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 A031704. 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 A031704 biospecimen collection, processing, and submission; including staff at satellite institutions.

2. Scope

This document applies to all biospecimens collected specifically for A031704 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

4. Contact Information

Protocol-related questions may be directed as follows:	
Questions	**Contact (via email)**
Questions regarding patient eligibility, treatment, and dose modification:	A031704@alliancenctn.org
Questions related to data submission, RAVE or patient follow-up:	Data Manager: Shauna Overton overton.shauna@mayo.edu
Questions regarding the protocol document and model informed consent:	Protocol Coordinator: Aishwarya Vijendran aishwaryav@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 alliance@email.wustl.edu
Questions regarding drug supply	PMB
Questions regarding drug administration	Pharmacy Contact: Jerline Hsin, PharmD jhsin@coh.org

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 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 A031704 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 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.

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)	Biospecimen	Quantity	Collection / Processing Method	Shipping	Notes
For patients registered to A031704-ST1						
Prior to treatment	N	Fixed tissue block	1	Fixed tissue blocks (9.2)	Ambient	1, 2
Prior to treatment	N	Unstained tumor tissue slides	25	Fixed tissue slides (9.3)	Ambient	1, 2
Prior to treatment	N	Fixed tissue cores	2	Fixed tissue cores (9.4)	Ambient	1, 2
Prior to treatment	N	Optional Research Biopsy- Tumor tissue	2-4	Formalin Fixation (9.5)	Ambient	1, 3
Prior to treatment	N	Optional Research Biopsy- Tumor tissue	1-2	Frozen Tissue (9.6)	Dry Ice	1, 3
Prior to treatment	Y	Whole blood for serum	3 x 1ml aliquots	Frozen serum (10.1)	Dry Ice	1
Prior to treatment	Y	Whole blood for plasma	6 x 1ml aliquots	Frozen plasma (10.2)	Dry Ice	1, 4
Prior to treatment	Y	Whole blood for “buffy coat”	2 aliquots	“Buffy Coat” (10.3)	Dry Ice	1, 4
Prior to treatment	Y	Whole blood (ACD tubes)	3 x 10 ml	Whole Blood- ACD tubes (10.4)	Ambient	1
Prior to treatment	Y	Whole blood (Streck BCT)	2 x 10 ml	Plasma for cfDNA (10.5)	Ambient	1
Cycle 1, Day 1 after registration step 2	Y	Whole blood for serum	3 x 1ml aliquots	Frozen serum (10.1)	Dry Ice	1, 5
Cycle 1, Day 1 after registration step 2	Y	Whole blood for plasma	6 x 1ml aliquots	Frozen plasma (10.2)	Dry Ice	1, 4, 5
Cycle 1, Day 1 after registration step 2	Y	Whole blood for “buffy coat”	2 aliquots	“Buffy Coat” (10.3)	Dry Ice	1, 4, 5
Cycle 1, Day 1 after registration step 2	Y	Whole blood (ACD tubes)	3 x 10 ml	Whole Blood- ACD tubes (10.4)	Ambient	1, 5
Cycle 1, Day 1 after registration step 2	Y	Whole blood (Streck BCT)	2 x 10 ml	Plasma for cfDNA (10.5)	Ambient	1, 5
End of Study Treatment (All pts)	N	Fixed tissue block	1	Fixed tissue blocks (9.2)	Ambient	1, 7

End of Study Treatment (All pts)	N	Unstained tumor tissue slides	25	Fixed tissue slides (9.3)	Ambient	1, 7
End of Study Treatment (All pts)	N	Fixed tissue cores	2	Fixed tissue cores (9.4)	Ambient	1, 7
End of Study Treatment (All pts)	Y	Whole blood for serum	3 x 1ml aliquots	Frozen serum (10.1)	Dry Ice	1, 6
End of Study Treatment (All pts)	Y	Whole blood for plasma	6 x 1ml aliquots	Frozen plasma (10.2)	Dry Ice	1, 4, 6
End of Study Treatment (All pts)	Y	Whole blood for "buffy coat"	2 aliquots	"Buffy Coat" (10.3)	Dry Ice	1, 4, 6
End of Study Treatment (All pts)	Y	Whole blood (ACD tubes)	3 x 10 ml	Whole Blood- ACD tubes (10.4)	Ambient	1, 6
End of Study Treatment (All pts)	Y	Whole blood (Streck BCT)	2 x 10 ml	Plasma for cfDNA (10.5)	Ambient	1, 6

Notes:

1. Collection is optional for patients but requires all sites offer to patients to consent. Please see protocol-specific consent documents.
2. Submission of archival tissue from the nephrectomy or biopsy of primary or metastatic site is optional. Submission of either a representative, archived tumor tissue block, **OR** 25 unstained tumor tissue slides AND two (2) 2 mm cores from such a block is requested, if available. An archival pathology block submission is strongly preferred. If fewer than 25 unstained slides and 2 cores can be submitted, please submit as many as possible.
3. If archival diagnostic tissue is not available or sufficient for submission, there is an optional research biopsy at baseline to collect tissue. At least 3 but up to 6 cores (18G needle or larger) should be submitted. At least 1 core should be flash frozen **AND** at least 2 should be formalin fixed. If submitting 6 cores, 2 cores should be flash frozen **AND** 4 cores should be formalin fixed. Please see study funding sheet regarding site reimbursement for this research biopsy. The submission of these samples is optional for all patients registered to this study, including those who are found to be ineligible and those who do not receive protocol therapy. For additional details, please refer to **sections 9.5** and **9.6.**
4. Plasma and "buffy coat" (white blood cells) are obtained from the same tubes of whole blood.
5. Specimens to be collected in all patients proceeding to Step 2 registration.
6. Blood specimens to be collected from **ALL** patients when study treatment is completed, including those who complete study treatment prior to randomization, and those who discontinue treatment due to toxicity, disease progression, or any other reasons.
7. Submission of leftover FFPE tissue collected under standard of care at disease progression should be submitted, if available. A fixed tumor tissue block, **OR** 25 unstained tumor tissue slides AND two (2) 2 mm cores from such a block is requested, if available. An archival pathology block submission is strongly preferred. If fewer than 25 unstained slides and 2 cores can be submitted, please submit as many as possible.

7. Biospecimen Collection Kits

7.1 Blood Specimens

7.1.1 To facilitate the proper collection and shipping of whole blood, buffy coat, plasma, and serum specimens, 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 biospecimens back to the Alliance Biorepository at Washington University in St. Louis via priority overnight shipping.

7.1.1.1 NOTE: Kits will be sent via FedEx 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.

7.1.2 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.

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

7.1.4 Kit contents and specific instructions for use of the kit are provided in the kit box. Please return any used collection materials with the kit**. 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.**

7.1.5 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.

7.1.6 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.

7.1.7 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.

7.1.8 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).

7.1.9 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 out-going and in coming kits are tracked, and sites that have requested many more kits than they have returned will be charged for non-returned kits.

7.1.10 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.

7.1.11 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.

7.2 Tissue Specimens

7.2.1 There is no independent "kit" for submission of paraffin blocks, cores, or slides.

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

7.2.3 During warm weather months, paraffin block, cores, 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.

7.2.4 Frozen tissue specimens should be shipped in insulated containers with tissue covered in at least 2 inches of dry ice.

7.2.5 Please see **Section 11 – Biospecimen Shipping** for specific instructions on shipping to ABWUSTL.

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 and specimen type (i.e. serum, plasma, buffy coat).

8.2 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 or cores are being submitted instead of the block, each tissue section slide or tube should be labeled with the Alliance patient ID number, institutional surgical pathology number, the block identifier, and the serial section number. Provide **a de-identified copy of the surgical pathology report**, labeled with the Alliance patient ID number, corresponding to the blocks or slides submitted. **Please ensure the institutional surgical pathology number and block ID are maintained on the surgical pathology report**. See **section 9** for additional details.

8.3 Label all containers and vials with an indelible, solvent-resistant marker when they are at ambient temperature.

8.4 Do not affix any labels to vials, slides or tubes. Label the collection containers directly with the marking pen.

8.5 All biospecimens that are collected and sent 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.

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

9.1.2 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.

9.2 Diagnostic Pathology Fixed Tissue Blocks.

9.2.1 This protocol requests submission of ONE representative, diagnostic pathology, formalin fixed paraffin embedded tumor tissue block from nephrectomy or biopsy of primary or metastatic site. An additional block is requested from disease progression if leftover tissue collected under standard of care is available.

9.2.2 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 end points have been met.

9.2.3 In the event that an institution will not release tumor tissue blocks, the institution may instead submit tissue sections, mounted and unstained to glass slides.

9.2.4 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 Unstained Slides from Diagnostic Fixed Tissue Blocks

9.3.1 In cases where institutions are unable or unwilling to submit the requested tissue blocks, a set of at least 10 but up to 25 unstained tissue slides may be sent as an alternative for each block. 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.

# of slides	Section thickness	Slide type	Purpose
10-25	10 micron	Non-Charged	DNA, RNA, Protein-based biomarker

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

9.3.3 Cut sections at 10 micron thickness as indicated onto non-charged slides.

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

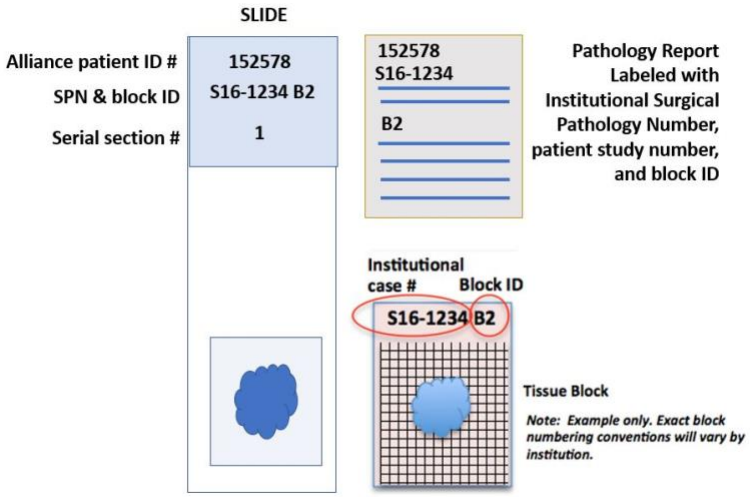
9.3.5 Do not label slides with adhesive labels. Write or print information on the textured surface of the slide with indelible, solvent-resistant ink.

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

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

9.3.8 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.

9.3.9 See figure below for proper mounting and labeling.



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

9.3.11 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.

9.3.12 Include a copy of a **de-identified pathology report** with all slide submissions.

9.3.13 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.

9.4 Tissue Cores from Diagnostic Fixed Tissue Blocks

9.4.1 In cases where an institution is unwilling or unable to submit tissue blocks, two (2), 2mm cores may be submitted from each block, **in addition to** the unstained tumor tissue slides.

9.4.2 Place the tissue cores directly into a microcentrifuge tube or any other suitable container. Label the tube of tissue following the guidelines outlined in **section 9.3.**

9.5 Formalin Fixation and Frozen Tissue from Research Biopsy

9.5.1 In cases where archival diagnostic tissue is not available or sufficient for submission, an optional research biopsy can be performed to collect tissue. Please follow institutional procedures to ensure research biopsy tissues are obtained from the safest / most accessible site and preferably not a sclerotic bone lesion. At least 3 but up to 6 cores (18G needle or larger) should be submitted. At least 1 core should be flash frozen AND at least 2 should be formalin fixed. If submitting 6 cores, 2 cores should be flash frozen AND 4 cores should be formalin fixed (see section 6 collection schema footnote 3). Please see **section 9.6** for instructions of preparing flash frozen tissue cores.

9.5.2 Label the formalin fixative vial with the Alliance patient ID number, as instructed in **section 8**. Be certain to record the date and time that the tissue is placed into the formalin vial.

9.5.3 Place the fresh tissue core into the vial and secure the lid with parafilm. Ensure that the tissue is completely submerged into the formalin fixative.

9.5.4 Store and ship the formalin fixed tissue at ambient temperature. If possible, to avoid prolonged fixation, ship the tissue on the same day it is collected.

9.6 Frozen Tissue from Research Biopsy

9.6.1 In cases where archival diagnostic tissue is not available or sufficient for submission, an optional research biopsy can be performed to collect tissue. Please follow institutional procedures to ensure research biopsy tissues are obtained from the safest / most accessible site and preferably not a sclerotic bone lesion. At least 3 but up to 6 cores (18G needle or larger) should be submitted. At least 1 core should be flash frozen AND at least 2 should be formalin fixed. If submitting 6 cores, 2 cores should be flash frozen AND 4 cores should be formalin fixed (see section 6 collection schema footnote 3). Please see **section 9.5** for instructions of preparing formalin fixed tissue cores.

9.6.2 Prior to procurement, prepare tissue for freezing by placing approximately six pounds of crushed dry ice into the bottom compartment of a Styrofoam cooler. Place a metal freezing plate on top of the dry ice and allow the surface of the plate to reach the approximate temperature of the dry ice.

9.6.2.1 An alternative method is to use the freezing plate found on a pathology cryostat.

9.6.2.2 An alternative method is to use a flat surface of a dry ice block.

9.6.2.3 An alternative method is to use a commercially available Cryocooler (OPS Diagnostics) which uses a metal platform and a liquid nitrogen saturated “pillow” to achieve freezing temperatures of -130 degrees C.

9.6.2.4 Do not freeze tissue by placing warm tissue in a -70 to -90 degree C ultralow freezer.

9.6.2.5 Do not freeze tissue using a dry ice ethanol bath.

9.6.2.6 Do not freeze tissue by submersion in an isopentane cryobath.

9.6.3 Label one tissue cryomold for every tissue core that is to be frozen. Ensure that the cryomold(s) and tissue bag(s) are labeled with the Alliance patient ID number as instructed in **section 8.**

9.6.4 Working quickly, gently place the tissue length-wise in the mold. Place the cryomold on the level cold plate or flat, level surface of dry ice. Allow the tissue to freeze for 3-5 minutes.

9.6.5 Once frozen, quickly wrap the mold with the tissue block in cooled foil and place the block in the corresponding labeled tissue bag. Maintain the tissue block buried in dry ice, in a -70 to -90 degree C ultralow freezer, or in liquid nitrogen vapor (not liquid phase) until ready for shipment.

9.6.6 Repeat the above steps for each individual tissue core or biopsy specimen that is to be frozen.

10. Blood Collection Methods

10.1 Serum Processing

10.1.1 Collect 10 ml of whole blood by standard venous phlebotomy technique into the red top (plain glass with clot activator) tube. Do not collect whole blood into a "tiger top" / "SST" / "gel tube." Invert tube 10 times

10.1.2 Allow blood to clot for 30 minutes.

10.1.3 Label 3 cryovials as instructed in **section 8**. Make certain each vial is labeled completely and identically.

10.1.4 Spin blood in vacutainer tube at 4 degrees Celsius in a clinical centrifuge using standard programming for serum separation. Usually this is 1200 xG (actual speed will depend upon the centrifuge) for 10 minutes.

10.1.5 Carefully remove 3 ml of serum (without touching the clot layer) and divide into 3, 1 ml labeled cryovials.

10.1.6 Freeze serum containing cryovials on dry ice or a -70 to -90 degree C ultralow freezer. Store at -70 to -90 degrees C until ready for shipment on dry ice.

10.1.7 Please be aware that it is important the serum to be processed **within 4 hours** after blood draw

10.2 Plasma Processing

10.2.1 Collect 20 ml of whole blood by standard venous phlebotomy technique into the purple top (EDTA) tubes. Invert tubes 10 times.

10.2.2 Within 30 minutes of collection, spin the vacutainer tubes at room temperature in a clinical centrifuge using standard programming for plasma separation. Usually this is 2500 xG (actual speed will depend upon the centrifuge) for 15 minutes. Transfer the upper layer of plasma from each tube into two separate clean 15 ml polypropylene tubes. **Repeat the centrifugation** at the same condition as before to create platelet poor plasma.

10.2.3 Label 6 cryovials as instructed in **section 8**. Make certain each vial is labeled completely and identically.

10.2.4 Carefully remove about 6 ml of plasma (without touching the white, buffy coat layer) and divide into 6, 1 ml labeled cryovials. Keep the vacutainer tubes containing the white, buffy coat layer for white blood cell isolation **(section 10.3).**

10.2.5 Freeze plasma containing cryovials on dry ice or a -70 to -90 degree C ultralow freezer. Store at -70 to -90 degrees C until ready for shipment on dry ice.

10.3 "Buffy Coat" (White Blood Cell) Processing

10.3.1 Follow procedures in **section 10.2** for collecting and processing plasma from EDTA tubes.

10.3.2 Label 2 cryovials as instructed in **section 8.**

10.3.3 After removing the plasma, carefully remove the white, "buffy coat" white blood cell layer, avoiding the red blood cell mass as much as possible.

10.3.4 Transfer the buffy coat layer (approximately 0.2 – 0.5 ml) from each EDTA tube into the labeled cryovials. Immediately freeze the cryovials of buffy coat on dry ice or in liquid nitrogen vapor. Do NOT freeze buffy coat cells by placing a warm tube in a -70 to -90 degree C ultralow freezer. Once completely frozen, the cryovials containing the buffy coat cells may be stored at -70 to -90 degrees C until ready for shipment on dry ice.

10.4 Whole Blood- ACD tubes (no processing)

10.4.1 Collect 10 ml of blood into each of the ACD tubes using standard venous phlebotomy. Invert tubes 10 times.

10.4.2 Store ACD tubes with whole blood at ambient temperature until shipping. Do not freeze the tubes. **Blood should be collected Monday—Thursday only. Due to required processing, the tubes MUST be received at the Biorepository within 24 hours of collection.** Ensure that the ACD 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.**

10.5 Plasma Nucleic Acid (Streck) Tube Processing

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

10.5.2 Store Streck tubes with whole blood at room temperature. Do not freeze or refrigerate the tubes. The tubes may be stored for up to 72 hours at ambient temperature before shipment. Ensure that the Streck 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.**

11. Biospecimen Shipping

11.1 Overview

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

11.1.2 If sending frozen tissue, place tissue bag containing the tissue specimen into an insulated shipping container and immediately cover with at least 2 inches of dry ice. **Do not tape shipping container closed.**

11.1.3 Place the original, completed copy of the BioMS packing manifest in the shipment. If sending tissue, include a copy of the de-identified 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.

11.1.4 All biospecimens should be shipped on the same day that they are collected (Monday – Thursday). Biospecimens must be received by the recipient lab within 24 hours of collection. If collected biospecimens cannot be shipped on the same day that they are collected (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.

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

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

Ship to:

Alliance Biorepository
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. 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 Frozen aliquoted biofluids will be stored under liquid nitrogen vapor.

12.7 Fixed tissue biospecimens will be processed and embedded into paraffin using TPC standard operating procedures.

12.8 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
3.1	Updated title of study, added contact table, added info about kit requests,	KL	07/11/2023

	removed reference to blank waybill being provided		
3.0	Added tissue collection at EOT	PAA	11/29/2021
2.3	Updated shipment requirements for ACD tubes Include instructions for shipping in warm weather Corrected minor typos and grammatical errors	PAA	06/17/2021
2.2	Updated effective date to align with protocol posting date	PAA	02/01/2021
2.1	Updated time point in biospecimen collection schedule	PAA	11/06/2020
2.0	Updated biospecimen collection schedule to remove progression time point Updated biospecimen collection schedule to make tissue submission optional Updated Biorepository email addresses	PAA	11/25/2019
1.5	Updated shipment requirements for ACD tube	PAA	04/23/2019
1.4	Clarified optional biopsy	YW, PAA	03/06/2019
1.3	Updated contact email for BioMS helpdesk	PAA	02/21/2019
1.2	Added tissue requirement at progression	YW, PAA	01/08/2019
1.1	Included instructions for shipping frozen tissue	PAA	11/14/2018
1.0	New	PAA	10/04/2018