CIBMTR SC21-07 / BMT CTN 2101

Prospective observational study of the immunogenicity of mRNA vaccines for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine after autologous hematopoietic stem cell transplantation (HCT), allogeneic HCT, and chimeric antigen receptor T-cell therapy

RESEARCH SAMPLE INFORMATION GUIDE

Version v6.0

January 17, 2023

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BMT CTN 2101
Research Sample Information Guide

This guide includes the collection, processing, and shipping information for the following samples collected for this study as well as future assays of T-cell responses to vaccine:

➢ Study Samples

Schedule for Specimen Collection*		
Visit	**Visit Description**	**Visit Window[1]**
Time-point 1	Baseline: Pre-Vaccine #1	Within 14 days prior to vaccine administration
Time-point 2	Post Vaccine #1	Single dose vaccines: 14-35 days after dose #1 Two-dose vaccines: within 7 days prior to dose #2
Time-point 3	Post-Vaccine #2 (or similar time frame after a single dose vaccine) / Pre-vaccine dose #3 (Booster)	Single dose vaccines: 4-8 weeks after specimen obtained for Time-point 2 Two-dose vaccines: 3-8 weeks after dose #2. If vaccine #3 (booster) is planned, the sample should be drawn within 7 days prior to booster administration.
Time-point 3b *(only required for patients receiving a booster >8 weeks after dose #2)*	Pre-vaccine dose #3 (booster) **This sample is obtained only if there are >8 weeks between dose #2 and booster dose**	Obtain sample within 7 days prior to booster administration only if there are >8 weeks (56 days) between dose #2 and booster dose
Time-point 4 *(only required for patients receiving booster)*	Post-vaccine #3 (booster) **This sample is obtained only if the patient is receiving a booster dose**	Obtain sample between 7 – 35 days following the booster
Time-point 5	Final Post-Vaccine	7 – 9 months after dose #1, ideally at 8 months ± 28 days

***The CIBMTR Research Sample Repository Protocol v13.0 and the associated v3.0 consent/assents for this study (CIBMTR SC21-07/BMT CTN 2101) MUST be IRB approved by sites. Patient consent (re-consent for already enrolled subjects) must be obtained prior to collecting 50 ml samples at any visit and/or prior to collecting any booster-related blood draws (Time-point 3b and 4). If IRB approval has yet to be received at a site, only up to 30 ml samples are to be drawn at each time-point and samples for Time-point 3b and 4 cannot be obtained.**

[1]Visits post-vaccine #1 should occur at closest routine clinical visit during the visit windows where possible. Ideally visits and samples are completed within the visit windows specified. However, as this is an observational study, data should still be collected for out of window assessments. The only exception is that Visit 1 MUST be collected within 14 days prior to vaccination #1, otherwise the patient is not eligible to enroll.

- **Baseline (Pre-Vaccine #1),** collect the following samples (GlobalTrace visit **V1**):
  - Collect 5 ml peripheral blood sample in one BD Vacutainer® tube containing Silica Clot Activator, Polymer Gel, Silicone-coated interior (gold or red/gray top SST) **GlobalTrace sample type**: Whole Blood and **Global Trace purpose**: Research Sample (Serum)
  - Collect 45* mL of peripheral blood in appropriately sized BD Vacutainer® tubes containing Sodium Heparin additive (green top) – **GlobalTrace sample type**: Whole Blood and **Global Trace purpose**: Research Sample (PBMC)

- **Post Vaccine #1**, collect the following samples (GlobalTrace visit **V2**):
  - Collect 5 ml peripheral blood sample in one BD Vacutainer® tube containing Silica Clot Activator, Polymer Gel, Silicone-coated interior (gold or red/gray top SST) **GlobalTrace sample type**: Whole Blood and **Global Trace purpose**: Research Sample (serum)
  - Collect 45* mL of peripheral blood in appropriately sized BD Vacutainer® tubes containing Sodium Heparin additive (green top) – **GlobalTrace sample type**: Whole Blood and **Global Trace purpose**: Research Sample (PBMC)

- **Post-Vaccine #2 or similar time frame after a Single Dose Vaccine/Pre-vaccine dose #3*,** collect the following samples (GlobalTrace visit **V3**):
  - Collect 5 ml peripheral blood sample in one BD Vacutainer® tube containing Silica Clot Activator, Polymer Gel, Silicone-coated interior (gold or red/gray top SST) **GlobalTrace sample type:** Whole Blood and **Global Trace purpose**: Research Sample (serum)
  - Collect 45* mL of peripheral blood in appropriately sized BD Vacutainer® tubes containing Sodium Heparin additive (green top) – **GlobalTrace sample type:** Whole Blood and **Global Trace purpose**: Research Sample (PBMC)

- **Pre-Vaccine dose #3* (booster) collected only if there are more than 8 weeks (56 days) between dose #2 and booster dose,** collect the following samples (GlobalTrace visit **V3b**):
  - Collect 5 ml peripheral blood sample in one BD Vacutainer® tube containing Silica Clot Activator, Polymer Gel, Silicone-coated interior (gold or red/gray top SST) **GlobalTrace sample type:** Whole Blood and **Global Trace purpose**: Research Sample (serum)
  - Collect 45* mL of peripheral blood in appropriately sized BD Vacutainer® tubes containing Sodium Heparin additive (green top) – **GlobalTrace sample type:** Whole Blood and **Global Trace purpose**: Research Sample (PBMC)

- **Post-Vaccine dose #3* (booster) collected only if patient is receiving a booster dose,** collect the following samples (GlobalTrace visit **V4**):
  - Collect 5 ml peripheral blood sample in one BD Vacutainer® tube containing Silica Clot Activator, Polymer Gel, Silicone-coated interior (gold or red/gray top SST)

GlobalTrace sample type: Whole Blood and **Global Trace purpose**: Research Sample (serum)

- Collect 45* mL of peripheral blood in appropriately sized BD Vacutainer® tubes containing Sodium Heparin additive (green top) – **GlobalTrace sample type:** Whole Blood and **Global Trace purpose**: Research Sample (PBMC)

- **Final Post-vaccine,** collect the following samples (GlobalTrace visit **V5**):
  - Collect 5 ml peripheral blood sample in one BD Vacutainer® tube containing Silica Clot Activator, Polymer Gel, Silicone-coated interior (gold or red/gray top SST) **GlobalTrace sample type**: Whole Blood and **Global Trace purpose**: Research Sample (serum)
  - Collect 45* mL of peripheral blood in appropriately sized BD Vacutainer® tubes containing Sodium Heparin additive (green top) – **GlobalTrace sample type**: Whole Blood and **Global Trace purpose**: Research Sample (PBMC)

➢ Research Sample Collection, Processing and Shipping

1. Blood Collection Tubes

The **transplant center site** will need to supply the following blood collection tubes for the collection of peripheral blood research samples listed in section 2.5 of the study plan that are being sent to the BMT CTN Repository:

a. 10.0 mL fill green-top plastic Vacutainer® tubes containing Sodium-Heparin anticoagulant (**Fisher Scientific cat no.:02-689-6, BD cat no.:367874**)

b. 6.0 mL fill green-top plastic Vacutainer® tubes containing Sodium-Heparin anticoagulant (**Fisher Scientific cat no.:02-685-114A, BD cat no.:367878**)

c. 5.0 mL fill gold top plastic BD SST™ Vacutainer® tube containing Silica Clot Activator, Polymer Gel, Silicone-Coated Interior (**Fisher Scientific, cat. no.: 02-683-97, BD Vacutainer®, Catalog # 367986**).

OR

7.5 mL fill red/gray top plastic BD SST™ Vacutainer® tube containing Silica Clot Activator, Polymer Gel Silicone-Coated Interior, **(Fisher Scientific, cat no.: 02-683-95, BD Vacutainer® Catalog #367987**).

Note: Comparable smaller fill volume tubes may be used as long as the requested peripheral blood sample volumes are indeed submitted to the BMT CTN Repository.

2. Labels for Research Whole Blood

The BMT CTN will provide labels for all research samples that are being shipped to the BMT CTN Repository. A label set will consist of the following labels: Patient File and Sample (**see Appendix I**). One label set will be used for each Vacutainer® tube to be subsequently shipped to the BMT CTN Repository.

The sample labels will be distributed by The Emmes Company (Emmes). Please contact Emmes (bmtctnac@emmes.com with bmtctn2101@emmes.com copied) when you need additional labels. This request should be submitted at least 48 business hours prior to needing the requested labels to ensure shipments arrive in time.

3. Sample Shipping Kits

a. Inmark will provide each site with **insulated** ambient shipping kits for **ONLY** those laboratory samples being shipped priority overnight to the BMT CTN Repository. Upon approval of this study, you will be instructed to submit a request for an initial order of **twenty (20) insulated ambient shipping kits**. As you begin to use the kits in the initial supply, additional kits may be ordered so that you have a sufficient supply for new patients being accrued. **Please be good stewards of this kit ordering process, so that you are ordering only the number of kits that you will actually need and use for this project.** An order form for Inmark can be found at the end of this Research Sample Information Guide (**Appendix II**). The guide and a fillable copy of the order form is posted on the BMT CTN website (https://bmtctn.net).

4. Peripheral Blood Sample Collection and Processing Procedures:

a. Study Sample Processing and Storage:

Centers should arrange to have patient samples collected on Monday-Friday of a given week.

~For pediatric patients, where the collection of the full 50* mL sample exceeds the maximum volume allowed per institutional guidelines, the 5 mL serum sample should be prioritized, with the remainder of allowable blood volume dedicated to the PBMC research sample collection.

- Whole blood sample collection procedure:
  - Collect 5 mL of blood in a single SST BD Vacutainer® tube containing Silica Clot additive and polymer gel (gold or red/gray top SST)
    i. Gently mix the sample by inverting the tube 1-2 times
    ii. Label the tube with a unique BMT CTN sample label
    iii. Let the sample sit upright in a rack for 45-60 minutes to allow it to clot
    iv. Promptly centrifuge the sample at 1100-1300 x g for at least 10 minutes to separate serum (supernatant above gel separator) from the clot
    v. Complete the required Specimen Acquisition/Laboratory form in Advantage eClinical
    vi. Keep the tube at ambient temperature prior to shipping
    vii. Shipped to the BMT CTN Repository using the ambient insulated kit

  - Collect 45* mL of blood in BD Vacutainer® tubes containing Sodium Heparin additive

i. Gently mix the sample with heparin by inverting each tube 8-10 times.

ii. Label each of the tubes with a unique BMT CTN sample label.

iii. DO NOT centrifuge these blood tubes

iv. Complete the required Specimen Acquisition/Laboratory form in Advantage eClinical

v. Let sample sit upright in rack at ambient temperature until time of shipment.

vi. Shipped to the BMT CTN Repository using the ambient insulated kit

- Enter each unique sample ID number into Global Trace, followed by all required patient and sample collection information according to instructions provided in the Global Trace manual. Sample collection time and date should be the same as the information entered into Advantage eClinical Specimen Acquisition/Laboratory form.

5. Same-Day Shipment of Samples to the BMT CTN Repository.

If you cannot make your last local FedEx pick up time, please store the samples at ambient temperature overnight and ship the following day. Please note this is not an option for Friday collections.

a. Preparing Global Trace Shipping Manifest

1. Prepare shipping manifest in Global Trace, including the FedEx tracking number associated with your sample shipment. Be sure that the Vacutainer® tube(s) being shipped are added to the manifest and are included in the shipping kit being shipped to the BMT CTN Repository.
2. **Be certain that the correct shipping destination is selected in Global Trace**.
    a. **BMTLB** - BMT CTN Repository
3. Print a Global Trace shipping manifest to be included in your shipping box.
4. On the day of shipment, press “Send Shipment” to send the electronic Global Trace manifest to the laboratory/repository, notifying them of your shipment to arrive the next day via priority overnight FedEx service.

b. Complete FedEx Air Bill for Same-Day Sample Shipments

Complete a Fed Ex air bill with the following information:

1. Section 1: Complete with your institution’s shipping address
2. Section 2: The Internal Billing Reference Section **must** have the following information “**COVID 2101**”.
3. Section 3: Complete with the appropriate Repository shipping information:

Address for Shipment
Attn: BMT CTN Research Sample Repository **2900 Centre Pointe Drive** **Roseville, MN 55113** **Phone: 651-746-5008** **Email: BMTCTNRepository@nmdp.org**

4. Section 4a: Check "**FedEx Priority Overnight**" box.
5. Section 5: Check the "**Other**" box.
6. Section 6: Check "**No**" for dangerous goods
    a. If sending on **FRIDAY**: Check "**SATURDAY delivery**" box.
        i. If available, add a FedEx "Saturday delivery" label to outside of package.
7. Section 7: Check "**Third Party**" billing box and enter the following BMT CTN account number **2167-0913-7**

c. Packaging the Study Samples for Shipment (Instructions Page – Appendix III, also included in kit). Use **only** the ambient shipping kits received from Inmark. A printed copy of the following sample packaging instructions will also be included in each insulated ambient shipping kit.

1. Lay the first blood tube on the supplied bubble wrap sheet. Bring the end of the bubble wrap sheet over the tube, completely surrounding it in the bubble material. Place the second tube next to it and continue to roll the tubes up in the protective bubble material. Continue until all tubes are wrapped in bubble wrap. Secure bubble wrap with supplied tape.
2. Insert the wrapped vials in the Biohazard Bag **without the absorbent material**. IMPORTANT, bleed as much air as possible out of the bag prior to sealing. Peel the tape from the top of the bag and seal.
3. Insert the sealed bag into the Biohazard Bag **containing the absorbent material**. IMPORTANT, bleed as much air as possible out of the bag prior to sealing. Peel the tape from the top of the bag and seal.
4. Place the sealed Biohazard Bag in the double Styrofoam insulated shipping box and re-place the Styrofoam lid.
5. Include the printed copy of the Global Trace shipping manifest in the shipping kit.
6. Loosely fold over the plastic liner bag.
   Close the box and fully seal the top seams with tape.

6. Back-up Research Sample Collection Option for use in Post-Vaccination Study Visits

This backup sample collection option is to be reserved for those cases that truly require an off-site collection to be done for a patient not returning to the center. It is expected that samples for study visit V1 will be collected at the Transplant Center. The offsite blood draw option is available for V2, V3, V3B, V4 and V5 study visits. This offsite option is ONLY available to patients that can have the full 50* mL blood sample collected as allowed per institutional guidelines. There are a limited number of spots available for use for this study. Once a case has been determined to need this alternative back-up collection procedure the

site must:

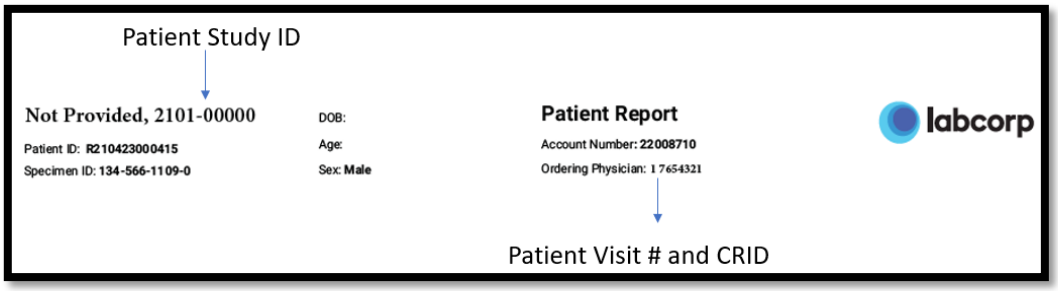
a. Procedure before the patient research sample collection visit

1. Determine the LabCorp Patient Service Center (PSC) that the patient will go to have their blood drawn at.
2. LabCorp PSC can be looked up by using the following website: https://www.labcorp.com/precheck
    a. Enter the address or zip code that is convenient for the patient
    b. Select “Routine Lab work” as the reason for your visit
3. Determine collection window target dates. The LabCorp PSC site requires a limited collection window of a Target date **±3 days**.
    a. Please be sure that the patient understands that they will need to go to THIS specific site on one of the days within that window for the blood draw.
4. Complete the LabCorp PSC Appointment Form (Appendix IV) with the details for this specific patient/visit.
    a. A completed copy of this form must be sent to ResearchKits@nmdp.org **IN ADVANCE** of the start of the target window to allow for the kit to be shipped to the LabCorp PSC ahead of the patient visit.
    b. A completed copy should also be provided to the patient (email, printed or both) to have them bring WITH to the LabCorp PSC.

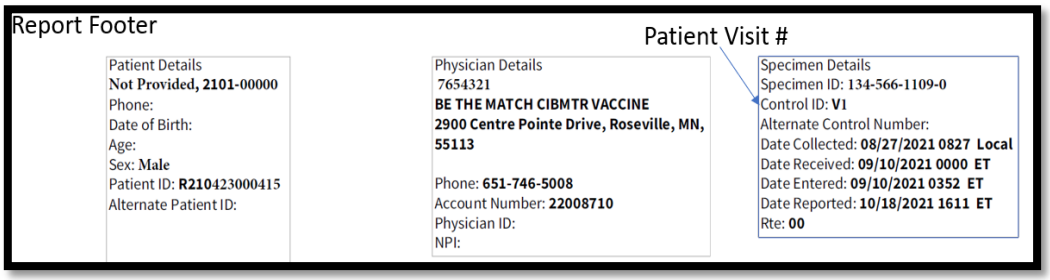
b. Procedure after the visit

1. Patient CBC result will be provided to the study team via excel file which will be added to the study database. These research results will not be provided back to the Transplant Center.
2. **For all Patient visits** (blood draws done at Study site & LabCorp)**:** Patient specific Serum Antibody results will be made available electronically to the Transplant Center.
    a. The CIBMTR will download Patient specific PDF results from LabCorp system and upload them into FormsNet3 by patient CRID.
    b. The results will be available to share with the Study PI and the patient from there.
        i. In FormsNet3, in the Recipient Forms tab, enter the CRID in the search box and click “search”.
        ii. Scroll to the bottom of the page and expand the Attachments grid.
        iii. Look for attachments with a file description of “**SC21-07/BMT CTN 2101**”
        iv. Click on the paperclip icon to view the attachment (example shown below):

c. Anticipated turnaround time for results from sample collection date is 3-6 weeks.
d. Example LabCorp Report headers for samples collected on or before September 24, 2021:



e. Example LabCorp Report header and footer for samples collected on or after September 25, 2021:



7. Primary BMT CTN Contact for Study, Advantage eClinical & Global Trace Questions

Task/Topic	Contact Information
Protocol Coordination	bmtctn2101@emmes.com
Advantage eClinical Data Entry and Forms	bmtctn2101dm@emmes.com
Advantage eClinical Training/Access	bmtedc@emmes.com

8. Primary BMT CTN Contacts for all Sample Collection, Processing, Shipping and Laboratory Services

Stephanie Waldvogel
BMT CTN DCC/NMDP
Principal Immunobiology Research Scientist – BMT CTN
Email: swaldvog@nmdp.org
Telephone: 763-406-8637

Ashley Spahn
BMT CTN DCC/NMDP
Manager, Clinical Sample Research
Email: aspahn@nmdp.org
Telephone: 763-406-4850

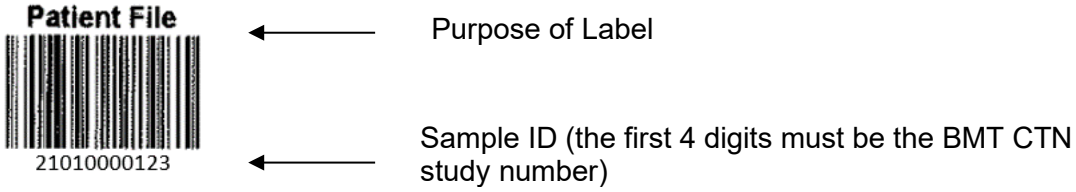
Hannah Florin
BMT CTN DCC/NMDP
Immunobiology Research Scientist – BMT CTN
Email: hflorin2@nmdp.org
Telephone: 763-406-4432

Appendix I: Labels for all Research Samples

The labels used for samples being shipped to the BMT CTN Repository will be provided by Emmes. Please contact Emmes (bmtctnac@emmes.com with bmtctn2101@emmes.com copied) when you need additional labels. This request should be submitted at least 48 business hours prior to needing the requested labels to ensure shipments arrive in time.

Detailed View of Each Label Set:

Components of Each Label:



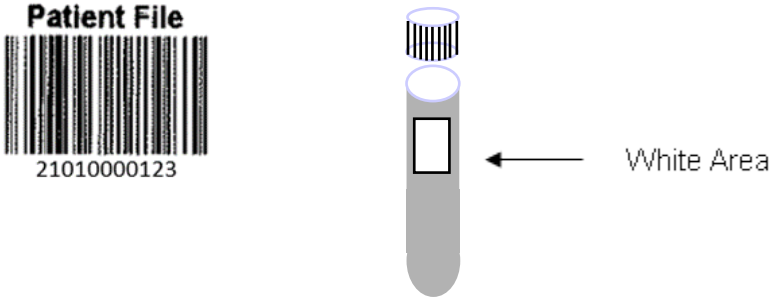
The **Purpose of Label** is where each label should be used:

a. **Patient File** – keep this label in you patient's files for record.
b. **Sample** – use this label on the specimen vial.

The first 4 digits of the Sample ID indicate the study for which the labels are designated. Be sure to use only the "2101" labels for this study. Please note: the specimen IDs for 2101 are 11 digits in total length.

Labeling Vials

a. Apply the barcode label on the Vacutainer tube as shown in the following diagram.
b. Do NOT write on the labels. There should be no patient identifying information on the barcode labels or Vacutainer tubes.



Appendix II: Insulated Ambient Sample Shipping Kit Order Form for Inmark

Order Form

CIBMTR SC21-07/ BMT CTN Study 2101

Prospective observational study of the immunogenicity of mRNA vaccines for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine after autologous hematopoietic stem cell transplantation (HCT), allogeneic HCT, and chimeric antigen receptor T-cell therapy

Insulated Ambient Sample Shipping Kits

DATE: _____

CENTER/SITE: _____

ORDERED BY: _____

PHONE NUMBER: _____

EMAIL: _____

Part No.	QTY	Description
ME-H2101BV06BMT		Patient Sample Kit, Insulated Ambient, 1-6 tubes (Assembled). For Use with **CIBMTR SC21-07**/ BMT CTN Study 2101 Only

Ship to: _____

_____

_____

_____

_____

Special Instructions: _____

_____

Email completed order form to ResearchKits@nmdp.org

Appendix III: Insulated Ambient Kit Packaging Instructions

EXAKT-PAK®

ASSEMBLY INSTRUCTIONS

This package is specifically designed to transport EXEMPT ANIMAL or HUMAN specimens that appropriately fit within the supplied Biohazard Bags. It MAY NOT transport a liquid amount in excess of 120 mL.

IMPORTANT - READ OTHER SIDE FIRST

1

Lay the vial on the supplied bubble wrap sheet. Bring the end of the bubble wrap sheet over the vial, completely surrounding it in the bubble material.

2

Continue until up to 6 vials are wrapped. Secure bubble wrap with supplied tape.

3

Insert the wrapped vials in the empty Biohazard Bag **without the absorbent**.

4

IMPORTANT: Bleed as much air as possible out of the small bag prior to sealing. Peel the tape from the top of the bag.

5

To seal the bag, fold the top of the bag over **AT THE SLIT** and orient lines onto corresponding lines. **GENTLY** tack together, working outward from the center. **PRESS HARD** from the **CENTER** working outward, making sure the bag is completely sealed.

6

Insert the sealed bag into the Biohazard Bag **containing the absorbent material.**

7

IMPORTANT: Bleed as much air as possible out of the outer bag prior to sealing. Peel the tape from the top of the outer bag.

8

To seal the bag, fold the top of the bag over. **AT THE SLIT**. Gently tack together, working outward from the center. **PRESS HARD** from the **CENTER** working outward, making sure the bag is completely sealed.

9

Place the sealed bag(s) UPRIGHT in the outer box.

10

Replace top EPS foam.

11

Place any necessary documentation on top of the white EPS foam lid.

12

Loosely fold over plastic liner bag.

13

Close box. Fully seal top and side seams with tape.

14 **Apply the appropriate shipping documents to the outside of the box.**

 IS4752BMT (05/21/2009)

Appendix IV: LabCorp Patient Service Center (PSC) Appointment Form

LabCorp Patient Service Center (PSC) Appointment Form – Blood draw for CBC w/ differential and Research Sample kit

For Study: CIBMTR SC21-07/ BMT CTN Study 2101
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LabCorp Account# 22008500

Study Patient ID: _____

Patient CIBMTR CRID: _____

Purpose of LabCorp Visit:

- Collection & Shipment of Biorepository Research Samples (Kit provided to PSC by NMDP)
- Research CBC w/ differential (LabCorp PSC requisition in kit provided by NMDP)

Study Visit Number (V2, V3, V3B, V4 or V5): _____

Target Date: _____ Visit range (-3 days): _____ to (+3 days) _____

Address of Selected LabCorp PSC: _____

_____

_____

_____

_____

_____

Phone number of Selected LabCorp PSC: _____

- **Form should be completed by Transplant Center**
  - A copy (email or printed) should be given to the patient to bring with to their blood draw at LabCorp PSC **AND**
  - Email completed form to ResearchKits@nmdp.org – for shipment of Kit to LabCorp PSC
    - **MUST BE DONE AHEAD OF TIME TO ALLOW FOR KIT TO ARRIVE PRIOR TO BLOOD DRAW**