MEDPACE
REFERENCE LABORATORIES

Laboratory Manual

Sonoma Biotherapeutics

Protocol Number: SBT777101-01

A Phase 1 Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Activity of Single Ascending Doses of SBT777101 in Subjects with Rheumatoid Arthritis

Version/Date: V1 29-AUG-2022

Region: US

Table of Contents

1 Laboratory Information

The first section of the Laboratory Manual provides an overview of basic laboratory information such as contact information, specimen collection and processing instructions, shipping guidelines, laboratory reporting details, and accreditation certificates. The study-specific section provides detailed instructions related to a particular study.

1.1 Contact Information

Medpace Reference Laboratories (MRL)

5365 Medpace Way

Cincinnati, Ohio, US 45227

Phone: +1.513.366.3270 or +1.800.749.1737 (North America sites only)

Fax: +1.513.366.3273 or +1.800.705.2177 (North America sites only)

Client Services
The extension for the Project Manager assigned to your protocol is in the study-specific laboratory manual. Contact client services to clarify sample collection procedures or shipment temperature, request additional laboratory supplies, or re-send laboratory reports.

Critical Values Department
Contact the Critical Values Department (extension 11120) to obtain and acknowledge receipt of critical values. You should have the following information available each time you contact MRL:

- Sponsor name
- Protocol number
- Site number
- Subject ID (laboratory number, randomization number and/or initials [where applicable])
- Date of collection and visit

1.2 MRL Hours of Operation and Holiday Observances

Monday - Friday
8:00am - 5:00pm (ET)

Saturday
8:00am - 4:30pm (ET)

Sunday and Public Holidays
Closed*

*Couriers do not deliver specimens on those days. Sites will be notified in advance if shipping adjustments are required because of public holidays.

2022	2023	2024	2025	US Laboratory Public Holiday
01 January	01 January	01 January	01 January	New Year's Day
30 May	29 May	27 May	26 May	Memorial Day
04 July	04 July	04 July	04 July	Independence Day
05 September	04 September	02 September	01 September	Labor Day
24 November	23 November	28 November	27 November	Thanksgiving Day
25 December	25 December	25 December	25 December	Christmas Day

2 Laboratory Materials

MRL provides sites with study-specific supplies, including (as applicable):

- **Laboratory Manual**: general and study-specific
- **Quick Reference Chart**: laboratory schedule and abbreviated sample processing instructions
- Visit-specific laboratory kits
- Extra laboratory supplies
- Subject requisition forms
- Packaging and shipping materials (boxes, pre-printed airbills, labels)
- Letter indicating the latest time that the local courier can be contacted to ensure same-day pick-up

2.1 Specimen Collection Supplies

Each visit-specific kit is labeled with the Sponsor Name, Protocol Number, Visit(s) the kit is to be used for, and Expiration Date of the kit. Lab kit labels have a peel-off barcode label that must be removed from the used lab kit's label and affixed to the requisition form for the corresponding visit. If there are multiple pages of requisitions provided for a given visit, affix the lab kit barcode label to the first requisition page. There is space on the requisition form to place the lab kit barcode label (refer to section 3.1).

Extra laboratory supplies are provided in the initial supply shipment for unscheduled visit testing or in cases where additional supplies are needed (e.g., vacutainer tube included in lab kit does not contain vacuum).

Prior to phlebotomy, ensure that laboratory kits are not expired. Expiry date is indicated on the laboratory kit label. Pay particular attention to the expiration date of each component taken from extra supplies prior to use.

To request additional laboratory supplies, please order via web at www.medpace.com within the **study-specific** MRL ClinTrak web portal. As secondary/back-up options, please send the Laboratory Re-Supply Form (Appendix I) via fax (513.366.3273), e-mail (MRL-US-PA@medpace.com), or contact the Client Services Department via phone (513.366.3270 ext. 11304). Allow five (5) business days for delivery.

3 Specimen Labeling (Requisition Forms)

Each set of requisition forms is subject-specific and includes forms for all study visits with laboratory assessments. Forms for early termination and unscheduled visits, if applicable, are provided in the back of each set. We recommend keeping the requisition set in a unique location per subject, like the subject file.

3.1 Overview of the Requisition Form

Standard demographic information collected on a requisition form may include (see Figure 1):

- Subject randomization number
- Subject sex
- Subject age at time of collection
- Date of collection
- Time of collection (24-hour clock)
- Is Subject Fasting?
- Childbearing Potential

Refer to Section 8 for the study-specific demographic information collected on the requisition form.

Important: Incomplete or illegible information prompts immediate site contact for verification. In cases where the issue cannot be resolved promptly, sending the laboratory report may be delayed.

Space is identified in the header of the first requisition page of each visit to affix the peel-off barcode label from the lab kit used for that visit (Figure 1).

Important: Remember to provide this barcode for every subject visit so that MRL can track the number and expiration date(s) of kits remaining at the site.

The columns of the Requisition Form have specific uses (Figure 1).

Column	Information
1	Small labels are provided for site use
2	Abbreviated specimen processing and shipping instructions
3	Labels provided to place on the primary collection tube (vacutainer or urine cup)
4	Labels are provided for placement on secondary containers (transfer vial or slide mailer as applicable)
5	Labels are provided for placement on the individual hematology blood slides (as applicable)

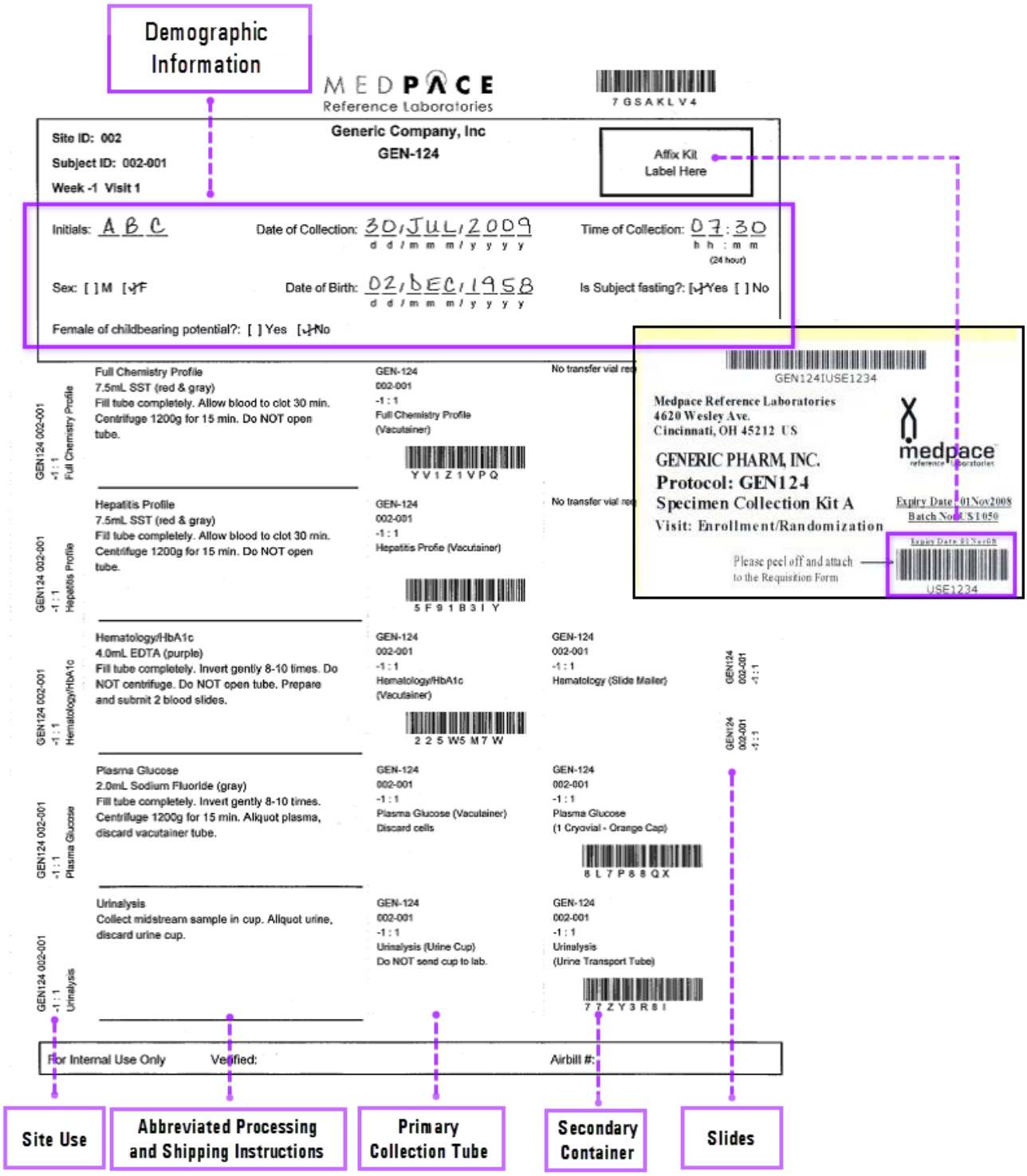


Figure 1 – Requisition Form

Secondary Container labels (Figure 2) should be placed on the corresponding tube lengthwise in the middle of the tube or vial as shown in Figure 3. Labels should not cover the cap of the tube.

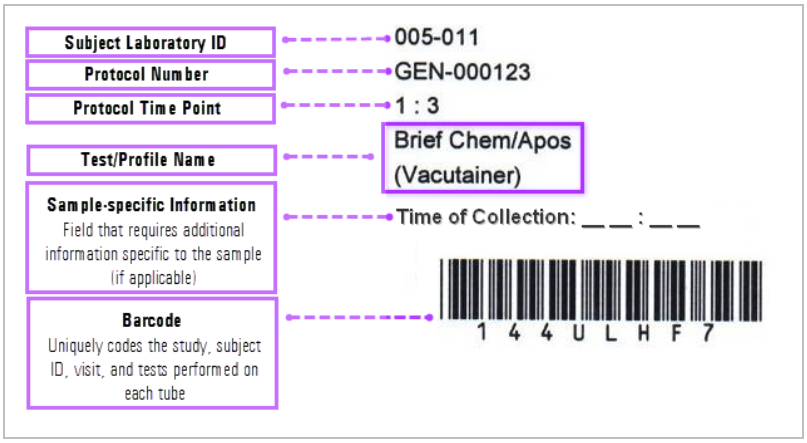


Figure 2 – Example Specimen Label

Correct labeling:

Lengthwise. Do NOT cover cap of the tube.

Incorrect labeling:

This label is not lengthwise.

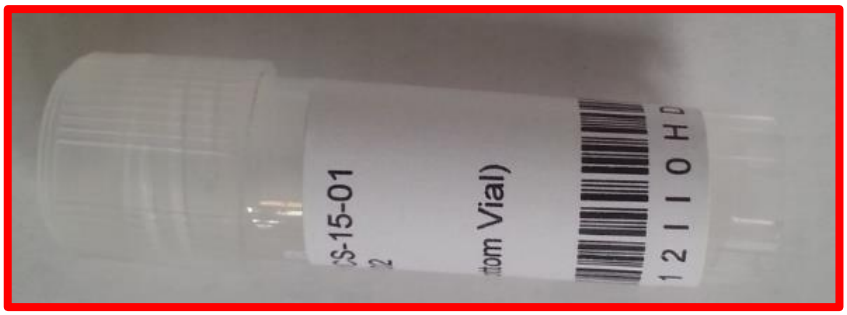


Figure 3 – Label Placement

3.2 Submitting Requisition Forms

Submit completed requisition forms to MRL in the shipment box together with the corresponding samples. In cases where back-up aliquots are shipped separately from the primary sample, the original completed requisition form must be copied PRIOR to the first shipment and a copy included with the subsequent shipments.

Requisition forms for samples shipped periodically in batches should be kept at the site with the samples until shipment. Photocopies of completed requisition forms, along with the shipment tracking number, should be maintained in site files.

If multiple forms are available for an unscheduled visit, ALL forms should be completed with the requested demographic information and submitted to the laboratory, even if no labels from a particular page are used.

In cases where a sample is not collected (e.g., difficult venipuncture, error, or subject unable to void a urine sample), leave the barcode label for that sample affixed to the requisition and make a notation next to the label the reason why the sample was not submitted. Refer to the example in Figure 4:

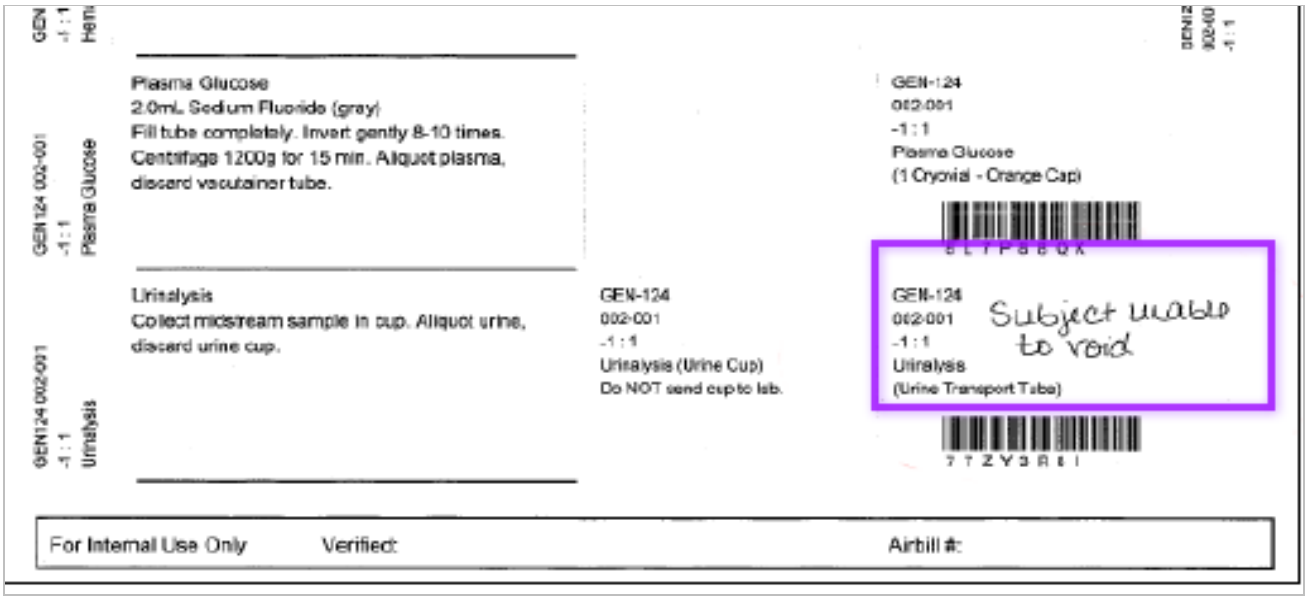


Figure 4 – Example Notation

4 Specimen Shipping

Sites are responsible for obtaining training of their staff for the shipment of diagnostic specimens.

If safe transport of specimens cannot be guaranteed within three to four (3-4) days of collection, contact the study-specific MRL Project Manager. Refer to Appendix G, Alternate Specimen Handling/Shipping Arrangements for instructions on how to proceed in emergency or other unusual circumstances that interrupt or affect normal shipping or delivery of samples to the MRL US facility.

4.1 Shipping Supplies

All shipping supplies provided by MRL are in compliance with international regulations (IATA PI650 / UN3373). Pre-printed airbills are provided that contain the site address as the shipper, MRL address, description of contents, and overnight shipment designation.

4.1.1 Dry Ice

MRL US does not routinely provide sites with dry ice, although we can assist in locating dry ice providers in the vicinity of the site. Contact the study-specific MRL Project Manager should you have difficulty, or require assistance, in obtaining dry ice for specimen shipments.

4.1.2 Instructions for Completing the List of Contents

An itemized List of Contents must be included in each shipment, as required by current shipping regulations for biological substances. This complies with International rules & regulations pertaining to the transport of Diagnostic Specimens/Biological Substances Category B (IATA UN3373 – Packing Instruction 650). This is required by IATA for transportation, is valid for such purposes only, and is not subject to any internal audit or archiving obligations.

STEP 1 The List of Contents is incorporated onto the **inner lid** of the shipping boxes. Please note picture of box in section 4.2.1 STEP 2.

STEP 2 One itemized List of Contents must be completed for the entire contents of each shipping box (one List of Contents per outer container).

STEP 3 Complete the List of Contents, indicating the Protocol number and site number associated with the samples. Check the box next to each sample type included in the shipment and enter the quantity of vials included for each sample type on the line to the right of the description.

Note: Serum separator tubes (red or gold tops) are classified as whole blood. The person who packed the shipment and completed the List of Contents must print his/her name, sign and date the bottom of the form (Figure 5).

Packing - Shipping List (List of Contents)

Protocol Number GEN123 Site Number 001

Check the box next to each sample type included in this shipment and enter the number of each sample type on the line to the right of the description:

☒ Human blood (whole) x 1 tubes x 2 blood smears

☒ Human urine x 1 vials

☒ Human serum x 2 vials

☐ Human plasma x _____ vials

☐ Human tissue x _____ slides / biopsies in solution / other_____(Circle the appropriate medium)

☐ Other: _____ x _____ quantity

Specimens packed by:

Name (Printed) Jane Smith

Signature *Jane Smith*

Date 04Jun2020

This document complies with International rules & regulations pertaining to the transport of Diagnostic Specimens/Biological Substances Category B (IATA UN3373 - Packing Instruction 650).

This document is required by IATA for transportation, is valid for such purposes only and is not subject to any internal audit or archiving obligations.

Figure 5 – Itemized List of Contents

4.2 Preparing Specimens for Shipment

4.2.1 Ambient Shipments

Ambient temperature shipments are defined as shipments in the temperature range of +20°C ± 5°C. Specimens intended for ambient shipment should be shipped on the day of collection if possible. If shipment cannot be performed on the day of collection, please hold samples at their specific temperature defined in section 9 and ship the following day.

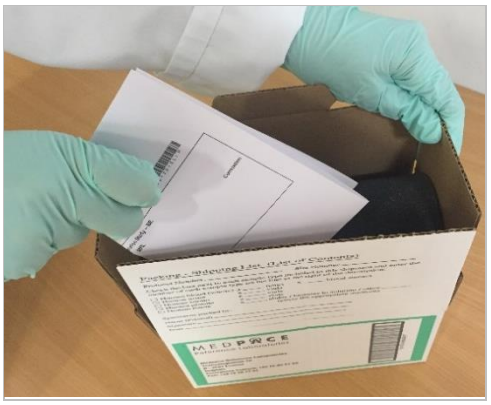
STEP 1 Ambient shipping materials are provided flat and each set includes five (5) shipping boxes, ten (10) 95kPa absorbent safety specimen bags, five (5) small Ziploc® baggies for slide mailers (if required), and cushioning material.

STEP 2 Confirm that all demographic information is filled out on the requisition form(s) and that all tubes are properly labeled. Assemble the shipping box by folding the numbered flaps in numerical order. Push the tab on the final flap (number 4) inside of the first three flaps to secure the bottom of the box.

STEP 3 Place the tubes in the 95kPa absorbent safety specimen bag(s) and seal the bag(s) (maximum 7 tubes per bag) as per the instructions on the bag.

STEP 4 Wrap the safety specimen bag(s) and the Ziploc baggie containing the slide mailer in the cushioning material.

STEP 5 Place the wrapped specimens and slides into the shipping box. Fold and place the requisition form(s) into the box.



STEP 6 Complete the List of Contents on the inner lid of the box, close the box, and secure with tape.

STEP 7 When utilizing ambient shipping boxes, a courier envelope may be used, or the airbill may be affixed directly to the shipping box in the designated area.

STEP 8 Insert the ambient shipping box(es) into the courier envelope.

STEP 9 To seal the bag, place the bag on a firm surface and peel off the plastic strip. Press down along the adhesive strip from the center out to the edges until it is completely sealed.

STEP 10 Complete the courier airbill as outlined in section 4.3.2.

4.2.2 Refrigerated/Ambient Shipments

Refrigerated temperature shipments are defined as shipments in the temperature range of 2°C to 8°C. Ambient temperature shipments are defined as shipments in the temperature range of 15°C to 25°C. Specimens intended for refrigerated and ambient shipment should be shipped on the day of collection whenever possible.

STEP 1 Refrigerated/Ambient boxes will arrive at your site compressed. **Please open the compressed box at least 24 hours before you intend to use it**, so that the foam insulation may fully expand. Assemble the shipping box by folding the numbered flaps in numerical order.

STEP 2 **Refrigerant packs included with compressed boxes should be frozen for a minimum of 24 hours at -20°C ±5°C prior to use.** Do NOT freeze refrigerant packs at ultralow temperatures (-75°C ±10°C), as this will result in samples freezing in transit.

STEP 3 Confirm that all demographic information is filled out on the requisition form(s), that the itemized List of Contents has been completed, and that all tubes are properly labeled.

4.2.2.1 Refrigerated Section

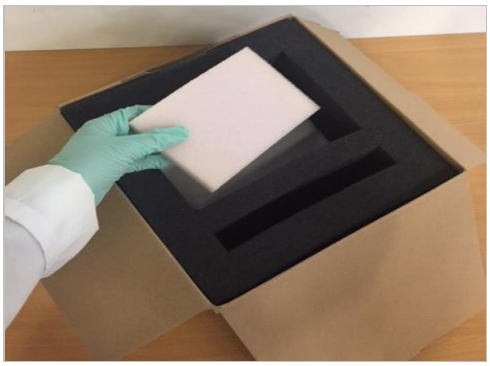
STEP 1 Place the tubes for refrigerated shipment in the 95kPa absorbent safety specimen bag(s) and seal the bag(s) (maximum 7 tubes per bag) as per the instructions on the bag.

STEP 2 Place the refrigerant pack (previously frozen at -20˚C ±5˚C for at least 24 hours) in the larger foam compartment.

Note: If using a saddle-bag refrigerant pack, one saddle-bag is sufficient. If using individual refrigerant packs, please use two packs per box.

Important: Do not freeze the refrigerant pack at ultra low temperatures (-75˚C ±10°C), as this will result in the samples freezing in transit.

STEP 3 Place the foam insert on top of the refrigerant pack.

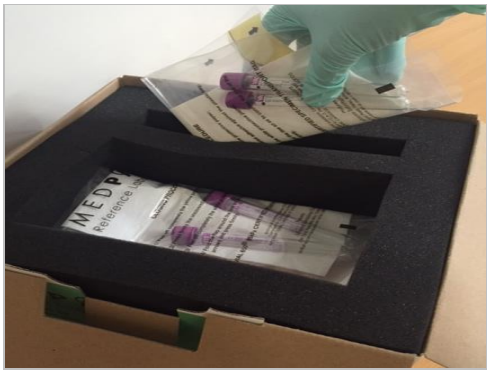


STEP 4 Place the refrigerated samples, in the 95kPa absorbent safety specimen bag(s), on top of the foam insert.

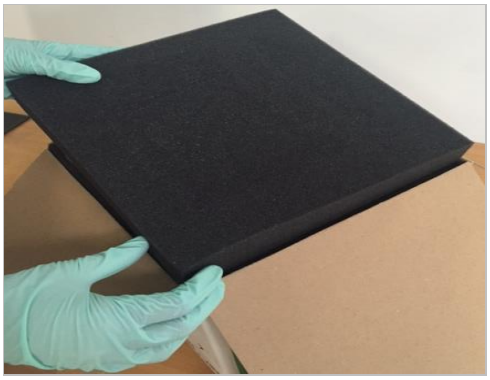
4.2.2.2 Ambient Section

STEP 1 Place the tubes for ambient shipment in the 95kPa absorbent safety specimen bag(s) and seal the bag(s) (maximum 7 tubes per bag) as per the instructions on the bag.

STEP 2 Place the Ambient samples, in the 95kPa absorbent safety specimen bag(s), into the smaller foam compartment.



STEP 3 Place the foam lid securely over the sample compartments.



STEP 4 Fold and place the requisition form(s) on top of the foam lid. Close and seal the box with shipping tape.

STEP 5 Complete the courier airbill as outlined in section 4.3.2.

STEP 6 Complete the List of Contents on the inner lid of the box, close the box, and secure with tape.

4.2.3 Frozen Shipments

Frozen temperature shipments are defined as shipments <-20ºC ±5°C. Frozen shipments are shipped Monday through Wednesday only (or Thursday if expected transit time does not exceed 24 hours) to ensure receipt during normal business hours. Refer to section 9.0. of this manual for study-specific instructions for the frequency of frozen shipments.

STEP 1 Confirm that all demographic information is filled out on the requisition form(s), that the itemized List of Contents has been completed, and that all tubes are properly labeled.

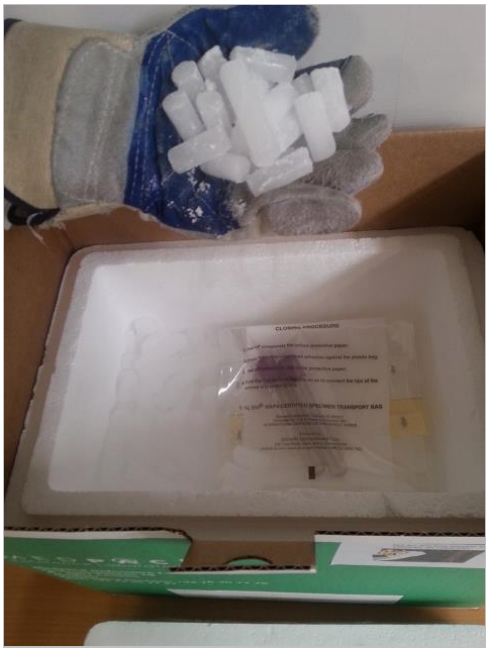
STEP 2 Place the tubes for frozen shipment in the 95kPa absorbent safety specimen bag(s) (maximum 7 tubes per bag) and seal the bag(s).

STEP 3 Line the bottom of the insulated cooler with at least 4 pounds (2 kg) of dry ice.

STEP 4 Place the safety specimen bag(s) into the insulated cooler on top of the dry ice.

STEP 5 Place at least an additional 4 pounds (2 kg) of dry ice in the insulated cooler around the specimens. Care should be taken not to overfill with dry ice so as to prevent the lid from being tightly fitted onto the cooler.

Important: Use granular dry ice—NOT chunks of dry ice—because chunks can damage samples in transit.



STEP 6 Place the lid on the insulated cooler, ensuring that it is inserted securely.

STEP 7 Place the completed requisition form(s) on top of the insulated cooler.

STEP 8 Close and seal the box with shipping tape.

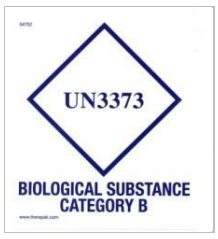
STEP 9 Record information on the dry ice label as outlined in section 4.3.1.

STEP 10 Complete the courier airbill as outlined in section 4.3.2.

4.3 Box Labeling and Courier Instructions

4.3.1 Box Labeling

- The outside of each shipping bag or box must clearly display the UN3373 and Biohazard symbols, as detailed below. All supplies provided by MRL for use as outer containers have these labels applied already.
- Shipments sent on a Thursday or Friday should be labeled with a Saturday Delivery label.
- If multiple ambient boxes are shipped inside of a courier envelope, an Overpack label must be used.



If shipping dry ice, record the information in Figure 6 on the dry ice label on the side of the box:

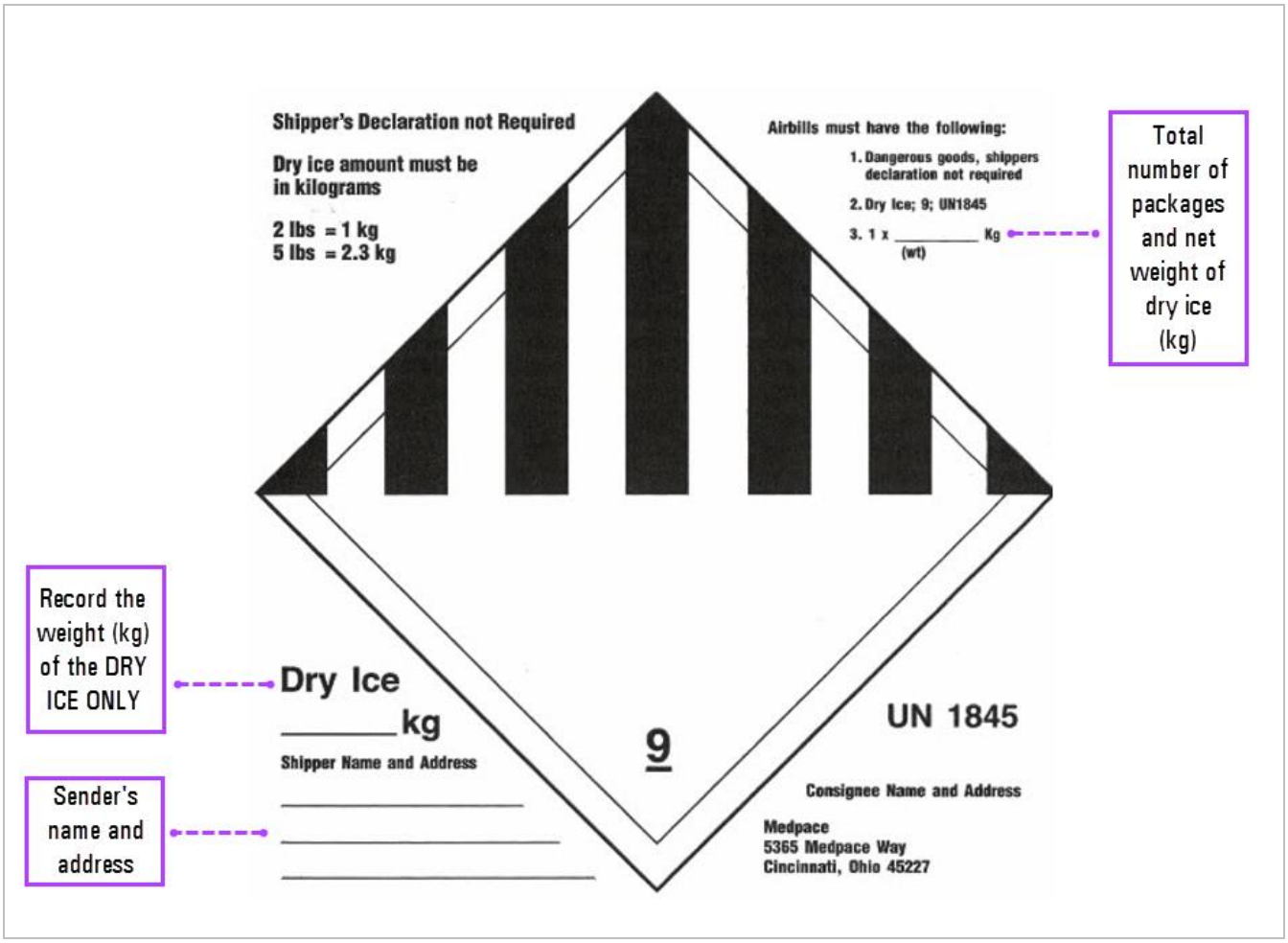


Figure 6 – Dry ice shipment information

4.3.2 FedEx Airbill Instructions

4.3.2.1 Ambient or Refrigerated Shipments, Thermal Label Airbill (US)

- Remove the thermal label from the backing.
- Keep the top portion of the label for your records (Figure 7).
- Place the adhesive label on the side of the bag or box. Place a Saturday Delivery sticker on the package if mailed on Thursday or Friday.

Important: Thermal label airbills contain a billing reference to the protocol and site number for tracking purposes; therefore, use airbills Only for shipping samples for the study for which they are provided.

Figure 7 – Ambient or Refrigerated Shipments, Thermal Airbill (US)

Note: When ordering additional thermal label airbills, you must specify whether you need labels for ambient/refrigerated or frozen shipments.

4.3.2.2 Frozen Shipments, Thermal Airbills (US)

Important: Ensure you are using a label specific for dry ice for all frozen shipments.

- Remove the thermal label from the backing.
- Keep the top portion of the label for your records (Figure 8).
- Place the adhesive label on the side of the bag or box. Place a Saturday Delivery sticker on the package if mailed on Thursday or Friday.

Important: Thermal label airbills contain a billing reference to the protocol and site number for tracking purposes; therefore, use airbills only for shipping samples for the study for which they are provided.

Figure 8 – Frozen Shipments, Thermal Airbill (US)

4.3.3 Scheduling Courier Pick-Ups

- A memo indicating the local courier contact information and the cut-off time by which the local courier must be contacted to ensure a same day pick-up is provided to each site as part of initial supplies. It is the site's responsibility to time collections so that samples can be shipped on the day of collection, if possible.
- Courier assignments are made based on efficiencies within each country or region. Sites may deviate from the courier assignment only with the written approval of the Sponsor or CRO.
- FedEx Account Number: 2986-1476-6
- **There are no pick-ups on Sundays or public holidays.**

4.4 International Shipping

4.4.1 Commercial Invoice

Non-US sites must include three copies of a Commercial Invoice with each shipment to MRL. An example of a Commercial Invoice can be found in Appendix E. The sites may use their own Commercial Invoice or photocopy this example onto their site letterhead. If a site chooses to use their own Commercial Invoice, the language included in the example in Appendix E should be incorporated into the document to ensure that there are no shipping delays due to incorrect documentation.

5 Laboratory Reports

5.1 Turn-Around Times

Routine laboratory testing will be completed, and a laboratory report faxed/emailed to the site within 24 hours of receipt of the samples. Certain tests may require additional time for analysis.

5.1.1 Expected Turnaround Times (> 24 hours)

SAMPLE NAME	TEST(S)	ANALYZING LAB	ANALYSIS SCHEDULE	FREQUENCY FOR BIOREPOSITORY TO MOVE SAMPLE(S) TO LABORATORY	COMPLETE SET VISITS	STABILITY
PBMC	PBMC Count Viable	MRL-US	Samples received before 3PM are analyzed day of receipt Mon-Sat. Samples arriving after 3PM may be processed day of receipt or stored at room temperature until the next day of lab operation in the dark upon Lab decision.	N/A Samples processed by the Biorepository Sample Processing Team	N/A	24-48 hours** ambient; 18-25c Samples processed after 48 hours will be marked as problem samples. Samples received after 72 hours will be discarded
	PBMC Count Nonviable					
	PBMC Initial Blood Volume					
	PBMC Concentration					
	PBMC Viability %					
	PBMC Total Volume					
	PBMC Total Count					
TBD	Cytokines	TBD	TBD	TBD	TBD	TBD
RF	TBD	TBD	TBD	TBD	TBD	TBD
ACPA - TBD	TBD	TBD	TBD	TBD	TBD	TBD

5.2 Repeat Testing

MRL will automatically repeat any result that fails internal pre-defined criteria based on absolute values and/or delta (changes) from previous visits. In addition, repeat testing may be performed at the request of the site or Sponsor, provided that the elapsed time does not exceed the established stability limits.

5.3 Samples Unacceptable for Testing

On occasion, laboratory samples may be unacceptable for testing. This may include, but is not limited to, extremely lipemic, icteric, or hemolyzed samples, clotted samples (for hematology or coagulation testing), improperly labeled or processed samples, or insufficient volume for testing. These conditions will be noted on the laboratory report.

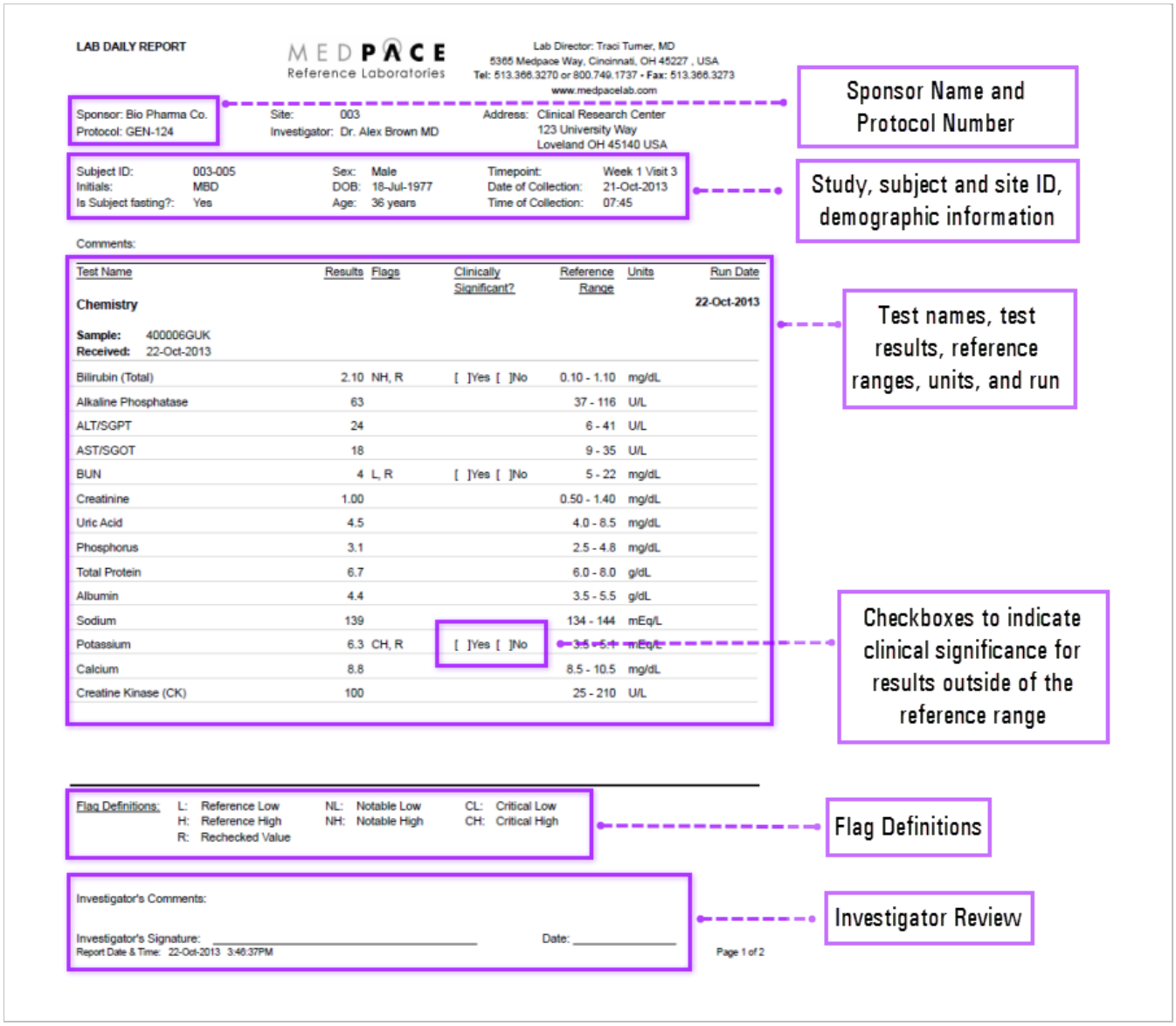


Figure 9 – Example laboratory request

5.4 Report Flagging

5.4.1 Outside of Reference Range, Notable, and Critical Values

Standard MRL report flagging and action taken are listed below:

Flag	Flag Definition	Action Taken to Communicate to Site
L or H Reference Low or Reference High	Result is outside of reference range	None (Standard faxing/email of lab report)
NL or NH Notable Low or Notable High	Moderately low or high result which warrants notification of site	None (Standard faxing/email of lab report)
CL or CH Critical Low or Critical High	Critically low or high result with potentially serious implications for subject safety	Fax/email notification to site and/or phone call to English-speaking sites as soon as result is verified by laboratory personnel

The site must send the critical value notification fax/email back to MRL or phone the critical values department (+1.513.366.3270, ext. 11120) as soon as possible to acknowledge receipt of the critical value. If the site has not acknowledged receipt of the critical result within a reasonable timeframe, the Sponsor will be notified.

5.4.2 Study-specific Report Flagging

Refer to the Study-specific Laboratory Manual section 0 for protocol-specific laboratory report flagging.

5.5 Re-sending of Laboratory Report

A copy of the original laboratory report can be re-sent upon request. Refer to section 1.1 and 7 of this manual.

5.6 Re-issue of Laboratory Report

A re-issued report is a newly generated laboratory report consisting of all tests performed at a particular protocol time point. This report will have a different report date/time than the original report. In cases where a report is re-issued, a “REISSUE” notation appears in the upper left-hand section of the report under the Lab Daily Report statement.

Example:

LAB DAILY REPORT

REISSUE

MEDPACE Reference Laboratories

Lab Director: Traci Turner, MD
5365 Medpace Way, Cincinnati, OH 45227 , USA
Tel: 513.366.3270 or 800.749.1737 • **Fax:** 513.366.3273
www.medpacelab.com

Sponsor: Bio Pharma Co.
Protocol: GEN-124

Site: 003
Investigator: Dr. Alex Brown MD

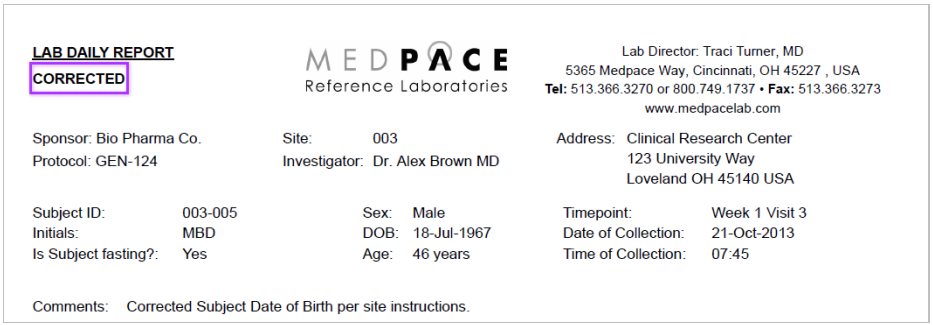
Address: Clinical Research Center
123 University Way
Loveland OH 45140 USA

Subject ID:	003-005	Sex:	Male	Timepoint:	Week 0 Visit 2
Initials:	MBD	DOB:	18-Jul-1977	Date of Collection:	01/MAY/2013
Is Subject fasting?:	Yes	Age:	35 years	Time of Collection:	08:45

Figure 10 – Example reissue of laboratory report

5.7 Corrected Laboratory Report

In cases where a report is re-issued due to changes in demographic information, Subject ID, protocol time point, or laboratory result(s), a “CORRECTED” notation appears in the upper left-hand section of the report under the Lab Daily Report statement.



LAB DAILY REPORT
CORRECTED

MEDPACE Reference Laboratories

Lab Director: Traci Turner, MD
5365 Medpace Way, Cincinnati, OH 45227 , USA
Tel: 513.366.3270 or 800.749.1737 • **Fax:** 513.366.3273
www.medpacelab.com

Sponsor: Bio Pharma Co.
Protocol: GEN-124

Site: 003
Investigator: Dr. Alex Brown MD

Address: Clinical Research Center
123 University Way
Loveland OH 45140 USA

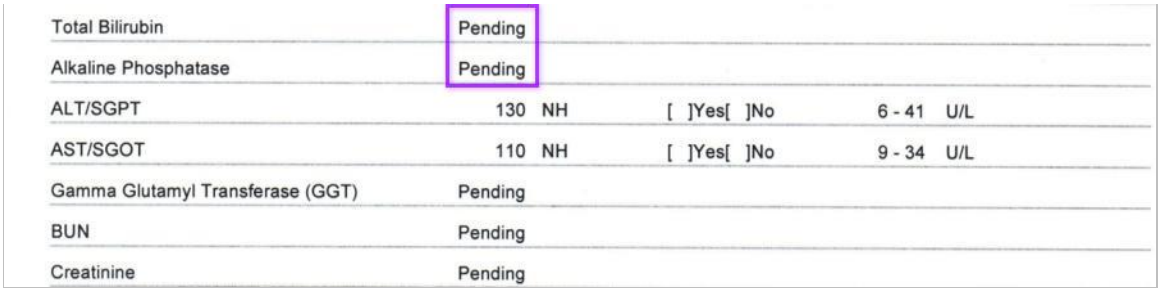
Subject ID:	003-005	Sex:	Male	Timepoint:	Week 1 Visit 3
Initials:	MBD	DOB:	18-Jul-1967	Date of Collection:	21-Oct-2013
Is Subject fasting?:	Yes	Age:	46 years	Time of Collection:	07:45

Comments: Corrected Subject Date of Birth per site instructions.

Figure 11 – Example corrected laboratory report

5.8 Pending Laboratory Results

In cases where a portion of the profile is performed but the profile has some tests pending, a report will be issued with the word “Pending” in the result field of those tests. When a result is available, ONLY the newly reported tests are reported on the subsequent report.

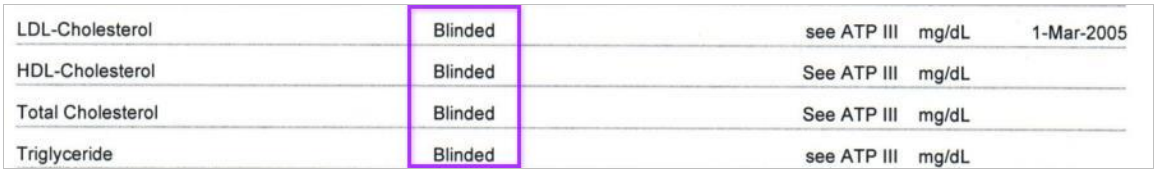


Total Bilirubin	Pending				
Alkaline Phosphatase	Pending				
ALT/SGPT	130	NH	[ ]Yes[ ]No	6 - 41	U/L
AST/SGOT	110	NH	[ ]Yes[ ]No	9 - 34	U/L
Gamma Glutamyl Transferase (GGT)	Pending				
BUN	Pending				
Creatinine	Pending				

Figure 12 – Example pending laboratory results

5.9 Blinded Laboratory Results

As indicated in the protocol, certain tests may be blinded at certain visits. The laboratory report will list the word “blinded” instead of listing a result.



LDL-Cholesterol	Blinded	see ATP III	mg/dL	1-Mar-2005
HDL-Cholesterol	Blinded	See ATP III	mg/dL	
Total Cholesterol	Blinded	See ATP III	mg/dL	
Triglyceride	Blinded	see ATP III	mg/dL	

Figure 13 – Example Blinded laboratory results

Study-Specific Instructions

Refer to sections 1-5 of this manual for general instructions and information.

6 SBT777101-01 Quick Reference Chart

- Refer to Appendix F | Quick Reference Chart for a listing of profiles/tests to be performed at each visit and abbreviated specimen collection and processing procedures, shipment temperatures, and shipment frequencies.
- The total blood volume required for this study for samples analyzed or managed by Medpace is 540 mL.

7 SBT777101-01 Contact Information

Re-sending of laboratory reports, additional supplies, or general questions:

- Contact Client Services at +1.513.366.3270/+1.800.749.1737
- MRL-US-PA@medpace.com

Complex Protocol-Related / Technical Questions:

- Contact Project Management at +1.513.366.3270 / +1.800.749.1737
- Project Coordinator: Amanda Rellahan x11504; a.rellahan@medpace.com
- Project Coordinator: Bradley Meyer x12581; b.meyer@medpace.com
- Project Coordinator: Riley Steward x16691; r.steward@medpace.com

8 SBT777101-01 Requisitions

Refer to section 3 of this manual for general information and instructions on the use of requisition forms.

Each subject will be given a Laboratory Subject ID which will be assigned sequentially at each site, be pre-printed on the requisition forms, and will remain consistent throughout the duration of the trial.

- The subject ID format for this trial will be XXX-YYY (3 digit site – 3 digit subject)
- The following information will be collected in the header of the requisition forms:

Visit	Information	Format	Notes
All Visits All Samples	Year of Birth	yyyy*	
	Age	_ _	
	Date of Collection	DD-MMM-YYYY	
	Time of Collection	___:___ (24-hour clock)	
	Sex	M / F (checkbox)	

- The following information will be collected on individual sample labels:

Visit	Information	Format	Test	Timepoint
Visit	Time of Collection	_ _ : _ _ (24-hour clock)		All

9 SBT777101-01 Sample Collection and Processing

- The phlebotomist should become familiar with the lab kit supplies, order of draw, and sample processing instructions prior to collection.

- Check the expiration date of laboratory supplies in advance.
- Prepare the requisition forms required for the specific visit corresponding to the subject's ID.
- Phlebotomy should be performed using universal precautions and according to site guidelines.
- All tubes should be filled completely to ensure adequate volume for testing.

9.1 Venous Blood Collection

9.1.1 Order of Tube Collection

Refer to the Quick Reference Chart for proper order of collection. Tubes must be collected in the same order as listed on the Quick Reference Chart to avoid carryover of additives.

SST >> CPT NaHep >> EDTA

9.1.2 Blood Specimens – Centrifugation

- We recommend using swinging bucket centrifuges for high-quality results.
- Refer to Appendix B, Centrifuge Conversion Chart, for sample-specific centrifugation time and force, in addition to instructions on the conversion from g(RCF) to RPM.
- Samples should always be visually inspected following centrifugation to ensure complete separation of the red cells below and a clear plasma/serum layer above.
- Troubleshooting: When looking at the tube in the upright position, if the gel does not form a horizontal barrier between serum (clear layer) and cells (see unspun or partially spun examples in Figure 14), please ensure that clotting time before centrifugation and resting time after centrifugation are respected for all future collections. In addition, please ensure centrifuge is well calibrated and that g(RCF) to RPM conversion was performed (refer to conversion table in Appendix B). **Do not** re-spin tube.

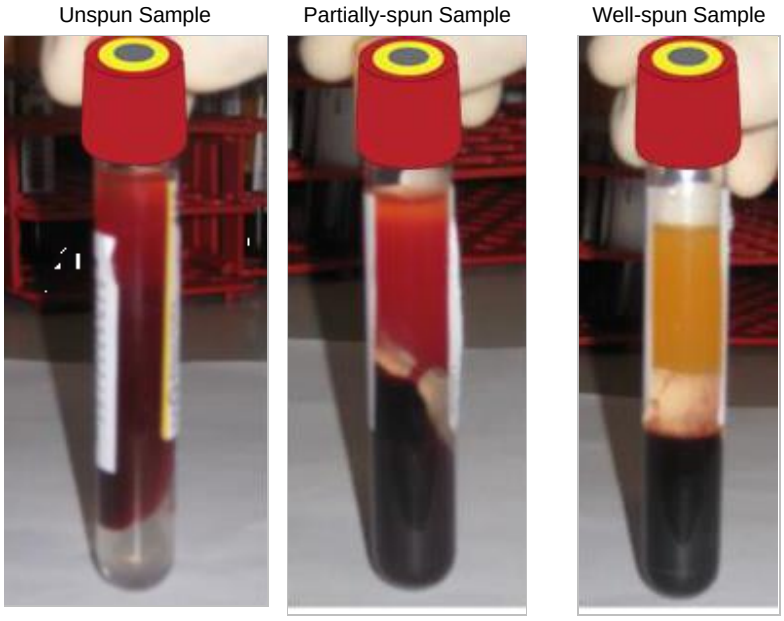


Figure 14 – Centrifuged Samples

9.1.3 **ADA**

7.0mL Serum Separator Tube/SST (Red or Gold Top) – Serum Sample

STEP 1 Fill the tube completely.

STEP 2 Mix immediately by gently inverting the tube 5 times.

STEP 3 Allow the blood to clot in the upright position for 30 to 60 minutes.

STEP 4 Within 60 min of collection, centrifuge the tube for 10 to 15 minutes at 1800 g to 2200 g *(RCF not RPM)*. **The SST tube should NOT be refrigerated prior to centrifugation.** There should be complete separation of serum and blood cells via the separation gel. To prevent the gel barrier from migrating in transit, it is recommended to allow the tube to sit upright at ambient temperature for 1 hour prior to shipping.

STEP 5 Using a transfer pipette, aliquot the serum sample into 4 x 2.0 mL cryovials, leaving a small amount on top of the separator gel. Discard the collection tube.

STEP 6 Ship cryovials to MRL frozen in weekly batches.

9.1.4 Serum Exploratory Inflammatory Markers

8.5mL Serum Separator Tube/SST (Red or Gold Top) – Serum Sample

STEP 1 Fill the tube completely.

STEP 2 Mix immediately by gently inverting the tube 5 times.

STEP 3 Allow the blood to clot in the upright position for 30 to 60 minutes.

STEP 4 Within 60 min of collection, centrifuge the tube for 10 to 15 minutes at 1800 g to 2200 g *(RCF not RPM)*. **The SST tube should NOT be refrigerated prior to centrifugation.** There should be complete separation of serum and blood cells via the separation gel. To prevent the gel barrier from migrating in transit, it is recommended to allow the tube to sit upright at ambient temperature for 1 hour prior to shipping.

STEP 5 Using a transfer pipette, aliquot the serum sample into 8 x 2.0 mL cryovials, leaving a small amount on top of the separator gel. Discard the collection tube.

STEP 6 Ship cryovials to MRL frozen in weekly batches.

9.1.5 **ACPA/RF**

8.0mL Serum Separator Tube/SST (Red or Gold Top) – Serum Sample

STEP 1 Fill the tube completely.

STEP 2 Mix immediately by gently inverting the tube 5 times.

STEP 3 Allow the blood to clot in the upright position for 30 to 60 minutes.

STEP 4 Within 60 min of collection, centrifuge the tube for 10 to 15 minutes at 1800 g to 2200 g *(RCF not RPM)*. **The SST tube should NOT be refrigerated prior to centrifugation.** There should be complete separation of serum and blood cells via the separation gel. To prevent the gel barrier from migrating in transit, it is recommended to allow the tube to sit upright at ambient temperature for 1 hour prior to shipping.

STEP 5 Using a transfer pipette, aliquot the serum sample into 3 x 2.0 mL cryovials, leaving a small amount on top of the separator gel. Discard the collection tube.

STEP 6 Ship cryovials to MRL frozen in weekly batches.

9.1.6 **PBMC**

8.0mL Sodium Heparin CPT (Red and Green Top)

STEP 1 Fill the tube completely.

STEP 2 Mix immediately by gently inverting the tube 8-10 times.

STEP 3 Within 120min of collection, centrifuge the tube for 30 minutes at 1500 g *(RCF not RPM)*. There should be complete separation of the plasma and blood cells.

STEP 4 Resuspend mononuclear cells into plasma by gently inverting tubes 5-10 times.

STEP 5 Ship tube to MRL refrigerated on day of collection.

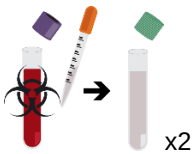
9.1.7 **Plasma Exploratory Inflammatory Markers** 4.0mL K2EDTA (Purple Top) – Plasma Sample

(K2 Ethylenediaminetetraacetate)

STEP 1 Fill the tube completely.

STEP 2 Mix immediately by gently inverting the tube 8-10 times and immediately place on wet ice.

STEP 3 Within 15 min of collection, centrifuge at 4°C for 10 to 15 minutes at 1800 - 2200 g *(RCF not RPM)*. There should be complete separation of the plasma and blood cells.



STEP 4 Using a transfer pipette, aliquot plasma into 2 x 2.0 mL cryovials and freeze until shipment.

STEP 5 Ship cryovials frozen.

9.1.8 **PK ddPCR**

3.0mL K2EDTA (Purple Top) – Plasma Sample

(K2 Ethylenediaminetetraacetate)

STEP 1 Fill tubes completely as a partial fill results in over anticoagulated plasma, impacting results of testing.

STEP 2 Mix immediately by gently inverting the tube 8-10 times.

STEP 3 Do NOT Centrifuge. Do NOT open tube.

STEP 4 Ship tube UNOPENED to CRL refrigerated, Day of Collection.

9.1.9 **Synovial Fluid (Supernatant and Cell Pellet)**

Green-top (heparin) tube

STEP 1 Fill tubes completely as a partial fill results in over anticoagulated plasma, impacting results of testing.

STEP 2 Within 4 hours of collection, centrifuge at room temperature at 500 g for 10 minutes.

STEP 3 The supernatant should be transferred into new and labeled tubes in 500 mL aliquots and placed in –80 °C.

STEP 4 The cell pellet should be resuspended in cold PBS.

STEP 5 Centrifuge at room temperature at 500 g for 10 minutes.

STEP 6 The new cell pellet should be resuspended in cold CryoStor CS10 media and immediately transferred to cryovials in 1 mL aliquots.

STEP 7 Transfer aliquots to pre-cooled controlled rate freezing container and place in -80 °C freezer prior to shipping.

STEP 8 Ship at least 24 hours and no longer than 7 days.

9.1.10 **Synovial Biopsy (Cryo and FFPE)**

Synovial tissue fragments should be placed on a sterile compress, soaked in physiological NaCl to keep the tissue moist, and within 1-2 minutes, should either be placed in 10% neutral-buffered formalin or Cryostor CS10 medium (provided in kit), with a minimum of 2 or 3 core fragments in each depending on size of joint biopsied. Please see below.

Large joints (knee/ankle):

	Intended analysis	Number of fragments	Format	Process
1	Fixed tissue	3-6†	Loose in 10% formalin in a histology pot	Place tissue directly into histology pot
2	Frozen tissue for subsequent disaggregation	3-6†	Loose in CryoStor CS10 medium in a cryovial	Place tissue into 1 mL cryovial

† Allocate 3 fragments first for fixation and then for freezing, then divide any additional fragments evenly between both, up to 12 fragments total

Small joints (wrist):

	Intended analysis	Number of fragments	Format	Process
1	Fixed tissue	2-4‡	Loose in 10% formalin in a histology pot	Place tissue directly into histology pot
2	Frozen tissue for subsequent disaggregation	2-4‡	Loose in CryoStor CS10 medium in a cryovial	Place tissue into 1 mL cryovial

‡ Allocate 2 fragments first for fixation and then for freezing, then divide any additional fragments evenly between both, up to 8 fragments total.

9.2 SBT777101-01 Shipment Information

FedEx is the courier for all sites in the study.

Ambient samples are shipped ambient on the day of collection.

The following samples will be shipped ambient for this study:

- PK ddPCR
- FFPE Synovial Biopsy

Refrigerated samples are shipped with refrigerant packs (4°C) on the day of collection. Each shipment should contain one (1) or two (2) refrigerant packs that have been frozen overnight for a minimum of twenty four (24) hours at-20°C ±5°C, NOT-75°C ±10°C, which would cause the samples to freeze during shipment. If using a saddle-bag refrigerant pack, one (1) saddle-bag per box is sufficient. If using individual refrigerant packs, please use two (2) refrigerant packs per box.

The following samples will be shipped refrigerated for this study:

- PMBC

Frozen samples are stored at the site frozen (-20°C ±5°C or below) and shipped to Medpace Reference Laboratories on dry ice. Frozen shipments should be sent according to the schedule noted below. For weekly or monthly batches, it is recommended that shipments occur on Monday, Tuesday, or Wednesday only.

The following frozen samples will be shipped on the day of collection:

The following frozen samples will be shipped in weekly batches:

- ADA
- Exploratory Inflammatory Markers - Serum
- ACPA/RF
- Exploratory Inflammatory Markers – Plasma
- Synovial Fluid Supernatant
- Synovial Fluid Cell Pellet
- Cyro Synovial Biopsy

The following frozen samples will be shipped in monthly batches:

Refer to section 4 of this manual for instructions on how to package samples for shipment at various temperatures.

9.3 SBT777101-01 Reflexive Testing

Originating Test	Criteria	Test Triggered
TBD	TBD	TBD

9.4 SBT777101-01 Blinded Tests

Sample	Test	Visit(s)	Reporting Flag	Blinding Flag
TBD	TBD	All	TBD	TBD

Reporting Key

Reporting Definition: Laboratory test names and subsequent results or result codes are visible on the laboratory reports.

Reporting Flags	
Definition	**Flag**

Reporting Flags	
Laboratory results reported to Sponsor/CRO only	TBD
Laboratory results reported to Investigator only	TBD
Laboratory results reported to both Sponsor/CRO & Investigator	TBD
Laboratory results are not reported	TBD

Blinding Key

Blinding Definition: True laboratory results are not populated for visibility. Results are noted as “Blinded” on the laboratory reports, ClinTrak Lab, and/or data transfers.

Blinding Flags	
Definition	**Flag**
Results are blinded to Sponsor/CRO only	TBD
Results are blinded to Investigator only	TBD
Results are blinded to Sponsor/CRO & Investigator	TBD
Results are not blinded	TBD

9.5 SBT777101-01 Report Flagging

Visit	Test	Criteria	Flag
//Visit//	IL-1, IL-6, IL-10, IL-15, IL-17, TNFα and interferon-gamma (IFNγ)	//Criteria//	Subject meets discontinuation criteria

- Refer to section 5 of this manual for general laboratory report information.

10 Appendix A | CAP and CLIA Certificates

(page 1 of 2)

COLLEGE of AMERICAN PATHOLOGISTS

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

The College of American Pathologists
certifies that the laboratory named below

Medpace Reference Laboratories
Cincinnati, Ohio
Traci Turner, MD, MT(ASCP)

CAP Number: 7185149
AU-ID: 1405873
CLIA Number: 36D1023277

has met all applicable standards for accreditation and is hereby accredited by the College of American Pathologists' Laboratory Accreditation Program. Reinspection should occur prior to May 18, 2022 to maintain accreditation.

Accreditation does not automatically survive a change in director, ownership, or location and assumes that all interim requirements are met.

Chair, Accreditation Committee

President, College of American Pathologists

CENTERS FOR MEDICARE & MEDICAID SERVICES

CLINICAL LABORATORY IMPROVEMENT AMENDMENTS

CERTIFICATE OF ACCREDITATION

LABORATORY NAME AND ADDRESS
MEDPACE REFERENCE LABORATORIES LLC
5365 MEDPACE WAY
CINCINNATI, OH 45227

CLIA ID NUMBER
36D1023277

EFFECTIVE DATE
06/03/2020

LABORATORY DIRECTOR
TRACI TURNER M.D.

EXPIRATION DATE
06/02/2022

Pursuant to Section 353 of the Public Health Services Act (42 U.S.C. 263a) as revised by the Clinical Laboratory Improvement Amendments (CLIA), the above named laboratory located at the address shown hereon (and other approved locations) may accept human specimens for the purposes of performing laboratory examinations or procedures.

This certificate shall be valid until the expiration date above, but is subject to revocation, suspension, limitation, or other sanctions for violation of the Act or the regulations promulgated thereunder.

CMS
CENTERS FOR MEDICARE & MEDICAID SERVICES

Karen W. Dyer, Director
Division of Laboratory Services
Survey and Certification Group
Center for Clinical Standards and Quality

11 Appendix B | Centrifuge Conversion Chart (RCF to RPM)

A certain relative centrifugal force (RCF) in g's is required to separate cells from serum/plasma. Centrifuges typically measure revolutions per minute (RPM) and not g's. The number of RPMs required to obtain a given g is calculated by the following equation:

$$RPM = \sqrt{\frac{RCF \times 10^5}{1.12 \times r}}$$

Centrifugal Force – The force that tends to make rotating bodies move away from the center of rotation (i.e., separation of cells and plasma/serum in a tube).

Relative Centrifugal Force (RCF) – The centrifugal force (see above), expressed as number of times greater than gravity (g). Example: 1200 x g, also written as 1200g.

Revolutions per Minute (RPM) – The number of rotations per minute of the centrifuge rotor (moving head).

Radius (r) – Swinging bucket centrifuges – the distance (in cm) from the center of the centrifuge head (post the head rests on) to the bottom of the bucket.

Fixed angle centrifuges – the distance (in cm) from the center of the centrifuge head (post the head rests on) to the middle of the sample compartment.

Centrifuge Radius (in cm)	Force of 1200g	Force of 1500g	Force of 1800g	Forge of 2200g
8	3600 rpm	4100 rpm	4500 rpm	5000 rpm
10	3300 rpm	3700 rpm	4000 rpm	4500 rpm
12	3000 rpm	3400 rpm	3700 rpm	4100 rpm
14	2800 rpm	3100 rpm	3400 rpm	3800 rpm
16	2600 rpm	2900 rpm	3200 rpm	3500 rpm

After centrifugation, there must be complete separation of the serum/plasma and cells.

12 Appendix C | Biotin Interference

Biotin is a B vitamin that is found in a variety of foods. It helps turn the carbohydrates, fats, and proteins into energy. The amount of biotin required daily depends on the individual's age, and it is recommended that adults receive 30 µg/day [1].

High levels of biotin may cause interference with certain immunoassays using biotin-streptavidin technology [2, 3, 4]. Typical dietary biotin intake does not reach amounts capable of causing interference, but high dose biotin, as sometimes recommended in the treatment of certain diseases/conditions (e.g., multiple sclerosis (MS) and dermatologic conditions) may be sufficient to impact laboratory tests using biotin-streptavidin technology. Also, multivitamins, biotin supplements, dietary supplements for hair, skin, and nail growth may contain amounts of biotin capable of interference with laboratory tests. Such interference may cause falsely high or falsely low results depending on the assay. Physicians should advise patients to abstain from high levels of biotin intake for at least 48 hours before the blood collection for immunoassay tests [5].

The FDA provides recommendations for Health Care Providers in safety communications regarding biotin [2, 3] that can be accessed at www.fda.gov/medical-devices/safety-communications/update-fda-warns-biotin-may-interfere-lab-tests-fda-safety-communication.

Laboratory Tests with Potential Interference by High Biotin Levels	
Adrenocorticotropic Hormone (ACTH)	Human Immunodeficiency Virus 1&2 p24 (HIV combi PT)
Alpha Fetoprotein (AFP)	Insulin
C-Peptide	Luteinizing Hormone (LH)
CA-125	Myoglobin
Calcitonin	Neuron Specific Enolase (NSE)
Carcinoembyonic Antigen (CEA)	Osteocalcin
Human Chorionic Gonadotrophin (ß-hCG)	Parathyroid Hormone (PTH), Intact
Cortisol	Pro BNP
Creatine Kinase MB Isoenzyme (CK-MB)	Procollagen Type 1 N-terminal Propeptide (P1NP)
Cytomegalovirus, IgG (CMV IgG)	Progesterone
Cytomegalovirus, IgM (CMV IgM)	Prolactin
Dehydroepiandrosterone Sulfate (DHEA-S)	Prostate Specific Antigen (PSA)
Estradiol	QuickVue Pregnancy Test
Ferritin	S-100
Folate	Sex Hormone Binding Globulin (SHBG)
Folicle Stimulating Hormone (FSH)	Telopeptide C Terminal, Type 1 Collagen (ß-Crosslaps)
Hepatitis A Virus Antibody (Anti-HAV), IgM, and Total	Testosterone, Total
Hepatitis B Core Antibody (Anti-HBc), IgM, and Total	Thyroid Stimulating Hormone (TSH)
Hepatitis B Envelope Antibody (Anti-HBe)	Thyroxine, Free (FT4)
Hepatitis B Envelope Antigen (Anti-HBe Ag) (Qualitative)	Thyroxine, Total (T4)
Hepatitis B Envelope Antigen (Anti-HBe Ag) (Quantitative)	Triiodothyronine, Free T3 (FT3)
Hepatitis B Surface Antibody (Anti-HBs)	Triiodothyronine, T3
Hepatitis B Surface Antigen (HBs Ag) (Qualitative)	Troponin I
Hepatitis B Surface Antigen (HBs Ag) (Quantitative)	Troponin T, High Sensitivity
Hepatitis B Surface Antigen Confirmatory (HBs Ag) (Qualitative)	Vitamin B12
Hepatitis C Virus Antibody (Anti-HCV)	Vitamin D, 25 OH

References:

[1] National Institutes of Health. Biotin fact sheet for consumers. ods.od.nih.gov/factsheets/Biotin-Consumer

[2] U.S. Food and Drug Administration. The FDA Warns that Biotin May Interfere with Lab Tests: FDA Safety Communication, November 28, 2017.
[3] U.S. Food and Drug Administration. UPDATE: The FDA Warns that Biotin May Interfere with Lab Tests: FDA Safety Communication. November 5, 2019.
[4] Roche Diagnostics. Biotin facts. biotinfacts.roche.com
[5] Chun KY. Biotin interference in diagnostic tests. ClinChem. 2017;63(2):619-620.
[6] U.S. Food and Drug Administration. Biotin Interference with Troponin Lab Tests – Assays Subject to Biotin Interference.

13 Appendix D | Commercial Invoice

MEDPACE
Reference Laboratories
www.medpacelab.com

Commercial Invoice

Complete and fax this form to Medpace Reference Laboratories at
001-513-366-3273 each time an international shipment is made.

Date of exportation: _____

Shipper/Exporter:	Consignee: **Patrick McDermott** **Medpace Reference Laboratories** **5365 Medpace Way** **Cincinnati, Ohio 45227** **United States** **T: 513.604.0485**
Country of Origin/Export:	Importer: **Same as above**
International Tracking Number	Country of Ultimate Destination: **United States**

Pkg. #.	No. of Vials	Unit	Description	Unit Value	Total Value
1		Each	Human specimens, non-infectious UN3373 Category B for diagnostic purposes only. No commercial value. Value for customs purposes only. Tariff code 3002.12.0090		$1.00
			Packed in Compliance with IATA Packing Inst. 650 / UN3373 Biological Substance Category B		
			Human blood, tissue or urine (human material that was neither inoculated with or exposed to infectious agents of agricultural concern, including zoonotic agents; the material contains no animal or non-human primate material and is not of tissue culture origin)		
			These are research specimens for investigational use only and are not for resale, having no commercial value. The declared value for customs purposes only is $1.00 (USD)		

Total # Packages	Total Weight	Total Specimen Volume (mL)	Total Invoice Value
1			$1.00 (USD)

THESE COMMODITITES ARE LICENSED FOR THE ULTIMATE DESTINATION SHOWN

Print Name _____ Title

Sign Name _____ Date _____

14 Appendix E | Alternate Specimen Handling/Shipping Arrangements

(page 1 of 2)

14.1 Alternate Specimen Handling/Shipping Arrangements

Sites in the following locations send specimen shipments to MRL Cincinnati, OH, USA: North America, and Central and South America.

These instructions apply to emergency or other unusual circumstances that interrupt or affect normal shipping or delivery of samples to the central laboratory. Sites will be notified by MRL or the Sponsor/CRO when circumstances are such that alternate specimen handling and shipping arrangements should be implemented. Be alert for a message with specific instructions. If a site has concerns about shipping and has not received a message, information should be obtained from their CRA, from their MRL Project Manager, or by checking the MRL website.

14.1.1 Suggested Contingency Specimen Handling

If safe transport cannot be assured within three to four days of collection, the Sponsor/CRO may direct that sites follow any of the suggested instructions:

- Perform safety chemistry, hematology, urinalysis, hemoglobin A1C, and other safety tests at a local laboratory.
- Retain an aliquot of 1 mL of safety chemistry serum, labeled with the chemistry specimen label, in a small transfer vial for later shipment to MRL. Freeze at -20°C ±5°C or below.
- Freeze serum or plasma for lipid profiles and reserves in the freezer at -20°C ±5°C or below.
- Maintain all frozen specimen at -20°C ±5°C or below until further notice.

14.1.2 Specimen Shipment to Alternate Central Laboratory

In emergency situations, sites in North America, and Central and South America might receive written instructions from the central laboratory or Sponsor/CRO to re-route specimens to the MRL EU location:

Medpace Reference Laboratories BVBA

Attn: George Andronos

Technologielaan 19

B-3001, Leuven Belgium

Tel: +32-16-407775

Fax: +32-16-407775

- A blank courier airbill should be obtained from the local courier.
- For receiver, enter the address of Medpace Reference Laboratories BVBA as listed above.

- For description of contents, enter:

BIOLOGICAL SUBSTANCE, CATEGORY B UN3373,
PACKED IN COMPLIANCE WITH IATA PACKING INSTRUCTION 650

- Prepare **three copies** of a commercial/proforma invoice with the address of Medpace Reference Laboratories BVBA as the receiver of the package. The commercial/proforma invoice must contain the following information/statements (see Appendix E, Commercial Invoice):
    - Number of samples, Total sample volume
    - Human Blood and Urine Specimens for Clinical Research / Diagnostic Purposes, Not Infectious / Not Contagious
    - Biological Substance, Category B; Packed in Compliance with IATA Packing Inst. 650 / Diagnostic Specimens UN3373
    - Human blood, tissue or urine (human material that was neither inoculated with or exposed to infectious agents of agricultural concern, including zoonotic agents; the material contains no animal or non-human primate material and is not of tissue culture origin)
    - These are research specimens for investigational use only and are not for resale, having no commercial value. Declared value for Customs purposes only.
    - These commodities are licensed for the ultimate destination shown.

Medpace Reference Laboratories will provide you with the proper courier account number and will assist you in shipping the specimens correctly.

15 Appendix F | Quick Reference Chart

MEDPACE Reference Laboratories

SBT777101-01
Quick Reference Chart

SONOMA BIOTHERAPEUTICS

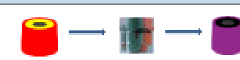
Label	Collection	Study Period	Screening	Pre-Treatment		Safety Follow Up															UV	ET
		Study Week	-8 to -7	-6 to -1		1				2		3	4	6	8	10	12	24	36	48/ES		
		Study Day (Visit Window)			-10 to -4	1	2	4 or 5	7±1	11±1	14±2	21±2	28±2	42±2	56±2	70±2	84±3	168±7	252±7	336±7		
		Testing																				
ADA	7 mL SST	ADA			x										x					x	x	x
Exp. Inflammatory Markers - Serum	8.5 mL SST	Exp. Inflammatory Markers, VICM, cytokines			x		x		x		x	x	x	x	x	x	x	x	x	x	x	x
ACPA/RF	8.0 mL SST	ACPA/RF			x						x	x	x	x	x	x	x	x	x	x		x
PBMC [b]	8.0 mL CPT NaHep	Cellular Immunogenicity, Exploratory Biomarkers, RCL			X (x3)		x	x	x	x	x	x	x	x	x	x	X (x2)	x	x	X (x2)	X (x2)	X (x2)
PK ddPCR	3.0 mL K2EDTA	PK ddPCR			x		X[a]	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Exp. Inflammatory Markers - Plasma	4.0 mL K2EDTA	Exp. Inflammatory Markers			x		x		x		x	x	x	x	x	x	x	x	x	x	x	x

Footnotes

[a] The PK sample collected on study Day 2 should be collected at approximately the same time of day that the infusion of study drug took place on study Day 1 (+/- 1 hour). An un scheduled PK sample should be collected within 30 minutes of a suspected infusion related event.

[b] 3 tubes will be collected at pretreatment. 2 tubes will be collected at Day 84, Day 336, UV, & ET. For all other visits only 1 tube will be collected.

Order of Draw



Medpace Reference Laboratories
Phone: 513.366.3270
Fax: 513.366.3273

Page 1 of 4

Quick Reference Chart
Date: 22Aug2022
Version 1

MEDPACE
Reference Laboratories

SBT777101-01
Quick Reference Chart

SONOMA BIOTHERAPEUTICS

		Study Period	Screening	Pre-Treatment		Safety Follow Up															UV	ET
		Study Week	-8 to -7	-6 to -1		1				2		3	4	6	8	10	12	24	36	48/ES		
		Study Day (Visit Window)			-10 to -4	1	2	4 or 5	7±1	11±1	14±2	21±2	28±2	42±2	56±2	70±2	84±3	168±7	252±7	336±7		
Label	Collection	Testing																				
Synovial Fluid Supernatant				X (a)									X (b) (c)				X (b) (c) (d)					X (c) (d)
Synovial Fluid Cell Pellet				X (a)									X (b) (c)				X (b) (c) (d)					X (c) (d)
Cryo Synovial Biopsy				X (a)									X (b) (c)									X (c) (d)
FFPE Synovial Biopsy				X (a)									X (b) (c)									X (c) (d)

Footnotes

(a) Synovial biopsy and/or synovial fluid collection during the Pre-treatment period should be performed after enrollment and at least one week prior to the planned dosing visit.

(b) The synovial biopsy/fluid collection can be performed at or up to 1 week after the scheduled assesment visit.

(c) The timing of the synovial biopsy and/or synovial fluid collection in may be changed based on evaluation of data from the first dose escalation cohot.

(d) The synovial biopsy sample/fluid collection at Week 12 and at the ET visit is optional.

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Sample	Tube	Collection & Processing	Aliquots	Shipping	Notes
ADA	 7.0 mL SST	Fill tube completely with blood. Immediately after collection, gently invert tubes 5 times. Allow tubes to clot for a minimum of 30 minutes post collection, keeping tubes vertical. Within 60 minutes of collection, centrifuge at 1,800- 2,200xg for 10-15 minutes to allow the gel barrier to migrate between the cell and serum layers. Using a transfer pipette, aliquot the serum sample into 4 x 2.0 mL cryovials, leaving a small amount on top of the separator gel. Discard the collection tube. Ship cryovials to MRL frozen in weekly batches.	4 x 2.0 mL Cryovials	Ship to MRL frozen in weekly batches	
Exp. Inflammatory Markers - Serum	 8.5 mL SST	Fill tube completely with blood. Immediately after collection, gently invert tubes 5 times. Allow tubes to clot for a minimum of 30 minutes post collection, keeping tubes vertical. Within 60 minutes of collection, centrifuge at 1,800- 2,200xg for 10-15 minutes to allow the gel barrier to migrate between the cell and serum layers. Using a transfer pipette, aliquot the serum sample into 8 x 2.0 mL cryovials, leaving a small amount on top of the separator gel. Discard the collection tube. Ship cryovials to MRL frozen in weekly batches.	8 x 2.0 mL Cryovials	Ship to MRL frozen in weekly batches	
ACPA/RF	 8.0 mL SST	Fill tube completely with blood. Immediately after collection, gently invert tubes 5 times. Allow tubes to clot for a minimum of 30 minutes post collection, keeping tubes vertical. Within 60 minutes of collection, centrifuge at 1,800- 2,200xg for 10-15 minutes to allow the gel barrier to migrate between the cell and serum layers. Using a transfer pipette, aliquot the serum sample into 3 x 2.0 mL cryovials, leaving a small amount on top of the separator gel. Discard the collection tube. Ship cryovials to MRL frozen in weekly batches.	3 x 2.0 mL Cryovials	Ship to MRL frozen in weekly batches	
PBMC	 8.0 mL CPT NaHep	Fill all tubes completely with blood. Gently invert 8-10 times to avoid clotting. Centrifuge within 2 hours of collection at 1500xg for 30 minutes. Resuspend mononuclear cells into plasma by gently inverting tubes 5-10 times. Ship tube to MRL refrigerated on day of collection	None	Ship to MRL refrigerated on day of collection	
Exp. Inflammatory Markers - Plasma	 4.0 mL K2EDTA	Fill tube completely. Mix tubes after collection by gently inverting 8-10 times and immediately place on wet ice. Within 15 minutes of collection, centrifuge at 4°C at 1800g - 2200g for 10-15 minutes. Using a transfer pipette, aliquot plasma into 2 x 2.0 mL cryovials and freeze until shipment. Ship cryovials to _____ frozen.	2 x 2.0 mL Cryovials	Ship to _____ frozen	

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SONOMA BIOTHERAPEUTICS

Sample	Tube	Collection & Processing	Aliquots	Shipping	Notes
PK ddPCR	 **3.0 mL K2EDTA**	Fill tubes completely as a partial fill results in over anticoagulated plasma, impacting results of testing. Mix tubes immediately after collection, gently inverting 8-10 times. Do NOT Centrifuge. Do NOT open tube. Ship tube UNOPENED to CRL refrigerated, day of collection.		**Ship to CRL ambient day of collection**	**DO NOT SEND TO MRL**
Synovial Fluid Supernatant		See Lab Manual for instruction.		**Ship to MRL frozen in weekly batches**	
Synovial Fluid Cell Pellet		See Lab Manual for instruction.		**Ship to MRL frozen in weekly batches**	
Cryo Synovial Biopsy		See Lab Manual for instruction.		**Ship to MRL frozen in weekly batches**	
FFPE Synovial Biopsy		See Lab Manual for instruction.		**Ship to Mosaic ambient day of collection**	**DO NOT SEND TO MRL**