# CORRELATIVE SCIENCE PROCEDURE MANUAL

## 1. Purpose

This document describes the procedures required for the collection, shipping, and processing of biospecimens from all patients enrolled or registered on A011801. This document also describes the procedures that will be followed subsequent to the receipt of biospecimens by the Alliance Biorepository (i.e. Siteman Cancer Center Tissue Procurement Core at Washington University), prior to their use for protocol-specified and future, unspecified correlative science research studies. This document should be used by staff involved with any aspect of the A011801 biospecimen collection, processing, and submission, including staff at satellite institutions.

## 2. Scope

This document applies to all biospecimens collected specifically for A011801 only. Please refer to the trial protocol-specific language for additional details regarding eligibility, participant enrollment, data submission, and specific procurement procedures. **Please ensure that you are reading the most updated version of this document. This document may experience minor updates, revisions, and clarifications independent of a formal protocol amendment. The most recent version of this document may be found on the Alliance website and CTSU.**

## 3. Definitions

| Term | Definition |
|---|---|
| ABWUSTL | Alliance Biorepository at Washington University in St. Louis |
| FFPE | Formalin fixed, paraffin embedded |
| H&E | Hematoxylin and Eosin |

## 4. Contact Information

Protocol-related questions may be directed as follows:

| Questions | Contact (via email) |
|---|---|
| Questions regarding patient eligibility, treatment, and dose modification: | Study Chair: Ciara C. O'Sullivan, MB, B.Ch, BAO osullivan.ciara@mayo.edu<br>Nursing Contact: Nicole Moxon, RN, BSN, OCN Nicole.moxon@providence.org<br>Protocol Coordinator: Laura Hoffman lhoffman22@bsd.uchicago.edu<br>Data Manager: Ann Hudson hudson.ann1@mayo.edu |
| Questions related to data submission, RAVE or patient follow-up: | Data Manager: Ann Hudson hudson.ann1@mayo.edu |
| Questions regarding the protocol document and model informed consent: | Protocol Coordinator: Laura Hoffman lhoffman22@bsd.uchicago.edu |
| Questions related to IRB review | Alliance Regulatory Inbox regulatory@allianceNCTN.org |
| Questions regarding CTEP-AERS reporting: | Alliance Pharmacovigilance Inbox pharmacovigilance@alliancenctn.org |
| Questions regarding specimens/specimen submissions: | Alliance Biorepository at Washington University in St. Louis (ABWUSTL) alliance@email.wustl.edu |
| Questions regarding drug supply | McKesson: CRS_intake@mckesson.com |
| Questions regarding drug administration | Pharmacy Contact: Myounghee Lee, PharmD, PhD, CCRP mlee1@umm.edu |

**4.1** For information on using the BioMS system, please refer to the 'Help' links on the BioMS webpage to access the online user manual, FAQs, and training videos. To report technical problems, such as login issues or application errors, please contact: 1-855-55-BIOMS or bioms@alliancenctn.org. For assistance in using the application or questions or problems related to specific specimen logging, please contact: 1-855-55-BIOMS or bioms@alliancenctn.org.

**4.2** For questions regarding Streck BCT tubes submitted directly to Epic Sciences, please contact Epic Sciences: 1-858-356-6610 or partners@epicsciences.com.

**4.3** For all other questions regarding biospecimen procurement and shipping procedures, please contact the Alliance Biorepository Program Manager: 1-314-747-4402 or alliance@email.wustl.edu.

## 5. Site Preparation

**5.1** Please refer to the A011801 protocol document for any specific requirements related to patient enrollment, registration, and regulatory compliance.

**5.2** Please ensure that you have appropriate log on credentials and can successfully access the BioMS application. The BioMS application is used for both requesting biospecimen collection kits and for logging the collection and shipment of biospecimens to Epic Sciences or to the Alliance Biorepository at Washington University. For training and assistance in using the application or questions or problems related to specific specimen logging, please contact: 1-855-55-BIOMS or bioms@alliancenctn.org**.**

**5.3** Prior to collection of biospecimens, a biospecimen collection kit must be at the collection site. Please see **section 7** for requesting biospecimen collection kits. Please allow at least 10 working days to receive the collection kit.

**5.4** Identify a reliable source of dry ice for freezing and shipping biospecimens and a -70 to -90 degree Celsius freezer ("ultralow") in which frozen biospecimens may be stored prior to shipment.

**5.5 Please confirm that your institutional pathology department is willing to submit tumor tissue blocks <u>OR</u> 1 H&E stained slide <u>AND</u> ten (10) 10 micron unstained slides from BOTH:**

- **a. the archived initial diagnostic biopsy specimen (prior to starting neoadjuvant therapy), <u>AND</u>**
- **b. the residual disease on the definitive surgical specimen.**

**An institution whose pathology department is unwilling to comply with mandatory block or slide submission should not enroll patients to this study.**

## 6. Collection Schema

The following biospecimens are to be collected at each of the time points. Please refer to individual collection kit instructions, biospecimen collection and processing methods, and specific shipping procedures below.

| Time Point | Kit (Y/N) | Kit Name | Biospecimen | Quantity | Collection / Processing Method | Shipping / Recipient Lab | Notes |
|---|---|---|---|---|---|---|---|
| **Mandatory for <u>all</u> patients registered to A011801** | | | | | | | |
| ≤ 28 days after registration | N | None | Fixed tissue block | 2 | Fixed tissue block (9.2) | Ambient / ABWUSTL | 1, 12, 13 |
| ≤ 28 days after registration | N | None | Fixed tissue slides- initial diagnostic biopsy | 1 H&E stained slide **<u>AND</u>** 10 (10 um) unstained slides | Fixed tissue slides (9.3) | Ambient / ABWUSTL | 1, 2, 12, 13 |
| ≤ 28 days after registration | N | None | Fixed tissue slides- definitive surgical specimen | 1 H&E stained slide **<u>AND</u>** 10 (10 um) unstained slides | Fixed tissue slides (9.3) | Ambient / ABWUSTL | 1, 2, 12, 13 |
| ≤ 28 days after registration | Y | Blood Collection- Epic Sciences | Whole blood (Streck BCT) | 2 x 10 ml | Plasma for cfDNA (10.1) | Ambient / Epic Sciences | 3 |
| | | | | | | | |
| Cycle 2, Day 1 Pre-dose, within 1 hour prior to administration of tucatinib/placebo | Y | Cycle 2, Day 1- Wash U Kit | Whole blood for plasma | 4 x 500 ul aliquots | Frozen plasma for PK analysis (10.2) | Dry Ice / ABWUSTL | 4, 5, 6 |
| | | | | | | | |
| Cycle 2, Day 1 Post-dose, within 1 hour after end of T-DM1 infusion | Y | Cycle 2, Day 1- Wash U Kit | Whole blood for plasma | 4 x 500 ul aliquots | Frozen plasma for PK analysis (10.2) | Dry Ice / ABWUSTL | 5, 6 |
| | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Cycle 3, Day 1 Pre-dose, within 1 hour prior to administration of tucatinib/placebo | Y | Cycle 3, Day 1- Wash U Kit | Whole blood for plasma | 4 x 500 ul aliquots | Frozen plasma for PK analysis (10.2) | Dry Ice / ABWUSTL | 4, 5, 6 |
| | | | | | | | |
| Cycle 3, Day 1 Post-dose, within 1 hour after end of T-DM1 infusion | Y | Cycle 3, Day 1- Wash U Kit | Whole blood for plasma | 4 x 500 ul aliquots | Frozen plasma for PK analysis (10.2) | Dry Ice / ABWUSTL | 5, 6 |
| | | | | | | | |
| At completion of study therapy (+/- 1 month) | Y | Blood Collection- Epic Sciences | Whole blood (Streck BCT) | 2 x 10 ml | Plasma for cfDNA (10.1) | Ambient / Epic Sciences | 3, 7 |
| | | | | | | | |
| 1 year after completion of study therapy (+/- 1 month) | Y | Blood Collection- Epic Sciences | Whole blood (Streck BCT) | 2 x 10 ml | Plasma for cfDNA (10.1) | Ambient / Epic Sciences | 3 |
| | | | | | | | |
| Recurrence | Y | Blood Collection- Epic Sciences | Whole blood (Streck BCT) | 2 x 10 ml | Plasma for cfDNA (10.1) | Ambient / Epic Sciences | 3, 8 |
| **A011801 Biobanking** | | | | | | | |
| ≤ 28 days after registration | Y | Less than 28 Days after Registration- Wash U Kit | Whole blood (Streck BCT) | 2 x 10 ml | Plasma for cfDNA (10.1) | Ambient / ABWUSTL | 10, 11 |
| | | | | | | | |
| At completion of study therapy (+/- 1 month) | Y | Completion of study- Wash U Kit | Whole blood (Streck BCT) | 2 x 10 ml | Plasma for cfDNA (10.1) | Ambient / ABWUSTL | 7, 10, 11 |
| | | | | | | | |
| 1 year after completion of study therapy (+/- 1 month) | Y | 1 Year After Completion- Wash U Kit | Whole blood (Streck BCT) | 2 x 10 ml | Plasma for cfDNA (10.1) | Ambient / ABWUSTL | 10, 11 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Recurrence | N | None | Fixed tissue block | 1 | Fixed tissue block (9.2) | Ambient / ABWUSTL | 8, 9, 11 |
| Recurrence | N | None | Fixed tissue slides | 1 H&E stained slide **AND** 10 (10 um) unstained slides | Fixed tissue slides (9.3) | Ambient / ABWUSTL | 8, 9, 11 |
| Recurrence | Y | Recurrence-Wash U Kit | Whole blood (Streck BCT) | 2 x 10 ml | Plasma for cfDNA (10.1) | Ambient / ABWUSTL | 8, 10, 11 |

**Notes:**

1. Submission of fixed tissue blocks **OR** fixed tissue slides from **BOTH** the archived initial diagnostic biopsy specimen (prior to starting neoadjuvant therapy) **AND** the residual disease on the definitive surgical specimen is required for all patients registered to A011801. **Block submission strongly preferred.** See **section 9.2** for additional information.
2. Submission of one (1) H&E stained slide **AND** ten (10) 10 um unstained slides is required for sites unable or unwilling to submit fixed tissue block. If unable to submit H&E stained slide, please submit an additional unstained slide, cut at 4-6 micron.
3. Whole blood (Streck BCT) for CTC analysis, submitted directly to Epic Sciences.
4. If a patient is scheduled for a morning appointment, their morning dose of tucatinib or placebo should be held until after PK sample collection prior to the start of T-DM1 infusion. If a patient is scheduled for an afternoon appointment, their morning dose should be taken as scheduled, and PK sample collection should be done at the time of their appointment prior to T-DM1 infusion, ahead of their evening dose. Dosing time (for both drugs) and time of sample collection must be accurately recorded in the patient records and in Medidata Rave.
5. A one-hour sampling window is acceptable for both pre- and post-dose samples.
6. A total of 5 mL of peripheral blood in an EDTA tube will be collected. Please submit plasma (4 x 500 ul aliquots), processed and frozen on site and shipped on dry ice.
7. Time point defined as the day of completion of the last planned dose of T-DM1 and study drug without disease recurrence.
8. Disease recurrence before completion of the last planned dose of study therapy, or within the follow-up period (10 years post-registration)

9. Tumor tissue from a site of recurrence (when applicable), only if tissue was collected per standard of care. No new research biopsy is required. A fixed tissue block **OR** one (1) H&E stained slide **AND** ten (10) 10 um unstained slides should be submitted. If unable to submit H&E stained slide, please submit an additional unstained slide, cut at 4-6 micron. **Block submission is strongly preferred.**
10. Whole blood (Streck BCT) for isolation of buffy coat and plasma at ABWUSTL. Please be certain to order kits for optional submission to ABWUSTL **AND** kits for mandatory submission to Epic Sciences. Kit names have been listed in the collection schema.
11. Collection is optional for patients but all sites must ask patients for their consent to participate. Please see protocol-specific consent documents.
12. If patient consents to biobanking, any remaining tissue will be stored at the Alliance Biorepository for unknown future use.
13. **For patients who previously participated in EA1181: The EA1181 patient ID numbers will be collected in the BioMS, OPEN, and Medidata Rave databases. If the tissue specimen was previously submitted for EA1181 and is therefore not available to submit for A011801, this will not be a protocol deviation. This should be recorded in the specimen submission CRF in Rave. Tissue should additionally be marked as "Not Collected" in BioMS.**

## 7. Biospecimen Collection Kits

**7.1** To facilitate the proper collection and shipping of blood biospecimens, biospecimen collection kits and materials will be provided. The cost of the kit and shipping the kit to the site will be paid for. The institution is expected to pay for shipping the kit with the blood biospecimens back to Epic Sciences and to the Alliance Biorepository at Washington University in St. Louis via priority overnight shipping.

**7.2** Kits will be sent via FedEx® Ground at no additional cost to the participating institutions. Kits will not be sent via rush delivery service unless the participating institution provides their own FedEx® account number for express service. The study will not cover the cost for rush delivery of kits.

**7.3** Kits should be requested at least 10 working days in advance of the anticipated collection date. As many as 2 kits can be requested at one time. Since the collection materials (vacutainer tubes) have expiration dates, do not request kits more than 90 days prior to their anticipated use. **All kits must be requested by using the BioMS system.**

**7.4** There are separate kits for the mandatory blood collection to Epic Sciences and the optional blood collection to the Alliance Biorepository at Washington University in St. Louis. Please ensure the proper kits are ordered depending on where the blood samples are being sent.

**7.5** Kit contents and specific instructions for use of the kit are provided in the kit box. **During warm weather months (i.e. June—August), a refrigerated pack (not frozen) should be included in the shipment to maintain ambient temperature. When shipping during other months of the year, a room temperature pack should be included in the shipment.**

**7.6** Once a kit is received, do not discard the outer cardboard overwrap. The kit, containing biospecimens, is to be shipped back in the same box.

**7.7** Please return all components of the kit, regardless of whether they have been used or not. Kits and kit components are recycled when possible, minimizing the kit cost.

**7.8** Well in advance of collecting biospecimens, inspect the biospecimen collection kit to ensure that all components are present and not expired, particularly if the kit has been onsite for longer than 30 days.

**7.9** Distributed kits will have a minimum shelf life of 90 days; unless precluded by the stability of a particular component.

**7.10** Note that individual kit components that are expired, damaged, or missing cannot be replaced. The remedy is to order a complete, new kit (Please note in your request that you are replacing an expired or damaged kit).

**7.11** Please return all kits that have expired or missing components. Return the ENTIRE kit using the cheapest possible shipping method at your expense. DO NOT DISCARD kits that have missing or expired components. Recycling kits keeps the cost of kit materials to a minimum. Please note that all outgoing and incoming kits are tracked, and sites that have requested many more kits than they have returned will be charged for non-returned kits.

**7.12** If a biospecimen collection component (e.g. vacutainer collection tube) is missing, damaged, or expired, the institution may substitute a like-kind collection tube from their own supply. However, note that while some kit components are generic (i.e. EDTA tubes), others are highly specialized (e.g. Streck BCT) and probably are not available at the institution.

**7.13** Note that protocol requirements are based on blood volumes, not tube sizes. If the protocol requires the collection of 8 ml of whole blood, generally a 10 ml tube is provided in the kit for convenience. If desirable or necessary to collect 8 ml in 3 x 3 ml tubes (for example), that is permissible.

**7.14 No kits are provided for submission of mandatory or optional tissue to ABWUSTL. Paraffin blocks or slides cut from such blocks should be sent independently of other biospecimens using the following guidelines:**

**a.** Blocks and slides should be packaged to avoid breakage using a padded envelope or, preferably, a small Styrofoam container.

**b.** During warm weather months, paraffin blocks and slides should be shipped in an insulated container that contains a refrigerant pack, to avoid heat > 25 degrees C (77 degrees F) that may melt paraffin and damage the tissue specimens.

**c.** Blocks and slides may be shipped for standard overnight delivery according to institutional policies and using the preferred vendor.

**7.15** Please see **Section 11 – Biospecimen Shipping** for specific instructions on shipping to ABWUSTL or to Epic Sciences.

## 8. Biospecimen Labeling and Tracking

**8.1** All research biospecimens (vacutainer tubes, cryovials, and tissue bags) MUST be labeled with the Alliance patient ID number, patient initials (Last, First, Middle), the date and time (if applicable) of collection, specimen type (e.g. plasma), and collection time point if applicable (e.g. “pre-dose” or “post-dose”).

**8.2** Kits from Epic Sciences will contain phlebotomist label sheets with a reference to “CTC requisition form”. **Please ignore this reference.** Labels should be attached to the tubes and to the BioMS manifest which serves as the requisition form. Containers and vials sent to ABWUSTL should be labeled with an indelible, solvent-resistant marker when they are at ambient temperature. Do not affix any labels to vials, slides or tubes submitted to ABWUSTL. Label the collection containers directly with the marking pen.

**8.3** Surgical pathology tissue blocks should not be labeled in any manner. The institutional surgical pathology number (e.g. “S16-1234”) and the individual block identifier (e.g. “A3”) should be readable on the block. If tissue sections are being submitted instead of a block, each tissue section slide should be labeled with the Alliance patient ID number, institutional surgical pathology number, the block identifier, section thickness, and the serial section number (if applicable).

**8.4** A **de-identified copy of the surgical pathology report**, labeled with the Alliance patient ID number, is required to accompany <u>all</u> tissue submissions to ABWUSTL. Usually, this is generated by obscuring all PHI (names and dates) with white-out or a black magic marker, labeling each page of the report with the Alliance patient ID number, and photocopying the report. Please ensure the institutional surgical pathology number (SPN) and block ID that match the SPN on the physical label on the tissue are maintained on the surgical pathology report. See **section 9** for additional details on tissue submission.

**8.5** All biospecimens that are collected and sent to Epic Sciences or to the Alliance Biorepository must be **logged and tracked in BioMS**. The BioMS system is a web-based application that tracks the collection and shipping of biospecimens. Once individual biospecimens are logged and 'shipped' in the BioMS system, a packing manifest will be created by the system. This manifest must be printed out and must accompany all biospecimen shipments. To become familiar with the BioMS system and for further information about training, access, and use, please contact the BioMS Help desk at: 1-855-55-BIOMS or bioms@alliancenctn.org.

**8.6** In the event that BioMS cannot be accessed, please complete a BioMS Specimen Log and Shipping Manifest form which can be found here- **http://tinyurl.com/alliance-bioms-contingency**.

## 9. Tissue Collection

### 9.1 Overview.

**a.** Please refer to protocol-specific instructions for procedures related to actual tissue procurement from individual participants. The method for tissue procurement (needle core biopsy, sampling of surgically resected tumor, or tumor 'debulking') is dependent upon the disease site and the individual patient.

**b.** When procuring tissue biospecimens by any method, when possible, avoid tissue that is grossly necrotic, hemorrhagic, fatty, or fibrous. If in doubt, briefly (1 min or less) place the tissue segment in a sterile specimen cup containing physiologic (normal) saline to rinse the tissue. Necrotic, hemorrhagic, and fatty tissue will generally dissolve or float on the surface while tumor and parenchymal tissue will remain intact and sink to the bottom of the cup.

**c.** **<u>For patients who previously participated in EA1181: The EA1181 patient ID numbers will be collected in the BioMS, OPEN, and Medidata Rave databases. If the tissue specimen was previously submitted for EA1181 and is therefore not available to submit for A011801, this will not be a protocol deviation. This should be recorded in the specimen submission CRF in Rave. Tissue should additionally be marked as "Not Collected" in BioMS.</u>**

### 9.2 Diagnostic Fixed Tissue Blocks

**a.** At time of registration, this protocol requires submission of TWO representative, diagnostic pathology, formalin fixed paraffin embedded (FFPE) tissue blocks. Blocks should be submitted from **<u>BOTH</u>** the archived initial diagnostic biopsy specimen (prior to starting neoadjuvant therapy) **<u>AND</u>** the residual disease on the definitive surgical specimen. For patients who consent to biobanking, an additional tumor tissue block is requested from a site of tumor recurrence (where applicable), if tissue was collected per standard of care.

**b.** DNA and RNA will be isolated from fixed tissue blocks for BC360 analysis. For those patients who consent to biobanking, remaining tissue will be stored at ABWUSTL for future use.

**c.** Any clinical surgical pathology block that is submitted for research studies will not be exhausted or rendered unsuitable for future diagnostic use. Any clinical surgical pathology block that is submitted will be returned within ten working days of written request, when needed for clinical management or clinical trial enrollment for a specific patient. Otherwise, all blocks will be returned to the submitting institution when the trial and correlative science study endpoints have been met.

**d.** In the event that an institution will not release tumor tissue blocks, the institution may instead submit one (1) H&E stained slide and ten (10) unstained slides from each of the requested blocks, as indicated in **section 9.3**. **Although slides will be accepted, tumor tissue block submission is strongly preferred.**

**e. During warm weather months, paraffin blocks and slides should be shipped in an insulated container that contains a refrigerant pack, to avoid heat > 25 degrees C (77degrees F) that may melt paraffin and damage the tissue specimens.**

### 9.3 Fixed Tissue Slides

**a.** In cases where an institution is unwilling or unable to submit the requested tissue blocks, a set of ten (10) unstained tumor tissue slides from each block can be submitted as an alternative. **An H&E stained slide should accompany each set of unstained slides. The H&E stained slide should be from the same block where the unstained slides were cut from. If an H&E stained slide from a block is not available, please submit an additional unstained slide, cut at 4-6 micron, in addition to the ten (10) unstained slides cut at 10 micron.**

**b.** Please follow the procedures below for submitting unstained tissue slides. If your pathology department is unwilling or unable to follow these tissue-sectioning instructions, please consider submission of tissue blocks, which can be cut at the biorepository and returned to your institution at a later date.

**c.** Include a copy of the corresponding, de-identified pathology report with all slide submissions.

**d.** Please follow the procedures below for submitting fixed tissue slides.

| # of slides | Section thickness | Slide type | Purpose |
|---|---|---|---|
| 10 | 10 micron | Positively Charged | DNA, RNA for BC360 |

**e.** Serial tissue sections should be cut fresh from the appropriate formalin fixed, paraffin embedded tissue block.

**f.** Cut sections at 10 micron thickness as indicated onto positively charged slides.

**g.** Ensure that each slide is labeled with the Alliance patient ID number, the institutional surgical pathology number and block ID, section thickness, and the slide serial section number (1, 2, 3, etc.).

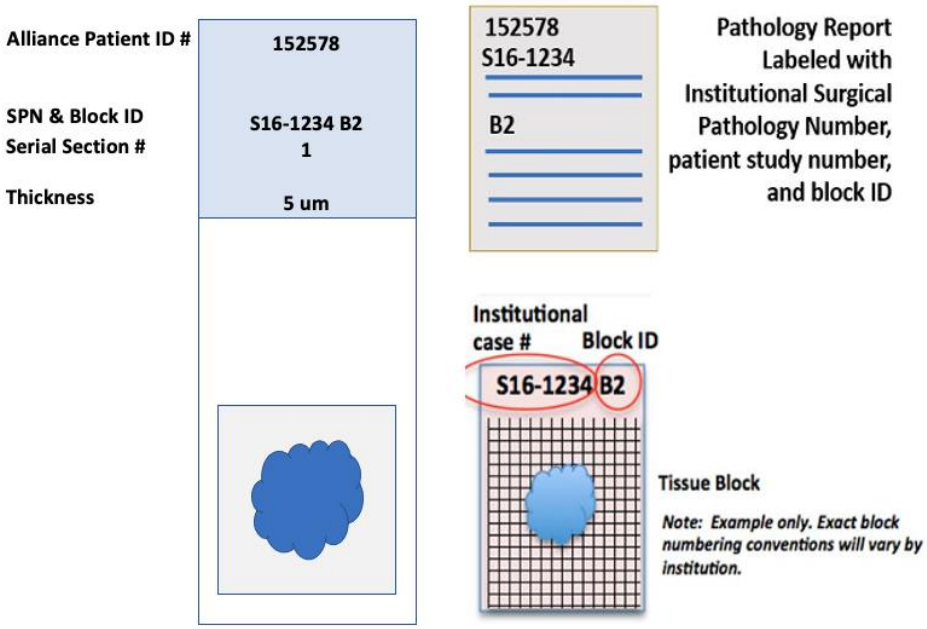
**h.** Do not label slides with adhesive labels. Write or print information on the textured surface of the slide with indelible, solvent-resistant ink.

**i.** No adhesives or other additives should be used in the water bath.

**j.** Mount only one tissue section per slide. Make certain sections are placed on the painted / textured side of the slide.

**k.** When placing the sections onto the slides, ensure that the tissue is placed on the bottom third of the slide. Ensure that each serial section from the block is placed in the same orientation on each slide.

**l.** See figure below for proper mounting and labeling.




**m.** Air dry slides for 12-24 hours prior to shipping. Do not oven dry slides.

**n.** Use slide mailers or a slide box to ship slides. Slides should not be touching each other. Ensure that slides from only one patient are placed in one slide mailer.

**o.** **During warm weather months, paraffin blocks and slides should be shipped in an insulated container that contains a refrigerant pack, to avoid heat > 25 degrees C (77degrees F) that may melt paraffin and damage the tissue specimens.**

## 10. Blood Collection Methods

### 10.1 Plasma Nucleic Acid (Streck) Tube Processing

**a.** Collect 10 ml of blood into each of the Streck BCT tubes using standard venous phlebotomy. Invert tubes 10 times.

**b.** Store Streck BCT tubes with whole blood at room temperature. Do not freeze or refrigerate the tubes.

**c.** **For blood submitted to Epic Sciences, the tubes must be shipped on the day of collection and received at the lab within 24 hours of collection. For blood collected for biobanking and submitted to ABWUSTL, the tubes may be stored for up to 72 hours at room temperature prior to shipment to ABWUSTL (i.e. blood collected on Friday may be stored over the weekend at room temperature for shipment to ABWUSTL on Monday).**

**d.** Ensure that the Streck BCT tubes are shipped at ambient temperature to avoid freezing. **During warm weather months (i.e. June—August), a refrigerated pack (not frozen) should be included in the shipment to maintain ambient temperature. When shipping during other months of the year, a room temperature pack should be included in the shipment.**

### 10.2 Plasma Processing for PK Analysis

**a.** Collect 5 ml of whole blood by standard venous phlebotomy technique into the purple top (K2EDTA) tube. Gently invert tube 10 times to disperse anticoagulant into the entire blood sample. Place blood tube on ice.

**b.** Within 30 minutes of collection, spin the vacutainer tube at room temperature in a clinical centrifuge at 1300 xG for 10 minutes. A refrigerated (4 degrees Celsius) centrifuge may be used, if available.

**c.** Label 4 cryovials as instructed in **section 8**. Make certain each vial is labeled completely and identically. **Please ensure aliquots are labeled with date and time of collection as well as time point (i.e. "pre-dose" or "post-dose").**

**d.** Carefully remove the plasma layer (~2 ml), without touching the white, buffy coat layer, and transfer 500 ul to each of the 4 labeled cryovials.

**e.** Immediately freeze plasma containing cryovials in a -70 to -90 degrees Celsius ultralow freezer. If an ultralow freezer is not immediately available, temporary storage on dry ice is acceptable. Store at -70 to -90 degrees Celsius until ready for shipment on dry ice.

## 11. Biospecimen Shipping

### 11.1 Overview

**a.** Please see the Directions for Use (DFU) document that is included in each kit for specific directions on how to package and ship blood biospecimens.

**b.** Place the original, completed copy of the BioMS packing manifest in the shipment. If sending tissue, include a de-identified copy of the surgical pathology report labeled with the Alliance patient ID number. Do not send specimens without a completed BioMS Packing Manifest or substitute "BioMS Downtime Form." Biospecimens cannot be accepted without this completed form.

**c.** All biospecimens should be shipped within the timeframes indicated above in **section 9** and **10.** If collected biospecimens cannot be shipped within the specified timeframe (e.g. Friday – Saturday or Holiday collections), please contact the Alliance Biorepository Program Manager: 1-314-747-4402 or alliance@email.wustl.edu for further instructions, at least 24 hours prior to anticipated collection. For questions regarding specimens shipping to Epic Sciences, please contact 1-858-356-6610 or partners@epicsciences.com.

**d.** **Do not ship on Friday, Saturday, Sunday or the day before a nationally recognized holiday.**

### 11.2 Shipping to Epic Sciences

Ship container for PRIORITY OVERNIGHT DELIVERY according to IATA guidelines and standard institutional policies and using the preferred vendor.

Ship to:

Epic Sciences
Attn: A011801
9381 Judicial Drive
Suite 200
San Diego, CA 92121
Phone: 858-356-6610

### 11.3 Shipping to ABWUSTL

Ship container for PRIORITY OVERNIGHT DELIVERY according to IATA guidelines and standard institutional policies and using the preferred vendor.

Ship to:

Alliance Biorepository at Washington University in St. Louis
c/o Siteman Cancer Center Tissue Procurement Core
Washington Univ. School of Medicine
425 S. Euclid Ave.
Room 5120
St. Louis, MO
63110-1005
Phone: 314-454-7615

## 12. ABWUSTL Biospecimen Receipt and Quality Assurance Measures

**12.1** Upon receipt, all biospecimens will be accessioned into the TPC informatics system, OpenSpecimen.

**12.2** All biospecimens will be logged, associated, and tracked by the unique patient biopsy control number.

**12.3** Each individual biospecimen will receive and be physically labeled with a unique biospecimen identifier, associated with the biopsy control number in the TPC informatics system.

**12.4** Upon receipt, all physical biospecimens received will be reconciled with what is recorded on the BioMS packing manifest. Any discrepancies noted will be communicated to the Program Manager who will contact the submitting site for reconciliation.

**12.5** Upon receipt, any biospecimen received that is not in appropriate physical condition (broken vials, frozen samples that are thawed, ambient samples that are frozen) will be reported to the Program Manager, who will contact the submitting site for reconciliation.

**12.6** Aliquoted biofluids will be stored under liquid nitrogen vapor.

**12.7** All biospecimens will remain in storage until additional processing or review is requested in writing by the appropriate protocol PI.

## 13. Document History

| Version | Description and Justification of Change | Author | Effective Date |
|---|---|---|---|
| 3.7 | Added contact table, included provisions for shipping during warm weather, added instructions for sites to ignore Epic Sciences reference to CTC requisition form in their kits | KAL | 06/07/2023 |
| 3.6 | Added info about kit shelf life and expedited shipping. Clarified instructions regarding pathology report submission in 8.3 | KAL | 4/5/2023 |
| 3.5 | Clarified shipping instructions to Epic Sciences | AAW | 08/16/2022 |
| 3.4 | Clarified instructions for ordering kits for Epic Sciences vs. ABWUSTL | AAW | 07/19/2022 |
| 3.3 | Clarified tissue requirements with regard to participants of study EA1181 | PAA | 10/26/2021 |
| 3.2 | Include provisions for shipping during warm weather<br>Minor clarifications to collection table | PAA | 06/21/2021 |
| 3.1 | Updated PK labeling instructions as requested by ABWUSTL | PAA | 05/26/2021 |
| 3.0 | Updated contact information for Epic Sciences | PAA | 05/17/2021 |

| | | | |
|---|---|---|---|
| | Corrected minor typos and grammatical errors | | |
| 2.1 | Updated PK labeling instructions | PAA | 11/30/2020 |
| 2.0 | Added details regarding PK collection<br>Updated hyperlinks | PAA | 11/04/2020 |
| 1.1 | Updated address for Epic Sciences | PAA | 09/14/2020 |
| 1.0 | New | PAA | 09/10/2020 |