blink, then the temperature is **WITHIN** temperature range.
      4. If the LED light is **BLINKING**, then the temperature is **OUTSIDE** of temperature range.

NOTE: If the temperature is indicating as outside of the required range, please notify Sonoma Patient Operations immediately for next steps and/or troubleshooting.

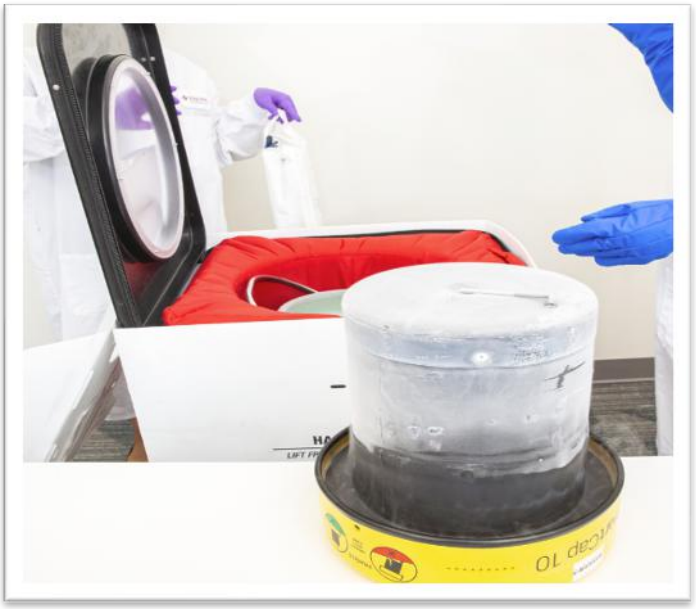
9. Access the document pouch, located within the Soft Pack of the shipper.
10. Verify subject is eligible and prepared for infusion.
11. Confirm the subject's identity and compare against the **CoR for Infusion** and the syringe labels.

    NOTE: Verification of the subject's identity by the study site staff should be performed per institutional policy.
12. Confirm that the IP is within expiration dating by checking the expiration date listed on the **CoR for Infusion**.
13. Confirm the serialized zip tie (eg, colored tag), securing the LN2 shipper cap/lid to the shipper, is intact and the serial number matches what is documented on the **IP Shipping and Receipt Form: Section 2**. Any discrepancies, contact Sonoma Patient Operations immediately.

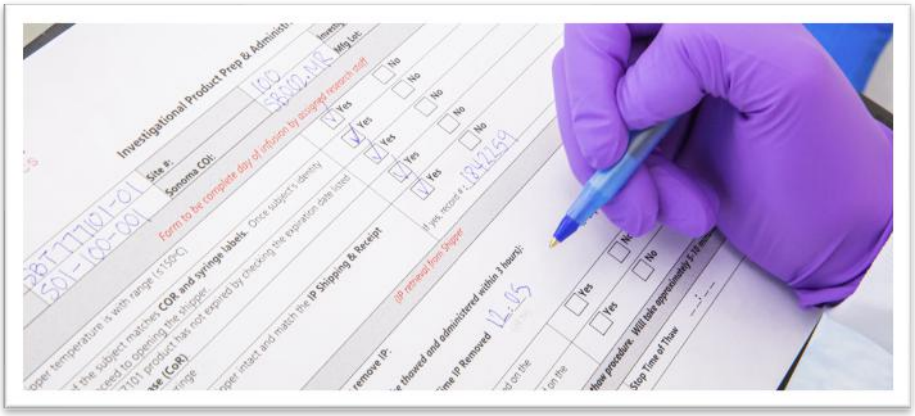
4.4.2 IP Retrieval from Shipper

Complete the **IP Preparation and Administration Form**, either manually or electronically, concurrently with the following steps.

1. Cut the serialized zip tie on the LN2 shipper and discard the zip tie.
2. Carefully remove the LN2 shipper cap/lid and place it upside down on a flat surface.



3. Using extreme care and wearing cryo gloves, remove the ModPak bag from the inner LN2 chamber.
4. Record the 'Date IP Removed' and 'Time IP Removed' from the shipper on the **IP Preparation and Administration Form: Section 3**.



5. Using extreme care, remove the cassette from the ModPak. Do not bend, shake, or put weight on the cassette. Review the label on the cassette to verify that the information on the label is consistent with the **CoR for Infusion**.
   NOTE: The cassette may be placed on dry ice or kept in a LN2 shipper when transporting the IP to another location for IP thaw and preparation. If transporting, prepare/thaw product immediately after transport is complete. Dimensions of the cassette are 6 3/8" x 3 5/8" x 3/8" without the hinges, and 6 1/2" x 3 5/8" x 3/8" with the hinges.

6. Carefully open the cassette and review the IP bag label to verify that the information on the label is consistent with the **CoR for Infusion**.
7. Carefully inspect the IP bag for any signs of damage (cracks, broken ports, discoloration, etc.). If any damage is present, contact Sonoma Patient Operations immediately.

4.5 Investigational Product Thaw and Administration

4.5.1 IP Thaw

Thaw the IP in a cell therapy laboratory or equivalent, prepare the dose and transport immediately to infusion area per institutional policy. Complete the **IP Preparation and Administration Form**, either manually or electronically, concurrently with the following steps.

1. Ensure the water bath is prepared and temperature set at 37°C. If using a dry automated thawer, ensure thaw temp is set to 35°C and thaw time to 6 minutes.

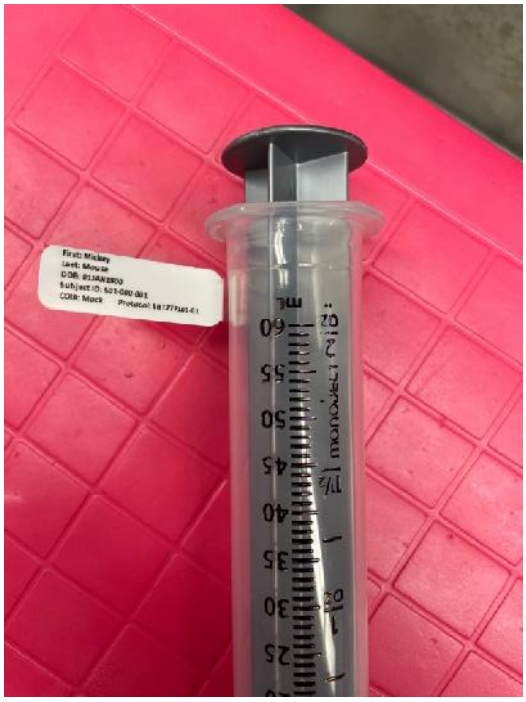
2. Carefully place O-Wrap overwrap pouch over the IP bag (follow applicable water bath or dry automated thawer methods).

3. Place the IP bag with the overwrap pouch in the water bath to commence the thaw procedure. This step will take approximately 5-7 minutes.

   OR if using a dry automated thawer place the IP bag with the overwrap pouch into the thawer and commence thaw for designated time.

4. Record the 'Start Time of Thaw' on the **IP Preparation and Administration Form: Section 4**.
5. Thaw until a small amount of ice remains in the IP bag. Gently massage the bag to mix the contents and until no ice crystals remain.
6. Place the thawed IP on the prepared work area.
7. Record the 'End Time of Thaw' on the **IP Preparation and Administration Form: Section 4**.
   i. Once the IP is fully thawed, it expires in **3 HOURS.** IP infusion must be completed within 3-hours of end of thaw.
   ii. Calculate the 'Expiration Time' by adding 3 hours to the 'End Time of Thaw'.
   iii. Record the 'Expiration Time' on the **IP Preparation and Administration Form: Section 4**.
8. Carefully remove the IP bag from the overwrap pouch.
9. Carefully inspect the IP bag for any signs of damage (cracks, broken ports, discoloration, etc.). If any damage is present, contact Sonoma Patient Operations immediately.
10. Adhere the verified syringe label to the syringe (ensure the volume markings are not obscured) and place the syringe in the work area.

    NOTE: Syringe labels are double-sided "flag" style. When removed from the backing the label is folded and then wrapped around the syringe.



11. Twist to remove the spike port cover from the IP bag.
12. Carefully wipe off the spike port with 70% IPA alcohol wipes.

13. Using extreme caution, spike the bag with the needle-free bag spike. It may be easiest to spike the bag by twisting the spike into the port. NOTE: It is normal to feel significant resistance when pushing and twisting the needle free spike into the port.

14. Attach the syringe to the plunger access port of the spike. (Luer Lock syringe)

15. Once the syringe is attached, carefully draw the intended volume of the IP ('Total Dosage Volume' on **CoR for Infusion**) into the syringe.
16. Record the 'Volume of IP Drawn into Syringe' on the **IP Preparation and Administration Form: Section 4**.
17. Verify the volume within the syringe matches the 'Total Dosage Volume' on the **CoR for Infusion**.
18. Transport the prepared syringe to the subject's bedside. Prepared syringes may be transported at ambient temperature.

4.5.2 IP Administration

IP Infusion must be completed before 'Expiration Time' (calculated 3-hours from 'End of Thaw Time'). Complete the **IP Preparation and Administration Form**, either manually or electronically, concurrently with the following steps.

1. Confirm the IP is within 'Expiration Time'.
2. Re-Confirm subject's identity and compare against the syringe labels.

   NOTE: Verification of the subject's identity by the study site staff should be performed per institutional policy.
3. Attach the syringe to the closest access port to the subject.
4. Record the 'Start Time of Infusion' on **IP Preparation and Administration Form: Section 5**.
5. Initiate IP administration at 3 mL/min (or fast push if dose volume is less than 3 mL).
6. The entire syringe volume must be administered unless an adverse event warranting interruption or termination occurs.

   NOTE: Refer to Section 4.6 for guidance on any interruption to IP administration. Any interruption should be recorded on the **IP Preparation and Administration Form: Section 6**.

7. Record the 'End Time of Infusion' on the **IP Preparation and Administration Form: Section 5**.
8. Record the 'Total Volume of IP Administered' on the **IP Preparation and Administration Form: Section 5**.
9. Following administration of the IP, flush with normal saline.

4.6 Interruptions To Investigational Product Administration

In the event of any interruption to IP administration, the 'Time of Interruption to IP Administration' and reason for interruption should be recorded on the **IP Preparation and Administration Form: Section 6** and Sonoma Patient Operations should be notified immediately.

If the reason for interruption is addressed and it is ultimately determined by the study site staff and Sonoma that it is safe to recommence IP administration:

1. Calculate time to completion and re-confirm IP is still within 3-hour window.
2. Record 'Re-Start Time of Infusion', 'End Time of Infusion' and 'Total Volume of IP Administration' on the **IP Preparation and Administration Form: Section 6a**.

If the reason for interruption cannot be addressed within the 3-hour window or it is ultimately determined by the study site staff and Sonoma that it is unsafe to recommence IP administration:

1. Record Reason for incomplete IP administration on the **IP Preparation and Administration Form: Section 6b**.
2. Calculate volume administered based on volume remaining in the syringe and record 'Estimated Volume of IP Administered' on the **IP Preparation and Administration Form: Section 6b**.

4.6.1 Infusion Related Reactions

Infusion related reactions are considered a potential risk for autologous cell therapies such as SBT777101, and therefore pre-treatment medications are required, as noted in Section 4.2.

- As per the clinical trial protocol, blood samples for potential analyses of infusion reaction mediators should be collected at the time of any infusion related reaction adverse event, using the unscheduled visit kit provided.

Follow the management guidelines of infusion reactions in accordance with the clinical trial protocol:

- For mild reactions (Grade 1) with onset during an IV infusion, continue infusion of IP at the same rate. Supportive care (eg, antipyretics and/or antihistamines) may be administered as clinically indicated.
- For reactions of Grade 2 severity, pause the IP infusion and administer supportive care. IP infusion may be re-initiated at a reduced rate (50%).
- For reactions of Grade 3 severity, pause the IP infusion and administer supportive care. If symptoms resolve to ≤ Grade 2, IP infusion may be re-initiated at a reduced rate (50%). If symptoms recur or worsen, discontinue infusion of the IP.
- For reactions of Grade 4, discontinue infusion of the IP.
- For reactions occurring after an IV infusion, apply supportive care as necessary.

Subjects experiencing anaphylaxis may not restart SBT777101 infusion.

4.7 Clinical Safety Monitoring

All subjects will be directly and continuously monitored during IV administration of SBT777101, and in the inpatient setting for the first 24 hours post-infusion of IP. Safety assessments pre-administration and during the post-administration monitoring period are described in the clinical trial protocol.

Due to the investigational nature of SBT777101, the safety profile is not yet established, and the risks are unknown. As a result, Sonoma recommends the following:

- Subjects should remain within approximately 60 minutes of the cell therapy treatment facility during the first 7 days following SBT777101 administration.
- Subjects have an adult companion or caretaker with them at all times for the first 28 days following SBT777101 administration to ensure the ability to seek medical care in the event of an emergency.

All subjects will be supplied with a study-provided thermometer and asked to check and record their temperatures into a paper diary at specified frequencies outlined in the clinical trial protocol until end of study following SBT777101 administration. Subjects will be instructed to seek medical attention for a temperature of ≥ 38°C (100.4°F).

5. INVESTIGATIONAL PRODUCT POST-ADMINISTRATION HANDLING PROCEDURES

5.1 Cell Product Disposal and Destruction

Any unused IP remaining within an IP bag (open/unopened) should be disposed of in accordance with the institution's biohazard disposal policy. Please do NOT return any unused product, packaging, or shipping materials back to the LN2 Shipper.

Residual SBT777101 containing material may include:

- SBT777101 product bag
- Absorbent barrier pads
- Any supplies used in the preparation process
- Syringes
- SBT777101 syringe labels
- ModPak and cassettes
- Other material used for IP Prep

Disposal of used or unused product and supplies is to be recorded on the **IP Disposal and Destruction Form**.

5.2 LN2 Shipper Return Instructions

The standard return pickup for all empty shipper returns is scheduled for 9 am local time ***one business day after the scheduled infusion***. The courier will arrive for the pickup at the same location it was delivered to. **The LN2 shipper must be empty.**

Should the infusion date be rescheduled or delayed, the LN2 shipper return pickup will be rescheduled accordingly by Sonoma Patient Operations. The courier assigned for the pickup of the LN2 shipper will bring a copy of the return waybill. Please contact Sonoma Patient Operations to request any return reschedules or pickup location changes.

APPENDIX 1: SBT777101 SPECIFICATIONS

Table 2: SBT777101 Specifications

Attribute	Analytical Procedure	Acceptance Criterion
% CD4+FOXP3+ cells	FACSLyric Flow Cytometer	≥ 70%
% CD4+ cells	FACSLyric Flow Cytometer	≥ 84%
% CD4 + EGFR+ cells (Transgene Expression)	FACSLyric Flow Cytometer	≥ 30%
% $CD4^{-}CD8^{+}$ cells	FACSLyric Flow Cytometer	≤ 5%
Mycoplasma in Drug Substance Cell Culture Supernatant	Rapid Detection of Mycoplasma by Real-Time PCR	Negative
Sterility in Pre-Formulation and of Final Drug Product	Sterility Evaluation by BACT/ALERT 3D System	No microbial growth
Endotoxin	Endotoxin Testing Using the Charles River Endosafe® nexgen-MCS™	≤ 3.5 EU/mL
Vector Copy Number	Determination of Gene Copy Number using Droplet Digital PCR (ddPCR)	≤ 5.0 copies per transduced cell
Vesicular Stomatitis Virus G (VSV-G) qPCR	qPCR Assay for the Detection of VSV-G Proviral DNA	Below Limit of Detection[1]
Viable Cell Count	Cell Counting Using NC-202	15 - 45 × 10^6 viable cells/mL
Viability	Cell Counting Using NC-202	≥ 70%

[1]Limit of Detection = 10 copies per reaction

APPENDIX 2: SBT777101 RELEASE CRITERIA

Table 3: Release Testing for Finished SBT777101 Drug Product

Attribute Category	Attribute	Specification
Identity	%$CD4^+$ $FOXP3^+$ cells	≥ 70%
	% $CD4^+$ cells	≥ 84%
	%$CD4^+$ $EGFR^+$ cells (Transgene Expression)	≥ 30%
Safety	Mycoplasma in Drug Substance Cell and Culture Supernatant	Negative
	Sterility in Pre-Formulation and of Final Drug Product	No Microbial Growth
	Endotoxin	≤ 3.5 EU/mL
	Vector Copy Number	≤ 5.00 copies per transduced cell
	Vesicular Stomatitis Virus G (VSV-G) qPCR	Below Limit of Detection[1]
Purity	% $CD4^-CD8^+$ cells	≤ 5%
Strength	Viable Cell Count	15 – 45 x 10^6 viable cells/mL
	Viability	≥ 70%