SONOMA BIOTHERAPEUTICS

SBT777101 HS SKIN BIOPSY AND PHOTOGRAPHY MANUAL

Study Number	SBT777101-02
Study Title	A Phase 1 Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Activity of Single Ascending Doses of SBT777101 in Subjects with Hidradenitis Suppurativa
Investigational Product	SBT777101
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Document Version Number	V4.0
Version Date	02JUL2025

Sponsor Signatory:

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Mei-Lun Wang, MD

7/2/2025

Date

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VERSION HISTORY

VERSION DATE	VERSION NUMBER	SUMMARY
18Mar2024	Version 1.0	Initial draft
29Mar2024	Version 2.0	Fixed Version Date in table on page 1 Added minor revisions to language and content regarding biopsy procedures and photographs
22May2025	Version 3.0	Renamed document to SBT777101 HS Skin Biopsy and Photography Manual Added Version History table Updated Section 4 Supplies and Equipment (which now includes the addition of a 'ruler') Removed optional procedure involving the placement of biopsy tissue in a petri dish containing PBS prior to transferring the biopsy tissue to formalin Added language and images for additional clarity surrounding photographs, which aligns with HS Protocol version 3.0, dated 01May2025
11Jun2025	Version 4.0	Clarified language in Section 5.2 to address photography involving vulnerable and PHI-sensitive areas of the body

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LIST OF ABBREVIATIONS

Abbreviation	Definition
A/N	abscess or nodule
CAR	chimeric antigen receptor
CRF	case report form
CTCAE	Common Terminology Criteria for Adverse Events
FFPE	Fixed formalin paraffin embedded
NBF	Neutral Buffered Formalin (also referred to as' formalin')
PD	pharmacodynamic
PHI	Protected Health Information
PK	pharmacokinetic
PPE	personal protective equipment
HS	Hidradenitis suppurativa
SOA	Schedule of Assessments
T_{reg}	regulatory T lymphocyte

1. INTRODUCTION

SBT777101 is a genetically engineered chimeric antigen receptor (CAR) regulatory T lymphocyte (Treg) cell therapy, designed to treat Hidradenitis suppurativa (HS) patients with Hurley stage 2 and 3 diseases. As part of this clinical trial, biopsies from an actively inflamed HS abscess or nodule (A/N) are required. All study participants will undergo 3 mandatory skin biopsies: at pre-treatment (Baseline), and post treatment Week 4 (WK4) and Week 12 (WK12). In addition, with subject consent, an optional skin biopsy may be performed at screening.

During the course of the study, 2 sets of photographs will be taken as follows:

1. The overall appearance and location of inflamed skin will be monitored by taking high resolution serial photographs of the affected skin taken at screening, pre-treatment, and post-treatment weeks 4, 8, 12, 18, 24, 36, and 48 (or End of Study).
2. Additionally, each time a biopsy is undertaken, photographs will be taken of each biopsy to document the location and size of the biopsied tissue.

2. SCOPE

The purpose of this biopsy and photography manual is to provide standard procedures for the acquisition, handling, processing, storage, and shipment of HS skin biopsies obtained by the clinical team at each clinical study site, and to provide standard procedures for photo-documentation of affected skin lesions at protocol-defined timepoints.

3. PERSONNEL

Biopsy Team: The team should be comprised of members with the following functional roles, who will fulfill the following responsibilities (Note: one person may fulfill more than one of these roles).

3.1. Proceduralist (i.e., Dermatologist, or designated qualified personnel)

A. Ensure the subject has been consented to study participation and is informed of the risks associated with the biopsy procedure.

B. Confirm the presence of a large, affected HS skin region with multiple active inflammatory A/N.

C. The proceduralist should - photo-document affected skin areas as instructed in Section 5.2 and Section 6.3.3.

D. Of note, the study site personnel involved in the biopsies will need to be trained by the Sponsor prior to undertaking the biopsies.

3.2. Specimen Manager

The Specimen Manager(s) should be staff members who have completed site protocol training and are acquainted with the study-specific supplies for specimen collection. Their responsibilities include:

A. Proper preparation of the specimen collection supplies, label and reagents prior to biopsy procedure.

B. Proper handling and processing of the study samples.

C. Proper storage and shipping of the study samples.

The Specimen Manager(s) should be notified with ample time prior to the start of the biopsy procedure, in order to allow for pre-procedure planning and preparation (Section 6.2).

4. SUPPLIES AND EQUIPMENT

4.1. Standard Site-Provided Supplies and Equipment for the skin biopsy procedure and processing

The following list of supplies and equipment are needed for the skin biopsy and are not provided by the study Sponsor:

- 1 or 2 % Lidocaine (max 4.5mg/kg)
- Sterile 2” x 2” 12-ply gauze pads (pack of 12)
- Tongue depressor
- Alcohol, at least 90% (e.g. ethanol, isopropyl)
- Saline solution
- Sterile gloves in sufficient quantity to double glove for all involved in the procedure
- Face masks and hair covers in sufficient quantity for all involved in the procedure
- 3M Coban self-adherent wrap
- Bacitracin ointment packets in sufficient quantity for wound care for 3 days after the procedure
- Access to a high-resolution camera and an ability to upload the photographs
- Ice bucket or other container to keep reagents cold

4.2. Sponsor-Provided Supplies and Equipment for skin biopsy procedure and process

Please use the Sponsor-provided supplies (e.g., vials, reagents) and associated labels according to the instructions provided in this manual.

- Biopsy Visit Requisition Form (Example in Appendix A)
- Bulk supplies
  - 6mm punch biopsy tool
  - Sterile forceps
  - Sterile scalpel
  - Ruler
  - Sterile pipettes (for transfer of reagents)
  - 20 mL vial pre-filled with 10% Formalin
  - 20 mL SecurTainer container (for use if biopsy samples in 10% formalin is not shipped within 24 hr)
  - 70% Reagent Grade Alcohol (for use if the biopsy samples in 10% formalin is not shipped within 24 hr)

5. PHOTO-DOCUMENTATION OF AFFECTED SKIN

5.1. Subject Consent

The informed consent form must be signed by the study investigator and subject prior to the initiation of any protocol-specific screening procedures.

5.2. Overview photography

- Photographs should be taken to document the appearance and location of all inflamed skin areas per protocol-defined timepoints
- For photographs of vulnerable areas such as the groin or buttocks, participants may choose to cover these areas with either underwear or draping, even if this may obscure some of the lesions. Similarly, identifiable marks such as face, tattoos, other and identifiable marks may also be covered with draping, even if this may obscure some of the lesions.
- In addition, photographs of identifiable marks which are not draped, such as the face, tattoos, other identifiable marks, may be taken and placed in the participant's binder, but will not be submitted to a sponsor.
- Set camera to highest resolution setting
- It is anticipated that multiple photographs will be needed to capture all affected regions.
    - Name each file with the affected region area: “SBT77710102 [Subject ID] [VISITCD]_[Region].jpeg” and store in the subject file

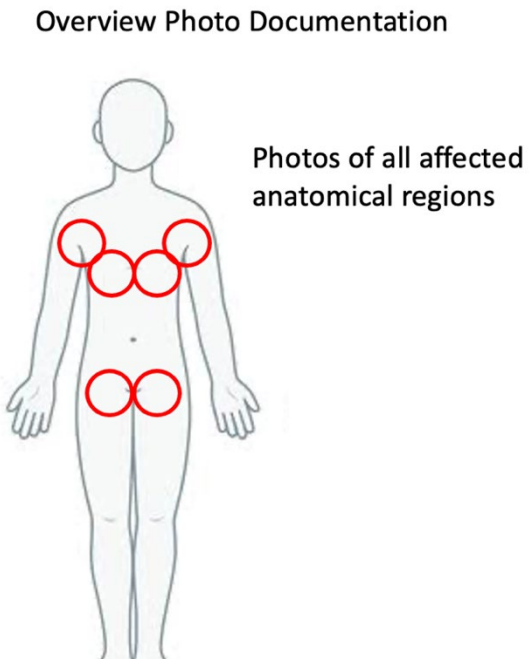

Figure 1: Overview photo documentation guide to demonstrate possible areas of inflamed skin that may need to be photographed at protocol-defined timepoints

6. PREPARATION OF BIOPSY PROCEDURE

6.1. Subject Consent

The informed consent form must be signed by the study investigator and subject prior to the initiation of any protocol-specific screening procedures.

6.2. Pre-Procedure Supplies and Preparation for Sample collection

The Specimen Manager should ensure that all necessary collection vials, reagents, and supplies are prepared and if needed brought to the procedure room.

- Vial containing 10% formalin, to be used for FFPE skin tissue fragment (20 mL)
- Sterile Forceps
- Identify appropriate labels from the requisition form for each sample type.

Note: Labels should only be removed from the requisition forms after biopsy collection and immediately prior to transferring the biopsies to the designated vials (see Section 9).

6.3. Pre-biopsy lesion Evaluation (Screening [optional], Baseline [pre-treatment], WK4 and WK12)

6.3.1. Screening biopsy (optional, prior to apheresis)

On the day of the screening biopsy, select an anatomical area with at least one lesion that can be biopsied. Please note, that if there is only one anatomical area with multiple A/N, that area should be reserved for the protocol-required biopsies at Baseline (pre-treatment), Week 4, and Week 12. In other words, the screening biopsy can be taken from an anatomical area which will not necessarily be biopsied a second time.

6.3.2. Baseline Biopsy (pre-treatment [Day-7 to Day 1])

On the day of the baseline biopsy, select the largest anatomical region with multiple A/N. Select an inflammatory lesion >1 cm for the biopsy and avoid *fibrotic tissue.*

Note: When conducting biopsies, ensure they are taken from inflamed areas of lesional skin and not solely from the center of the lesion. Avoid sampling pus.

6.3.3. Photo-documentation of the lesion

Photo-document the selected anatomical region. Two sets of photographs should be taken:

- Photograph set #1 - Overview photos to document the affected anatomical region with multiple lesions which will be used as a reference for the Week 4 and Week 12 biopsy (e.g. axilla)

  - Name the file: "SBT77710102 [Subject ID] [VISITCD]_[Location]_[Biopsy_Overview].jpeg" and store in the subject file

- Photograph set #2 – A/N close-up photographs to document the planned biopsy area (Baseline, Week 4 and Week 12). Place the provided ruler adjacent to the biopsy area and ensure it is captured and that the markings are in focus in the photograph.
  - Name the file: "SBT77710102 [Subject ID] [VISITCD]_[Location]_[Biopsy_Closeup].jpeg" and store in the subject file

Subsequent biopsies collected at Week 4 and Week 12 should also be photographed with a ruler (provided in the visit kit).

- Name the file: "SBT77710102 [Subject ID] [VISITCD]_[Location]_[Biopsy_Closeup].jpeg" and store in the subject file.
- Upon request, the photos may be transferred to the Sponsor per instructions in the ClinTrak Site Source Study Portal Quick Reference Guide (provided separately).

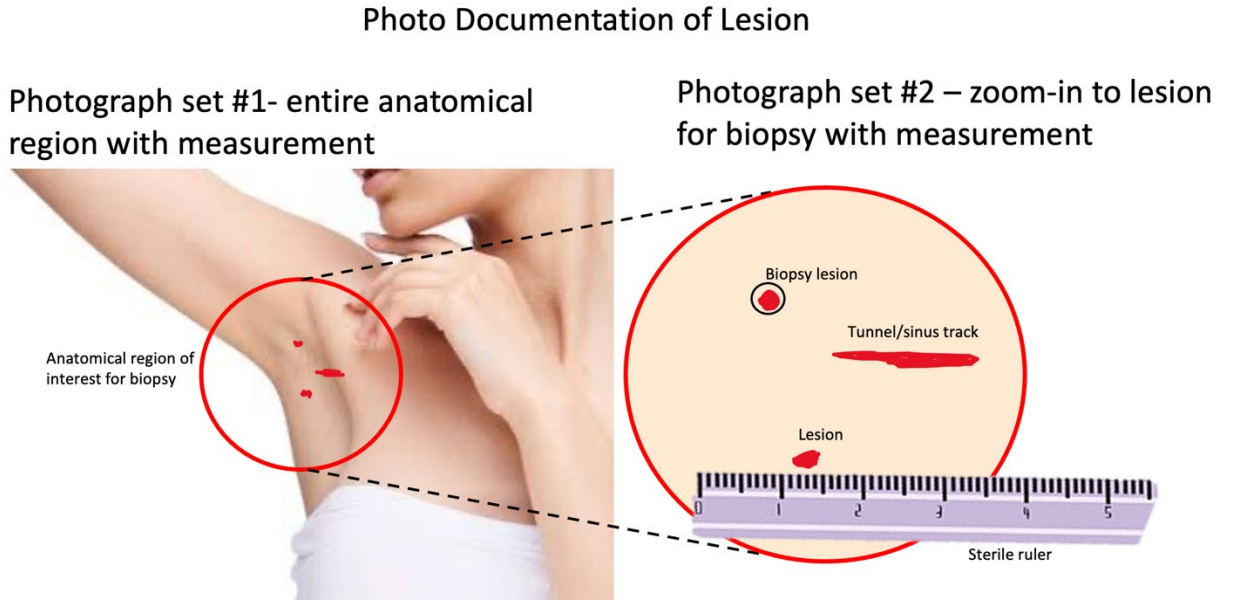

Figure 2: Photo documentation of lesional biopsy area

6.3.4. WK4 and WK12 Biopsy

At Week 4 and Week 12, a biopsy, and photographs, should be collected from the same anatomical region as baseline in the following order (Refer to the photo document from baseline):

- Biopsy an existing A/N. Refer to Baseline Photoset #1 to ensure that the A/N was present at baseline (see Section 6.3.3).

- *If* all the pre-existing A/Ns identified at the baseline timepoint are resolved, then the biopsy should be taken from a new lesion that was not present at baseline in the same anatomical area as the first biopsy.
- *If* no A/N are identified in the selected anatomical region, the biopsy should be obtained from the unaffected skin in the same anatomical area and close to the previously biopsied section (see section 6.3.3), with caution taken to avoid scar tissue.
- A perilesional biopsy may also be collected (**optional**) at each time point. Perilesional skin is defined as normal-appearing skin 2cm away from the inflammatory lesion (biopsied lesion).

  Note: The lesion morphology should be classified (e.g. inflammatory nodule, abscess) and the same type of lesion should be biopsied at each time point.

  Note: The location of all biopsies taken must be recorded on the requisition form and in the electronic data capture (EDC) system.

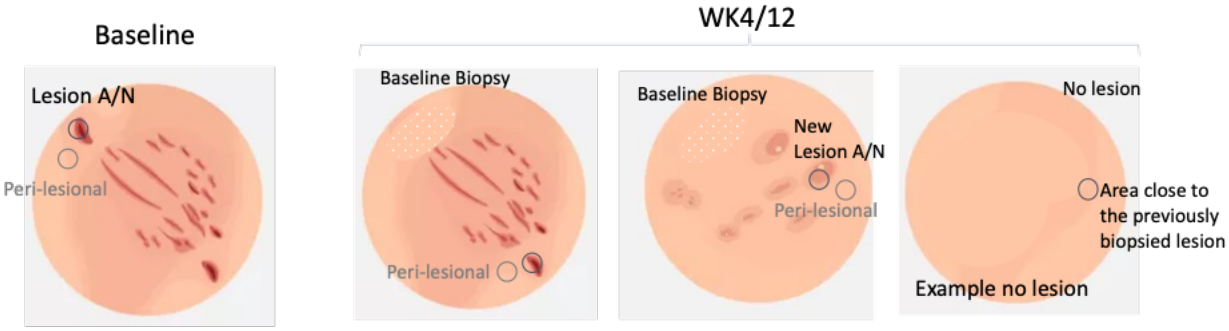

Figure 3: Baseline, WK4 and 12 biopsy planning

7. PUNCH BIOPSY PROCEDURE

7.1. Subject Preparation

Clean the selected skin area with your antiseptic of choice followed by local anesthesia as indicated by institutional standard operating procedures.

All medications used during the procedure should be recorded as concomitant medications on the study electronic case report form (eCRF).

7.2. Punch Biopsy Procedure

1. Photo-document the lesion: Photo 1 - Overview including the appropriate anatomic reference point, see Section 5.2 and 6.3.3.
2. Clean the selected skin area with the appropriate antiseptic.
3. Apply local anesthesia.
4. Use a circular 6 mm punch biopsy at the marked site of the biopsy. Rotate the punch biopsy tool through the skin using constant downwards pressure until the subcutaneous tissue has

clearly been entered. Ensure deep penetration of the punch biopsy tool. The punch biopsy tool should then be withdrawn.

5. Grasp the tissue biopsy with the forceps and detach the biopsy from its base (within the subcutaneous fat tissue) with a scalpel.
6. Immediately place the biopsy in the vial containing 10% formalin.

NOTE: the samples must be processed immediately after collection.

8. WOUND CARE

1. Once the biopsy tissue is removed, the preferred healing is by secondary intent, i.e. without suturing. However, use of sutures is permitted at the discretion of the investigator. If the lesion is draining, please do not pack the lesion with gauze and simply apply a dressing.
2. Apply bacitracin ointment at the biopsy site, cover the site with 2x2 inch gauze, and wrap the site with Coban.
3. A neurovascular assessment must be made of the respective extremities following the procedure and the results documented in the subject's medical record.
4. The subject should remain in the department for a minimum of 30 minutes after the procedure is completed.
5. The subject should change the dressing, daily and after the site has gotten wet (e.g. after a shower), for 3 consecutive days after the biopsy.
6. The subject must be informed that they may experience the following adverse events after the biopsy. The subject should be advised to contact their treating physician should any of the following events be present at a severity level that is above the typical symptom and severity that they experience from their underlying HS.
    - Pain at the injection sites
    - Evidence of swelling and tenderness
    - Evidence of significant oozing of serous fluid
    - Evidence or suspicion of an infection as manifested by redness and streaking
    - Evidence of bleeding
    - Evidence that the biopsy site is not healing well

9. SAFETY REPORTING

Adverse events will be reported and tracked as required in the clinical study protocol and are to be defined by the Common Terminology Criteria for Adverse Events (CTCAE)

10. SPECIMEN HANDLING, ALLOCATION, PROCESSING, AND STORAGE

This section describes the methods for handling, allocating, processing, and storage of skin tissue obtained from the biopsy. Tissue samples must be processed into 10% NBF immediately.

1. The Biopsy Visit Requisition Form for the formalin sample (FFPE skin Biopsy) sample should be filled out completely. Labels should be placed on the vials immediately before placing the sample in the designated vial.
    - Using a sterile needle, the flat edge sterile forceps or the flat edge of a sterile scalpel, transfer the biopsy into 10% formalin.

NOTE: Confirm vial label prior to depositing the sample into the vial.

Figure 4: Tissue Processing Workflow

Formalin-Fixed Biopsy Tissue Sample (FFPE) Processing – Additional Instructions

Please refer to the Sponsor-provided SBT777101-02 laboratory manual and use requisitions forms, supplies and associated labels as instructed in this manual.

Note: Ensure that the lesional biopsy is labelled as FFPE Biopsy Lesional and the optional peri-lesional biopsy if obtained is labelled as FFPE Biopsy Peri-Lesional.

- The biopsy tissue sample in 10% formalin (FFPE) should be kept refrigerated until shipment to Mosaic Laboratories, L.L.C. within 24 hr of collection (refer to the shipping section of the SBT777101-02 laboratory manual for specific shipping instructions).
- **If the 10% formalin (FFPE) biopsy sample cannot be shipped within 24 hr of collection, the following additional specimen processing steps for skin tissue samples are required to ensure specimen integrity:**
    1. Allow the samples to fix in 10% formalin vial for 24 hr.
    2. Fill the 20 mL SecurTainer container with 10 mL of 70% Reagent Grade Alcohol (provided by the sponsor).
    3. Identify the appropriate label from the requisition form and label the 20 mL SecurTainer container.
    4. Using sterile forceps, gently transfer formalin-fixed skin tissue samples from the formalin vial to the labelled SecurTainer container containing 10 mL of 70% Reagent Grade Alcohol (minimize formalin carryover into the new container).
    5. Store the SecurTainer container containing 70% Reagent Grade Alcohol and biopsy sample at 4°C until it is ready for shipment (the sample should be shipped within 24 hr after transfer to the SecurTainer container containing 70% Reagent Grade Alcohol).

11. TRANSPORT OF SPECIMENS

Please refer to the SBT777101-02 Lab Manual for detailed information about:

- Shipping supplies and labels
- Pre-shipping specimen preparation

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APPENDIX A. EXAMPLE OF REQUISITION FORM FOR BIOPSY SAMPLE

MEDPACE

REQUISITION FORM Pilot Pharma PILOT-001-001 PILOT1	PLACE REQUISITION FORM : STD BARCODE HERE	BARCODE FROM KIT

VISIT INFORMATION (Please Check the Visit Collected and Record Visit Date/Time of Collection)		
[ ] V2 [ ] V3 [ ] V5 [ ] U1 [ ] U2		
DATE OF COLLECTION: __ __ / __ __ __ / __ __ __ __ d d m m m y y y y	TIME OF COLLECTION: __ __ : __ __ (24 hour) h h m m	

PATIENT INFORMATION (Please Complete All Responses)		
LAB SUBJECT ID: __ __ __ - __ __ __ # # # # # #	AGE (YEARS): __ __ # #	SEX: [ ] Male [ ] Female
FASTING?: [ ] Yes [ ] No	YEAR OF BIRTH: __ __ __ __ y y y y	

SAMPLES AND INFORMATION (If Applicable, Please Provide Sample Information Below)
SAMPLE
Skin Biopsy
Chemistry - SER
Lipid Panel - SER
Exploratory Biomarkers Alq 1 - SER
Exploratory Biomarkers Alq 2 - SER
Hematology/HbA1c - WHBLD
Urinalysis - UR
PK Alq 1 - SER
PK Alq 2 - SER
PK Alq 3 - SER
PK Alq 4 - SER
PK Alq 5 - SER
PK Alq 6 - SER
PK Alq 7 - SER
PK Alq 8 - SER

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This page generated on 03-Feb-2023

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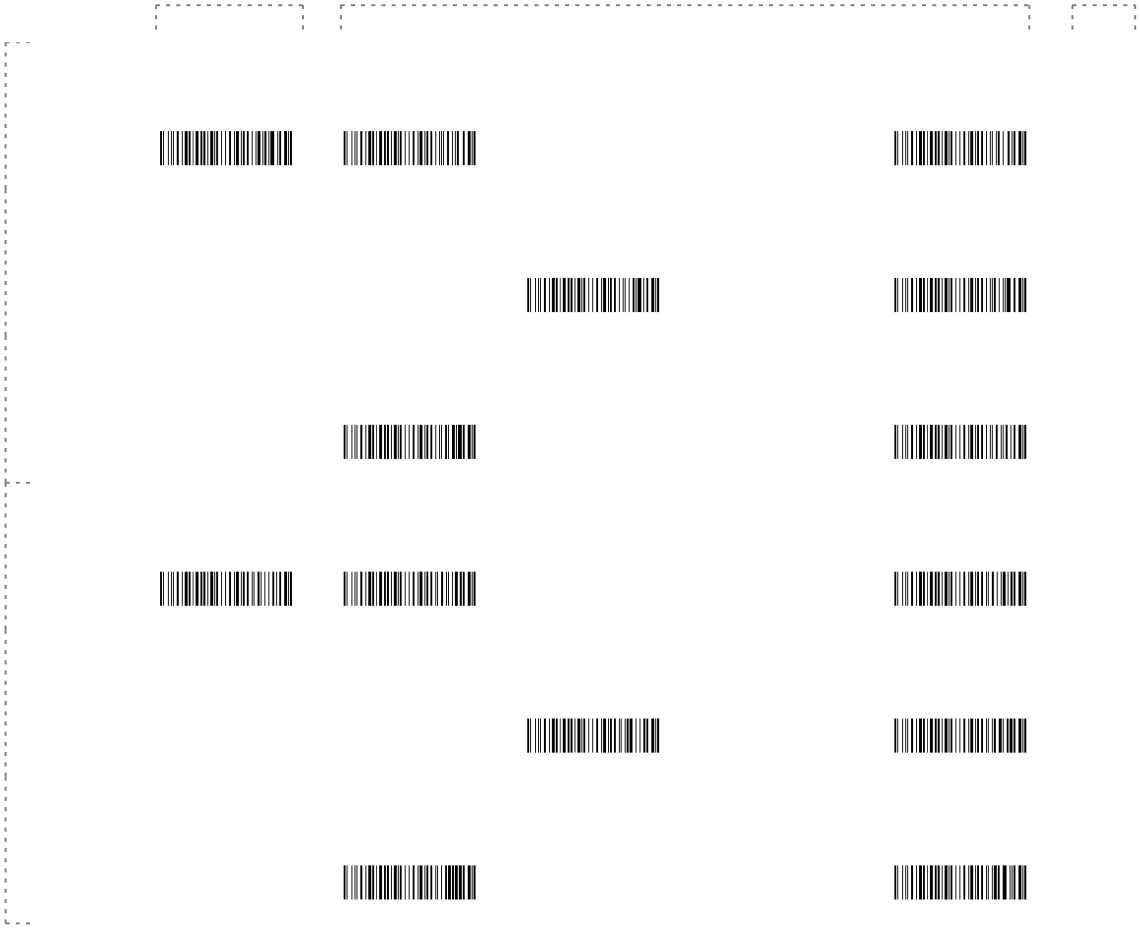
SPONSOR: Pilot Pharma
PROTOCOL: PILOT-001-001
STUDY CODE: PILOT1

MEDPACE Reference Laboratories



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