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 A042001. This document also describes the procedures that will be followed subsequent to the receipt of biospecimens by the Alliance Hematologic Malignancy Biorepository (HEME) or by Children's Hospital at Los Angeles (CHLA) 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 A042001 biospecimen collection, processing, and submission, including staff at satellite institutions.

2. Scope

This document applies to all biospecimens collected specifically for A042001 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
CHLA	Children's Hospital at Los Angeles
HEME	Alliance Hematologic Malignancy 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 questions regarding mandatory bone marrow aspirate submission to CHLA, please contact the CHLA Laboratory, 1-323-361-2423 or plmclinicalimmunologylaboratory@chla.usc.edu.

4.4 For specific questions regarding sample collection and submission to HEME, please contact the HEME Laboratory at AllianceLTB@osumc.edu or 1-614-688-4754.

4.5 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 A042001 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 CHLA. 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. Please refer to biospecimen collection and processing methods and specific shipping procedures below.

Time Point	Biospecimen	Quantity	Form Required	Collection / Processing Method	Shipping / Recipient Lab	Notes
Mandatory for <u>all</u> patients registered to A042001						
Pre-registration	Bone Marrow in Sodium Heparin tubes for MRD analysis at CHLA (If inaspirable, submit Whole Blood in EDTA tubes)	2 ml of bone marrow **<u>OR</u>** 5 ml of whole blood if inaspirable	Y	Bone Marrow Aspirate-Sodium Heparin (9.1) **<u>OR</u>** Whole Blood-EDTA (10.1)	Ambient / CHLA	1, 2
After Cycle 1	Bone Marrow in Sodium Heparin tubes for MRD analysis at CHLA	2 ml	Y	Bone Marrow Aspirate-Sodium Heparin (9.1)	Ambient / CHLA	1, 3
After Cycle 2	Bone Marrow in Sodium Heparin tubes for MRD analysis at CHLA	2 ml	Y	Bone Marrow Aspirate-Sodium Heparin (9.1)	Ambient / CHLA	1, 3
End Intensive Phase	Bone Marrow in Sodium Heparin tubes for MRD analysis at CHLA	2 ml	Y	Bone Marrow Aspirate-Sodium Heparin (9.1)	Ambient / CHLA	1, 3
For Patients Registered to A042001-LC1						
Pre-registration	Bone Marrow in EDTA tubes for MRD analysis by Adaptive (If inaspirable, submit Whole Blood in EDTA tubes)	2 ml of bone marrow **<u>OR</u>** 5 ml of whole blood if inaspirable	N	Bone Marrow Aspirate-EDTA (9.1) **<u>OR</u>** Whole Blood-EDTA (10.1)	Ambient / HEME	2, 5
After Cycle 1	Bone Marrow in EDTA tubes for MRD analysis by Adaptive	2 ml	N	Bone Marrow Aspirate-EDTA (9.1)	Ambient / HEME	3, 5
After Cycle 1	Whole blood in EDTA tubes for MRD analysis by Adaptive	5 ml	N	Whole Blood-EDTA (10.1)	Ambient / HEME	5

After Cycle 2	Bone Marrow in EDTA tubes for MRD analysis by Adaptive	2 ml	N	Bone Marrow Aspirate-EDTA (9.1)	Ambient / HEME	3, 5
After Cycle 2	Whole blood in EDTA tubes for MRD analysis by Adaptive	5 ml	N	Whole Blood-EDTA (10.1)	Ambient / HEME	5
End Intensive Phase	Bone Marrow in EDTA tubes for MRD analysis by Adaptive	2 ml	N	Bone Marrow Aspirate-EDTA (9.1)	Ambient / HEME	3, 5
End Intensive Phase	Whole blood in EDTA tubes for MRD analysis by Adaptive	5 ml	N	Whole Blood-EDTA (10.1)	Ambient / HEME	5
For patients consented to A042001 Biobanking						
Pre-registration	Bone marrow in EDTA tubes (If inaspirable, submit Whole Blood in EDTA tubes)	2 ml of bone marrow **OR** 5 ml of whole blood, if inaspirable	N	Bone Marrow Aspirate-EDTA (9.1) **OR** Whole Blood-EDTA (10.1)	Ambient / HEME	2
After Cycle 1	Bone marrow in EDTA tubes (If inaspirable, submit Whole Blood in EDTA tubes)	2 ml of bone marrow **OR** 5 ml of whole blood, if inaspirable	N	Bone Marrow Aspirate-EDTA (9.1) **OR** Whole Blood-EDTA (10.1)	Ambient / HEME	2
After Cycle 2	Bone marrow in EDTA tubes (If inaspirable, submit Whole Blood in EDTA tubes)	2 ml of bone marrow **OR** 5 ml of whole blood, if inaspirable	N	Bone Marrow Aspirate-EDTA (9.1) **OR** Whole Blood-EDTA (10.1)	Ambient / HEME	2
End Intensive Phase	Bone marrow in EDTA tubes	2 ml	N	Bone Marrow Aspirate-EDTA (9.1)	Ambient / HEME	4
Progression	Bone marrow in EDTA tubes	2 ml	N	Bone Marrow Aspirate-EDTA (9.1)	Ambient / HEME	4

Notes:

1. Submission is mandatory for **all** patients registered to A042001.
2. The samples should be from the first aspiration (i.e. first pull). Aspirate needle should be redirected if needed to get first pull bone marrow aspirate. Submit 5 ml peripheral whole blood in an EDTA tube to replace each sample if bone marrow inaspirable (i.e. 5 ml for MRD analysis at CHLA, 5 ml for Biobanking, 5 ml for Adaptive).
3. Samples for central MRD assessments should be from the first aspirate pull (sample may be split; if two pulls, first pull for flow MRD to CHLA, second pull to HEME for processing for future analysis by Adaptive).
4. Submit only if patient is undergoing bone marrow aspirate as standard of care.
5. **Specimen will be submitted to HEME for processing. Specimens should NOT be submitted directly to Adaptive.**

7. Biospecimen Collection Kits

7.1 Blood and Bone Marrow Specimens

7.1.1 There is no independent "kit" for submission of peripheral blood or bone marrow aspirates. Sites are responsible for acquiring materials for collection and shipping of these specimens.

7.1.2 Please see **Section 11 – Biospecimen Shipping** for specific instructions on shipping to HEME and to CHLA.

8. Biospecimen Labeling and Tracking

8.1 All research biospecimens (vacutainer tubes) MUST be labeled with the protocol number (A042001), Alliance patient number, patient initials (Last, First, Middle), the date and time (if applicable) of collection and specimen type (e.g. bone marrow, peripheral blood).

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 or to CHLA 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-bioms-contingency**.

9. Bone Marrow Collection

9.1 Aspirate- Sodium Heparin or EDTA tube

9.1.1 Collect 2ml of bone marrow following standard institutional protocol into the appropriate tube type as specified in the collection schema in **section 6** (EDTA or Sodium Heparin). Invert tube 10 times.

9.1.2 Store tube with bone marrow at ambient temperature. Do not freeze or refrigerate the tube. The tube must be shipped on the same day it is collected and must be received by the recipient lab within 24 hours of collection. **Please collect and ship specimens on Monday—Friday only. Specimens should not be collected or shipped on Saturday, Sunday, the day prior to a holiday, or on a holiday.** Ensure that the tube is shipped at ambient temperature to avoid freezing.

9.1.3 For all of the mandatory bone marrow submission timepoints (see section 6), the "Bone Marrow or Blood for MRD Analysis at CHLA" form must be submitted along with the bone marrow aspirate to CHLA. The form should also be emailed to the CHLA Laboratory, plmclinicalimmunologylaboratory@chla.usc.edu, at the time of shipment. Failure to submit this form with the specimens may delay turnaround time for analysis. The "Bone Marrow or Blood for MRD Analysis at CHLA" form can be located in Appendix 1 of this manual or on the A042001 protocol-specific page on the CTSU and Alliance websites.

10. Blood Collection

10.1 Whole blood (EDTA tubes- no processing)

10.1.1 Collect 5 ml of peripheral blood by standard venous phlebotomy technique into the EDTA tube. Invert the tube 10 times.

10.1.2 Store the EDTA tube with peripheral blood at ambient temperature. Do not freeze or refrigerate the tube. The specimen must be shipped on the same day it is collected and must be received at HEME within 24 hours of collection. **Saturday, Sunday, or holiday collections are NOT permitted.** Ensure that the EDTA tube is shipped at ambient temperature to avoid freezing.

11. Biospecimen Shipping

11.1 Overview

11.1.1 Peripheral 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 gel pack should be included to regulate temperature.

11.1.2 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.

11.1.3 The "Bone Marrow or Blood for MRD Analysis at CHLA" Form must be submitted along with the bone marrow aspirate at the mandatory timepoints (see section 6). This form can be located in Appendix 1 of this manual or is available for download on the A042001 protocol-specific page on CTSU and on the Alliance website.

11.1.4 Specimens should be sent according to IATA guidelines. 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.

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

11.1.6 All specimens should be shipped via priority overnight shipping.

11.1.7 Shipping to HEME

11.1.7.1 Ship container for PRIORITY OVERNIGHT DELIVERY according to IATA guidelines and standard institutional policies and using the preferred vendor.
Ship to:
Alliance Hematologic Malignancy Biorepository (HEME)
The Arthur G. James Cancer Hospital and Solove Research Institute
300 West Tenth Avenue, Lobby
Columbus, OH 43210
Phone: 614-688-4754
Fax: 614-688-4755

11.1.8 Shipping to CHLA

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:
Department of Pathology and Laboratory Medicine
Children's Hospital Los Angeles
4650 Sunset Blvd.
Dubuque Bldg, 2nd Floor, Room 2-290
Los Angeles, CA 90027
Phone: 323-361-2423

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
1.1	Added contact information for HEME Updated name of Biorepository Clarified footnotes	PAA	01/11/2023
1.0	New	PAA	04/06/2022

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Bone Marrow or Blood for MRD Analysis at Children's Hospital Los Angeles (CHLA)

Instructions: This form must be submitted along with bone marrow aspirate or blood to Dr. Brent Wood's lab at CHLA. The form must be completed by typing; ***do not handwrite. Failure to submit this form with the specimen may delay turnaround time for central MRD analysis.***

Patient Initials:_____ Patient ID:_____

Institution:_____Institution ID:_____

Collection Date: _____ Collection Time: _____ Sample Type: _____

Collection Timepoint:_____ Courier Tracking Number:_____

Responsible CRA Name: _____

E-mail Address: _____

Phone Number:_____Emergency Contact Number*: _____

Alternate CRA Name: _____

E-mail Address:_____

Phone Number: _____ Emergency Contact Number*_____

**Please provide a pager or cell phone number for questions outside of regular business hours.*

Comments (unusual circumstances during collection/processing of samples):

Shipped by: _____

After receiving the central review results form via e-mail, the institution must forward the form to plmclinicalimmunologylaboratory@chla.usc.edu in order to re-register the patient. The site will also be required to upload this form as Supporting Documentation using a report type of "Other" in Rave.

ver: 7/28/21.