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 A041701. This document also describes the procedures that will be followed subsequent to the receipt of biospecimens by the Alliance Hematologic Biorepository (HEME) and Hematologics, Inc., 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 A041701 biospecimen collection, processing, and submission; including staff at satellite institutions.

2. Scope

This document applies to all biospecimens collected specifically for A041701 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
HEME	Alliance Hematologic Biorepository

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 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.

4.3 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 A041701 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 logging the collection and shipment of biospecimens to HEME and to Hematologics, Inc. 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 Identify a reliable source of dry ice for freezing and shipping biospecimens and a -20 degree Celsius freezer in which frozen biospecimens may be stored prior to shipment.

6. Collection Schema

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

Time Point	Biospecimen	Quantity	Collection / Processing Method	Shipping / Recipient Lab	Notes
Mandatory for <u>all</u> patients registered to A041701					
At Pre-Registration	Bone Marrow Aspirate (EDTA / lavender top) **<u>OR</u>** Whole Blood (EDTA / lavender top)	5 ml Bone Marrow **<u>OR</u>** 30 ml Whole Blood	Bone Marrow Aspirate- EDTA (9.2) **<u>OR</u>** Whole Blood- EDTA (10.1)	Ambient / HEME (11.1.8)	1, 2
At Pre-Registration	Whole Blood (EDTA / lavender top)	10 ml	Whole Blood – EDTA (10.1)	Ambient / HEME (11.1.8)	1
For patients registered to A041701-LC1					
At Pre-Registration	Bone Marrow Aspirate (heparin / green top)	2 ml	Bone Marrow Aspirate- Heparin (9.1)	Ambient / Hematologics (11.1.9)	3
At Pre-Registration	Whole Blood (Sodium citrate / light blue top)	2.7 ml	Frozen Plasma (10.2)	Dry Ice / HEME (11.1.8)	3
End of Induction	Bone Marrow Aspirate (heparin / green top)	2 ml	Bone Marrow Aspirate- Heparin (9.1)	Ambient / Hematologics (11.1.9)	3
End of Induction	Whole Blood (Sodium citrate / light blue top)	2.7 ml	Frozen Plasma (10.2)	Dry Ice / HEME (11.1.8)	3
End of Consolidation	Bone Marrow Aspirate (heparin / green top)	2 ml	Bone Marrow Aspirate- Heparin (9.1)	Ambient / Hematologics (11.1.9)	3
For patients who consent to biobanking					
At Pre-Registration	Bone Marrow Aspirate (EDTA / lavender top) **<u>OR</u>** Whole Blood (EDTA / lavender top)	5 ml Bone Marrow **<u>OR</u>** 30 ml Whole Blood	Bone Marrow Aspirate- EDTA (9.2) **<u>OR</u>** Whole Blood- EDTA (10.1)	Ambient / HEME (11.1.8)	2, 4
At Pre-Registration	Whole Blood (EDTA / lavender top)	10 ml	Whole Blood – EDTA (10.1)	Ambient / HEME (11.1.8)	4

End of Induction	Bone Marrow Aspirate (EDTA / lavender top) **OR** Whole Blood (EDTA / lavender top)	5 ml Bone Marrow **OR** 30 ml Whole Blood	Bone Marrow Aspirate- EDTA (9.2) **OR** Whole Blood- EDTA (10.1)	Ambient / HEME (11.1.8)	2, 4
End of Induction	Whole Blood (EDTA / lavender top)	10 ml	Whole Blood – EDTA (10.1)	Ambient / HEME (11.1.8)	4
End of Consolidation	Bone Marrow Aspirate (EDTA / lavender top) **OR** Whole Blood (EDTA / lavender top)	5 ml Bone Marrow **OR** 30 ml Whole Blood	Bone Marrow Aspirate- EDTA (9.2) **OR** Whole Blood- EDTA (10.1)	Ambient / HEME (11.1.8)	2, 4
End of Consolidation	Whole Blood (EDTA / lavender top)	10 ml	Whole Blood – EDTA (10.1)	Ambient / HEME (11.1.8)	4
Relapse	Bone Marrow Aspirate (EDTA / lavender top) **OR** Whole Blood (EDTA / lavender top)	5 ml Bone Marrow **OR** 30 ml Whole Blood	Bone Marrow Aspirate- EDTA (9.2) **OR** Whole Blood- EDTA (10.1)	Ambient / HEME (11.1.8)	2, 4
Relapse	Whole Blood (EDTA / lavender top)	10 ml	Whole Blood – EDTA (10.1)	Ambient / HEME (11.1.8)	4

Notes:

1. Submission of a bone marrow aspirate (5 ml) and peripheral blood (10 ml) is required for all patients registered to A041701.
2. If marrow is inaspirable or if the patient has had a bone marrow aspiration prior to pre-registration and refuses to have another, submission of 30 ml of whole blood (EDTA) is permissible**. This whole blood is in addition to the 10 ml peripheral blood collection.**
3. Collection is optional for patients but requires all sites offer to patients to consent. Please see protocol-specific consent documents. Collection should only occur for those patients who consent to model consent question #2. No additional specimen will be required for RNA testing. The sample collected for E-selectin ligand testing will provide sufficient material for RNA aliquoting. If marrow inaspirable or if the patient has had a bone marrow aspiration prior to pre-registration and refuses to have another one performed, then the submitted 30 ml peripheral blood (EDTA/lavender top) used for all patients registered to A041701 will be used.

4. Collection is optional for patients but requires all sites offer to patients to consent. Please see protocol-specific consent documents. Collection should only occur for those patients who consent to model consent question #4.

7. Biospecimen Collection Kits

7.1 There are no kits, blood tubes, or collection / shipping materials provided for this study. Sites are responsible for acquiring materials for collection and shipping of all specimens to HEME and to Hematologics, Inc.

8. Biospecimen Labeling and Tracking

8.1 All research biospecimens (vacutainer tubes) MUST be labeled with the protocol number (A041701), Alliance patient number, patient initials (Last, First, Middle), the date and time (if applicable) of collection and specimen type (e.g. bone marrow, whole blood, plasma).

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 HEME and to Hematologics, Inc. 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.

8.5 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-biomscontingency**.

9. Bone Marrow Collection

9.1 Aspirate- Sodium Heparin Tube

9.1.1 Collect 2 ml of bone marrow following standard institutional protocol into a heparin / green top tube. Invert tube 10 times.

9.1.2 Store heparin tube with bone marrow at ambient temperature. Do not freeze or refrigerate the tube. The tube must be received at Hematologics, Inc. within 24 hours of collection. Ensure that the heparin tube is shipped at ambient temperature to avoid freezing.

9.2 Aspirate- EDTA tube

9.2.1 Collect 5 ml of bone marrow following standard institutional protocol into a EDTA / lavender top tube. Invert tube 10 times.

9.2.2 Store EDTA tube with bone marrow at ambient temperature. Do not freeze or refrigerate the tube. The tube must be received at HEME within 24 hours of collection. Ensure that the EDTA tube is shipped at ambient temperature to avoid freezing.

10. Blood Collection

10.1 Whole blood (EDTA- no processing)

10.1.1 Collect whole blood by standard venous phlebotomy technique into the EDTA tube. Invert tube 10 times.

10.1.2 Store EDTA tube with whole blood at 4 degrees Celsius (refrigerated). Do not freeze the tube. The tube must be received at HEME within 24 hours of collection (**i.e. Saturday, Sunday, or holiday collections are not allowed).** Ensure that the EDTA tube is shipped at ambient temperature to avoid freezing.

10.2 Frozen Plasma

10.2.1 Collect whole blood by standard venous phlebotomy technique into the sodium citrate tube. Invert tube 10 times.

10.2.2 Centrifuge tube with a recommended g-force relative to centrifugal force (rcf) of 1500 g for 15 minutes.

10.2.3 Remove plasma from the cells as soon as possible after separation. Samples should be aliquoted and must be stored frozen at -20 degrees Celsius until shipping to HEME to avoid loss of bioactive human sE-selectin. Plasma should be submitted to HEME within 30 days of collection. Batch shipping of plasma specimens is allowed.

11. Biospecimen Shipping

11.1 Overview

11.1.1 Whole blood and bone marrow aspirate specimens should be packaged to avoid breakage in a padded envelope or preferably a Styrofoam cooler. In warm weather months, a cold pack should be included to regulate temperature.

11.1.2 Frozen plasma aliquots should be placed in a biohazard bag inside of a Styrofoam cooler and covered with 3 to 4 lbs (2 kg) of commercially prepared dry ice. Pellets or chunks are preferred. Make sure the box is filled with dry ice and the weight of the dry ice is noted on the dry ice label on the outside of the shipping container. It is the local sites' responsibility to obtain dry ice when shipping frozen specimens.

11.1.3 Specimens should be sent according to IATA guidelines. Frozen aliquots should be shipped to HEME within 30 days of collection. Batch shipment of frozen aliquots is allowed.

11.1.4 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.

11.1.5 With the exception of plasma specimens which may be batched, all biospecimens should be shipped on the same day that they are collected (Monday – Friday). 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. Saturday, Sunday 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.

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

11.1.7 All specimens should be shipped via priority overnight shipping. Specimens shipped on Fridays must be sent using priority overnight shipping / FOR SATURDAY DELIVERY.

11.1.8 Shipping to HEME

11.1.8.1 Ship container for PRIORITY OVERNIGHT DELIVERY according to IATA guidelines and standard institutional policies and using the preferred vendor.
Ship to:
Alliance Hematologic Biorepository (HEME)
The Arthur G. James Cancer Hospital and Solove Research Institute
300 West Tenth Avenue, Lobby
Columbus, OH 43210
Phone: 614-366-6295
Fax: 614-688-4755

11.1.9 Shipping to Hematologics, Inc.

11.1.9.1 Ship container for PRIORITY OVERNIGHT DELIVERY according to IATA guidelines and standard institutional policies and using the preferred vendor.
Ship to:
Hematologics, Inc.
3161 Elliott Avenue, Suite 200
Seattle, Washington 98121
ATTN: Lisa Brodersen, PhD
Phone: 206-223-2700
Email: Lisa@hematologics.com

12. Biospecimen Receipt and Quality Assurance Measures

12.1 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.

12.2 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.

12.3 Aliquoted biofluids will be stored under liquid nitrogen vapor.

12.4 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
1.2	Updated HEME contact info	KL	01/15/2024
1.1	Clarified footnotes in section 6	PAA	09/20/2021
1.0	New	PAA	12/15/2020