CORRELATIVE SCIENCE PROCEDURE MANUAL

1. Purpose

This document describes the procedures required for the collection, shipping, and processing of biospecimens that are being submitted for patients enrolled or registered on A171901. This document also describes the procedures that will be followed subsequent to the receipt of biospecimens by the Alliance Biorepository at Mayo Clinic (ABMAYO) 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 A171901 biospecimen collection, processing, and submission, including staff at satellite institutions.

2. Scope

This document applies to all biospecimens collected specifically for the A171901 clinical trial study. Please refer to the trial protocol-specific language for additional details regarding eligibility, participant enrollment, and data submission. **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
ABMAYO	Alliance Biorepository at Mayo Clinic

4. Contact Information

4.1 For questions and problems related to protocol administration, eligibility, patient registration, and data submission, relevant contact information is listed on protocol pages 1 and 2.

4.2 For information on using the BioMS system, please refer to the 'Help' links on the BioMS webpage to access the on-line 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**.

4.3 For all other questions regarding biospecimen procurement and shipping procedures, please contact:

ABMAYO

- Blood samples:
  Roxann Neumann, RN, BSN, CCRP
  Phone: 1-507-538-0602
  Email: neumann.roxann@mayo.edu

5. Site Preparation

5.1 Please refer to A171901 protocol document for any specific requirements related to patient enrollment, registration, and regulatory compliance.

5.2 Please ensure that you have the appropriate log-in 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 Mayo Clinic. 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**.

6. Collection Schema

The following biospecimens are to be collected at each of the time points listed in the table below. Please refer to individual biospecimen collection and processing methods, and specific shipping procedures that are detailed in this manual.

Time Point	Kit (Y/N)	Biospecimen	Quantity	Collection / Processing Method	Shipping	Notes
Mandatory for ALL patients registered to A171901; submit the following for A171901-ST1 and A171901-PP1						
Day 1, Cycle 1	N	Whole Blood (EDTA tube)	3 x 10 mL	Whole blood EDTA (9.1)	Ambient cool pack/Ship overnight	1, 3, 5
Day 1, Cycle 1	N	Whole blood for serum	6 x 1 mL aliquots	Frozen serum (9.2)	Ship Frozen	1, 4, 5
Day 1, Cycle 2	N	Whole Blood (EDTA tube)	3 x 10 mL	Whole blood EDTA (9.1)	Ambient cool pack/Ship overnight	1, 3, 5
Day 1, Cycle 2	N	Whole blood for serum	6 x 1 mL aliquots	Frozen serum (9.2)	Ship Frozen	1, 4, 5
Day 1, Cycle 3	N	Whole Blood (EDTA tube)	3 x 10 mL	Whole blood EDTA (9.1)	Ambient cool pack/Ship overnight	1, 3, 5
Day 1, Cycle 3	N	Whole blood for serum	6 x 1 mL aliquots	Frozen serum (9.2)	Ship Frozen	1, 4, 5
Day 1, Cycle 6	N	Whole blood for serum	6 x 1 mL aliquots	Frozen serum (9.2)	Ship Frozen	4, 5
Day 1, Cycle 9	N	Whole blood for serum	6 x 1 mL aliquots	Frozen serum (9.2)	Ship Frozen	4, 5
End of Treatment	N	Whole Blood (EDTA tube)	3 x 10 mL	Whole blood EDTA (9.1)	Ambient cool pack/Ship overnight	1,2,3, 5

Notes:

1. Blood will be collected **prior to IV infusion** on Day 1 of Cycles 1, 2, and 3.
2. Blood should be collected within 7 days of the last day of treatment.
3. Whole blood to be used for biomarker analysis.
4. Serum from whole blood to be used for pharmacokinetic analysis. Cycle 6 and Cycle 9 samples required only for patients still receiving treatment (to be collected **prior to IV infusion**).
5. Submission of blood samples for review is required for all patients registered to this study, including those who are found to be ineligible and those who do not receive protocol therapy. Biomarker and pharmacokinetic studies will be performed. All patients who provide their consent to participate in the main study will have provided their consent to participate in A171901-ST1 and A171901-PP1.

7. Biospecimen Collection Kits

7.1 Blood Specimens

7.1.1 There are no "kits" provided for submission of blood specimens for this study. Sites are responsible for acquiring materials for collection and shipping of these specimens to the Biorepository.

7.1.2 Some examples of acceptable 2.0 mL cryovials for submission of serum samples are: Nalgene (Cat #5012-0020), Fisher (Cat #05-669-57), Corning (Cat #430488 or 430659), VWR (Cat #16001-1102), Thermo Scientific (Cat #5000-0020) or Sarsted (Cat #72.694.107).

8. Biospecimen Labeling and Tracking

8.1 All research biospecimens MUST be labeled with the Alliance study number, Alliance patient ID number, patient initials (Last, First, Middle), the date and time of collection and specimen type. Specimen labels must match BioMS records.

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

8.3 **Do not affix any labels to vials or tubes.** Label the collection containers directly with the marking pen.

8.4 All biospecimens that are collected and sent to ABMAYO must be **logged and tracked in BioMS** under A171901. Do not send samples to the Biorepository in which the patient has not been registered onto the study. 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**.

8.5 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. Blood Collection Methods

9.1 Whole blood (EDTA Tube- no processing)

9.1.1 Collect 3 x10mL of blood into the EDTA tube using standard venous phlebotomy. Invert tube 10 times.

9.1.2 Store EDTA tube with whole blood at ambient temperature until shipping. Do not refrigerate or freeze the tube. Biospecimens must be received by the recipient lab within 24 hours of collection. If blood must be collected on Friday, it can be shipped on Friday for Saturday delivery. Ensure that the EDTA tube is shipped with an ambient refrigerant pack to ensure proper temperature control.

9.2 Serum Processing

9.2.1 Collect 2 x10mL whole blood by standard venous phlebotomy technique into the red top (plain glass with clot activator) tubes. Do not collect whole blood into "tiger top" / "SST" / "gel tubes." Invert tubes 10 times

9.2.2 Allow blood to clot for 30 minutes until the clot forms.

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

9.2.4 Spin blood in vacutainer tube at 4 degrees 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.

9.2.5 Carefully remove 6 mLs of serum (without touching the clot layer) and divide into 6, 1 mL labeled cryovials.

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

10. Biospecimen Shipping

10.1 Place the original, completed copy of the BioMS packing manifest in the shipment. Do not send specimens without a completed BioMS Packing Manifest or substitute "BioMS Downtime Form." Biospecimens cannot be accepted without this completed form.

10.2 All biospecimens collected on the study should be shipped on the same day that they are collected. EDTA whole blood biospecimens must be received by the recipient lab within 24 hours of collection. If biospecimens cannot be shipped on the same day they are collected, please contact appropriate personnel listed in section 4.3 for further instructions, at least 24 hours prior to anticipated collection.

10.3 Ship container for PRIORITY OVERNIGHT DELIVERY according to IATA guidelines and standard institutional policies and using the preferred vendor. Ship specimens to ABMAYO on Monday through Friday only. Do not ship on Saturdays or on the day before a national holiday.

Ship to:
Alliance Biorepository at Mayo Clinic- BAP Freezer
ST-SL-16
150 Third Street SW
Rochester, MN 55902
Phone: 507-538-0602

11. ABMAYO Biospecimen Receipt and Quality Assurance Measures

11.1 All biospecimens sent to ABMAYO will be accessioned into the informatics system BioMS, at ABMAYO Research Laboratory Information Management System (RLIMS) which interfaces with BioMS.

11.2 All biospecimens received at the ABMAYO will be logged, associated, and tracked by the patient study ID number.

11.3 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 submitting site for reconciliation.

11.4 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.

11.5 All biospecimens submitted to ABMAYO will remain in storage until exhausted. In the event the patient withdraws consent, the specimens will be disposed/returned according to Alliance Policy and Procedure Chapter 11.

12. Document History

Version	Description and Justification of Change	Author	Effective Date
1.1	Updated EDTA storage to ambient temperature	GLS	12/16/2020
1.0	New	GLS	05/04/2020