

CHANGE- HD Manual of Procedures Update: Version 12.2024

December 2024

Section	Change
Document Footer	The date was updated for this amendment
Appendix I	Visits were added to the Specimen Collection and Processing Form



National Institute of Neurological Disorders and Stroke
Biorepository:

BioSpecimen Exchange for Neurological Disorders, BioSEND

Biospecimen Collection, Processing, and Shipment Manual for

Growth and Development of Striatal-Cerebellum Circuitry in
Subjects at Risk for Huntington's Disease
(ChANGE-HD)

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1.0 PURPOSE

The purpose of this manual is to provide collection site staff (PIs, study coordinators, and the sample collection and processing teams) at various study sites with instructions for collection and submission of biological samples. It includes instructions for biospecimen submission to the BioSpecimen Exchange for Neurological Disorders (BioSEND) located at Indiana University.

This manual includes instructions for the collection, processing, aliquoting and shipping of the following samples:

- Plasma
- Buffy Coat (for DNA extraction)
- Whole Blood (for banking)

These procedures are relevant to all study personnel responsible for processing blood specimens to be submitted to BioSEND.

2.0 ABBREVIATIONS

BioSEND	BioSpecimen Exchange for Neurological Disorders
EDTA	Ethylene Diamine Tetra-acetic Acid
IATA	International Air Transport Association
RBC	Red Blood Cells
RCF	Relative Centrifugal Force
RPM	Revolutions Per Minute

3.0 BioSEND INFORMATION

3.1 BioSEND Contacts

Tatiana Foroud, PhD, Principal Investigator

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Claire Wegel, Project Manager

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Email: cwegel@iu.edu

General BioSEND Contact Information

Fax: 317-278-1100

Email: biosend@iu.edu

Website: www.BioSEND.org

Sample Shipment Mailing Address

BioSEND

Indiana University School of Medicine

351 W. 10th Street. TK-217

Indianapolis, IN 46202-5188

3.2 Hours of Operation

Indiana University business hours are from 8 AM to 5 PM Eastern Time, Monday through Friday.

Frozen samples must be shipped Monday- Wednesday only.

For packaging and shipment details, please refer to Appendix K (Frozen Shipping Instructions).

Check the weather reports and the courier website to make sure impending weather events (blizzards, hurricanes, etc.) will not impact the shipping or delivery of the samples. Couriers often report anticipated weather delays on their website.

3.3 Holiday Schedules

- Please note that courier services may observe a different set of holidays. Please be sure to verify shipping dates with your courier prior to any holiday.
- **Weekend/holiday deliveries will not be accepted.**

3.4 Holiday Observations

Date	Holiday
January 1	New Year’s Day
3 rd Monday in January	Martin Luther King, Jr Day
4 th Monday in May	Memorial Day
June 19	Juneteenth (observed)
July 4	Independence Day (observed)
1 st Monday in September	Labor Day
4 th Thursday in November	Thanksgiving
4 th Friday in November	Friday after Thanksgiving
December 25	Christmas Day

Please see https://www.biosend.org/holiday_closures.html for additional information.

4.0 BIOSEND SAMPLE REQUIREMENTS

NINDS approves each study for a specific biospecimen collection protocol. Studies and study sites should make every effort to meet their approved biospecimen collection requirements. The expected number of samples from each site that should be returned to BioSEND are listed in [sections 4.1-4.2](#).

If a sample is not obtained at a particular visit, this should be recorded in the notes section of the **Sample Record and Shipment Notification Form (see Appendix I)**. These forms are submitted with your sample shipment to BioSEND.

4.1 Protocol Schedule for Biospecimen Submission to BioSEND-CHANGE-HD

Visit	BL	12M	24M	36M	48M	60M	72M
Plasma aliquots, 1.5ml	6	6	6	6	6	6	6
Buffy Coat	2	2	2	2	2	2	2
Whole blood, 3ml	2	2	2	2	2	2	2

*If participant is unable to donate blood, a saliva sample may be collected as an alternative (see Appendix R)

5.0 SPECIMEN COLLECTION KITS, SHIPPING KITS AND SUPPLIES

Research specimen collection kits as well as clinical lab supplies (except dry ice and equipment listed in Section 5.7) will be provided by BioSEND. These materials include blood tubes, boxes for buffy coats and plasma aliquots, as well as partially completed shipping labels to send materials to BioSEND. Barcoded kit labels, collection tube labels, and aliquot tube labels will all be provided by BioSEND. Collection tube labels and aliquot tube labels will be pre-printed with study information specific to the type of sample being drawn. BioSEND will provide a sufficient number of labels only for those specimens that are to be shipped back to the BioSEND repository (See the Protocol Schedule for Biospecimen Submission to BioSEND for your site in [Sections 4.1-4.2](#)); any tubes that will remain at the collection site should be labeled accordingly. Ensure that all tubes are properly labeled during processing and at the time of shipment according to [Section 6.2](#).

5.1 Kit Supply to Study Sites

Each individual site will be responsible for ordering kits from BioSEND. We advise sites to proactively confirm kits are on hand ahead of study visits.

Within the kit request module, there is a drop down menu to request kits based on site institution. Kits and individual items can be ordered as required through the kit request module.

The link to the kit request module is shown below:

- CHANGE-HD: <http://kits.iu.edu/biosend/changehd>

Please allow **TWO weeks** for kit orders to be processed and delivered.

5.2 Specimen Collection Kit General Contents

Collection kits contain the following (for each subject) as designated per your protocol and/or NINDS resource development agreement. Kits provide the necessary supplies to collect samples from a given subject. Do not replace or supplement any of the tubes or kit components provided with your own supplies unless you have received approval from the NINDS/BioSEND Study team to do so. *Please store all kits at room temperature until use.* Note that “supplemental” kits can be provided should you require additional supplies from those contained in the visit specific kits. Replacement supplemental kits can be requested on the kit request website. In addition, individual supplies can be requested as well.

BioSEND Supplies

Available upon request from the online kit request module ([Section 5.1](#))

General Items
25 cell cryobox
Cryogenic Vials
Envelope for airway bill
Shipping container for dry ice shipment (shipping and Styrofoam® box)
Sterile pipettes (3ml)
Plastic biohazard bag with absorbent sheet
Shipping label packet (dry ice, fragile, and UN3373 label)
Blood Collection Items
Purple-top EDTA blood collection tube (glass, 10 ml)
Purple-top EDTA blood collection tube (plastic, 3 ml)

5.3 Specimen Collection Kit Contents – CHANGE-HD

CHANGE-HD BL/Annual Collection Kit	
Supply	Amount
Purple cryogenic vial, 2ml	6
Grey cryogenic vial, 2ml	2
EDTA (glass) tube, 10ml	2
EDTA (plastic) tube, 3ml	2
Bubble-tube sleeve	3
Disposable pipet, 3ml	2
Cryobox, 25 cell	1
Biohazard bag w/ absorbent sheet	2
Fragile label	1
UN3373 label	1
Dry ice label	1
Waybill	1
Frozen shipper	1
Label set (case and collection tube labels)	1

CHANGE-HD Supplemental Kit	
Supply	Amount
Purple cryogenic vial, 2ml	10
Grey cryogenic vial, 2ml	10
EDTA (glass) tube, 10ml	5
EDTA (plastic) tube, 3ml	5
Bubble-tube sleeve	10
Disposable pipet, 3ml	10
Cryobox, 25 cell	2
Biohazard bag w/ absorbent sheet	5
Fragile label	5
UN3373 label	5
Dry ice label	5

5.4 Site Required Equipment

The following materials and equipment are necessary for the processing of specimens at the collection site and are to be **supplied by the local site**:

- Personal Protective Equipment: lab coat, nitrile/latex gloves, safety glasses
- Tourniquets
- Alcohol Prep Pads
- Gauze Pads
- Bandages
- Butterfly needles and hubs
- Microcentrifuge tube rack
- Test tube rack
- Sharps bin and lid

In order to process samples consistently across all projects and ensure the highest quality samples possible, project sites must have access to the following equipment:

- Centrifuge capable of ≥ 1500 rcf (1500 x g)
- -80°C Freezer

In order to ship specimens, you must provide:

- Dry ice (approximately 10 pounds per shipment)

6.0 SPECIMEN LABELS

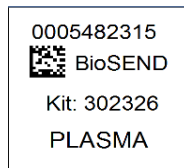
Labels must be affixed on all collection and aliquot tubes to ensure unique specimen identity. BioSEND provides labels for all samples being collected and returned to BioSEND. The site is responsible for providing labels for biospecimens that will be retained at the site.

6.1 Types of Labels

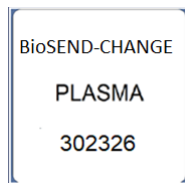
Each kit contains all labels required for the return of biospecimens to BioSEND.



The **Kit Labels** do not indicate a specimen type, but are affixed on BioSEND forms and on specific packing materials. See Appendix K for further instructions.



The **Collection Tube Labels for Blood** are placed on all blood collection tubes. See Appendices B-D for further instructions.

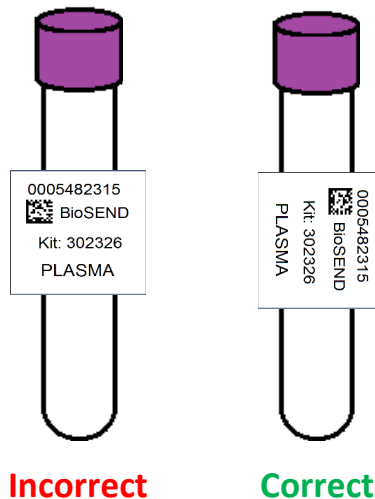


Plasma and Buffy Coat Aliquot Tubes will come pre-labeled with the study abbreviation, specimen type, and Kit number. The tube itself will have a unique barcode printed in both 2D format (on bottom of tube) and human readable formats (alongside of tube).

6.2 Affixing Labels

In order to ensure the label adheres properly and remains on the tube, follow these instructions:

- Place blood collection labels on **ALL** collection tubes **BEFORE** sample collection, sample processing, or freezing. This will help to ensure the label properly adheres to the tube before exposure to moisture or different temperatures.
- The blood collection tube labels contain a 2D barcode on the left hand side of the label. When turned horizontally, the barcode should be closer to the top (cap end) of the tube.
- Place label **horizontally** on the tube (wrapped around sideways if the tube is upright); see below.



- Take a moment to ensure the label is **completely affixed** to each tube. It may be helpful to roll the tube between your fingers after applying the label.

7.0 SPECIMEN COLLECTION AND PROCESSING PROCEDURES

Consistency in sample collection and processing is essential for biomarker studies. All samples are drawn in the same order and then processed in a uniform fashion. **Please read the instructions before collecting any specimens. Have all your supplies and equipment out and prepared prior to drawing blood.**

7.1 Collection Tubes for BioSEND

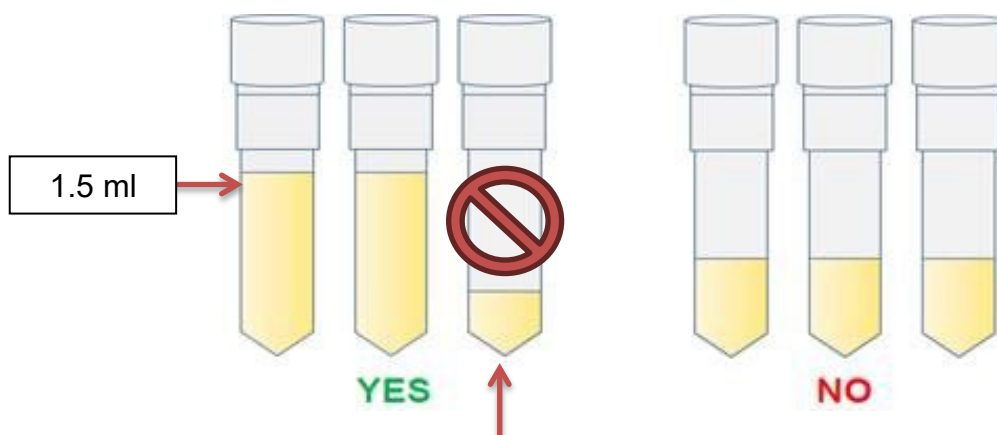
1. EDTA (purple top, 10ml) x 2 for plasma and buffy coat
2. EDTA (purple top, 3ml) x 2 for whole blood

7.2 Blood Collection Protocols

1. EDTA (purple top) blood collection for plasma (**Appendix B**)
2. EDTA (purple top) blood collection for Buffy Coat (**Appendix C**)
3. EDTA (purple top) blood collection for whole blood (**Appendix D**)

7.4 Filling Aliquot Tubes (Plasma and Buffy Coat)

In order to ensure that BioSEND receives a sufficient amount of sample for processing and storage, and to avoid cracking of the tubes prior to shipment, each aliquot tube should be filled to the assigned volume (refer to detailed processing instructions for average yield per sample). Over-filled tubes may burst once placed in the freezer, resulting in a loss of that sample. Each site is supplied with sufficient collection tubes to provide the specimen volume described in the Protocol Schedules for Biospecimen Submission ([see Section 4](#)). Specimens collected in addition to those described in Section 4 are collected at the site’s discretion and are not returned to BioSEND.



Please note: It is critical for the integrity of future studies using these samples that study staff **not submit** residual aliquot tubes (anything under 1.5 ml) to BioSEND.

Each aliquot cryovial will be have a color-coded cap as follows:

Cap Color	Specimen Type
Purple	Plasma
Grey	Buffy Coat

Please be sure to use the appropriate colored top for the appropriate sample type.

8.0 Packaging and Shipping Instructions

ALL study personnel responsible for shipping should be certified in biospecimen shipping. If not available at your University, training and certification is available through the CITI training site (Course titled “Shipping and Transport of Regulated Biological Materials” at <https://www.citiprogram.org/>).

8.1 Sample Record and Shipment Notification Form

All sample shipments to BioSEND must include the BioSEND Sample Record and Shipment Notification Form. The completed forms are:

- Emailed to BioSEND@iu.edu at the time the samples are being shipped
- And the original document should be Included in the shipment with the samples

8.2 Shipping Instructions

Frozen Shipment (baseline and follow-up). Reference Appendix K for frozen shipping instructions.

- Frozen 1.5 ml aliquots of plasma
- Frozen Buffy Coat
- Frozen 3 ml EDTAs for whole blood

*****Important Note*****

Please do not include more than 1-2 subjects worth of samples in a single shipper.

This ensures room for a sufficient amount of dry ice to keep samples frozen up to 24 hours.

8.3 Shipping Address

All samples are shipped to the BioSEND laboratory:

BioSEND
Indiana University School of Medicine
351 W. 10th Street. TK-217
Indianapolis, IN 46202-5188

9.0 Data Queries and Reconciliation

Appendix I must be completed the day that samples are collected to capture information related to sample collection and processing. This form includes information that will be used to reconcile sample collection and receipt, as well as information essential to future analyses.

The CHANGE-HD Study team will be collaborating with BioSEND to reconcile information captured in the database compared to samples received and logged at BioSEND. Information that appears incorrect in the clinical database will be queried through the standard system. Additional discrepancies that may be unrelated to data entry will be resolved with the Principal Investigator in a separate follow up communication. If applicable, a non-conformance report will be provided to sites.

Data discrepancies with samples shipped and received at BioSEND may result from:

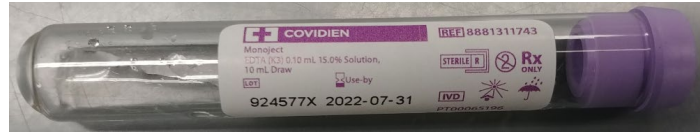
- Missing samples
- Incorrect samples collected and shipped
- Damaged or incorrectly prepared samples
- Unlabeled or mislabeled samples
- Discrepant information reported in the clinical database compared to information on Appendix I
- Samples frozen and stored longer than three months at the site

10.0 APPENDICES

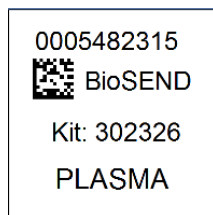
- Appendix B: Whole Blood Collection for Isolation of Plasma
- Appendix C: Whole Blood Collection for Isolation of Buffy Coat
- Appendix D: Whole Blood Collection for Banking
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- Appendix K: Frozen Shipping Instructions
- Appendix O: Low Fat Diet Menu Suggestions
- Appendix Q: UPS ShipExec™ Thin Client Instructions
- Appendix R: Saliva Collection for DNA

Appendix B – Whole Blood Collection for Isolation of Plasma

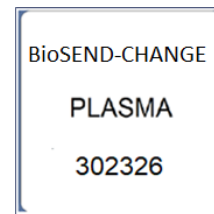
Whole Blood Collection for Isolation of Plasma: 10 ml Purple-Top EDTA tube(s) and cryovials are provided by BioSEND for the collection of plasma.



1. **CRITICAL STEP:** Store empty purple-top EDTA tubes at room temperature 64°F – 77°F (18°C to 25°C) prior to use.
2. Place provided “PLASMA” labels on 10 ml purple-top EDTA tube(s); the six 2 ml purple cryovial tubes will already be labeled. These six cryovials will be shipped to BioSEND. Any remaining cryovials can be retained by the site and labeled per site standards. Labels for aliquots kept by the site are not provided by BioSEND.



Collection Tube Label



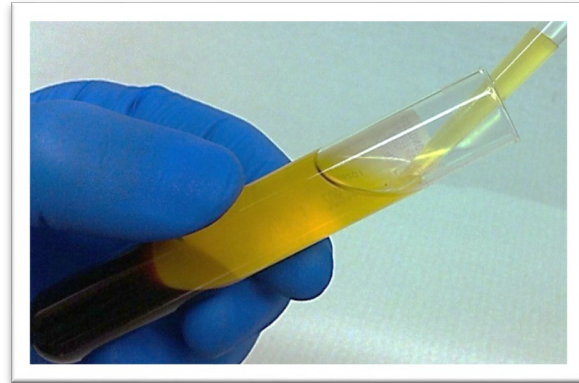
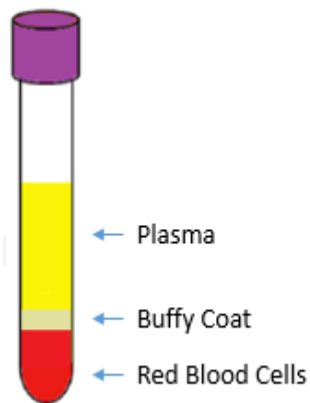
Label on cryovials

3. Pre-chill the cryovials on wet ice for at least 5 minutes.
4. Set centrifuge to 4°C to pre-chill before use. Time needed to pre-chill the centrifuge will depend on your centrifuge model.
5. Using a blood collection set and a holder, collect blood into the **purple top 10 ml EDTA tube(s)** using your institution's recommended procedure for standard venipuncture technique.

The following techniques shall be used to prevent possible backflow:

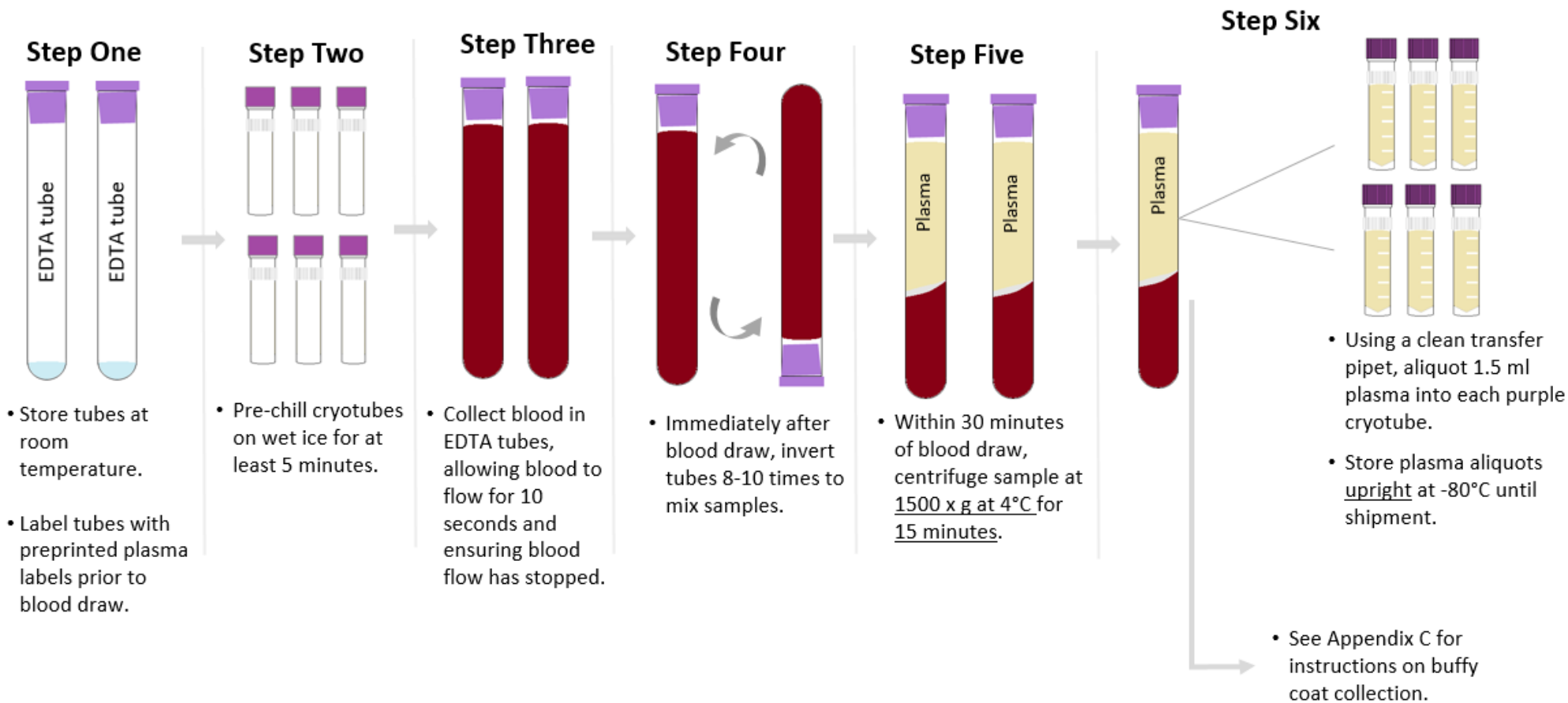
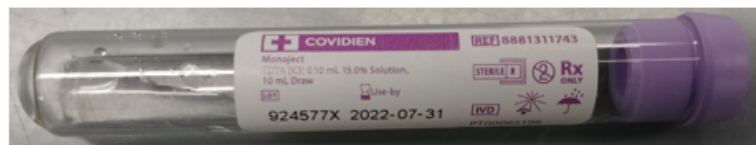
- a. Place donor's arm in a downward position.
- b. Hold tube in a vertical position, below the donor's arm during blood collection.
- c. Release tourniquet as soon as blood starts to flow into the tube.
- d. Make sure tube additives do not touch stopper or end of the needle during venipuncture.

6. Allow at least 10 seconds for a complete blood draw to take place in each tube. **Ensure that the blood has stopped flowing into the tube before removing the tube from the holder.** The tube vacuum is designed to draw 10 ml of blood into the tube.
7. **CRITICAL STEP: Immediately after blood collection, gently invert/mix (180 degree turns) the purple-top EDTA tube(s) 8 – 10 times. Do not shake the tubes!**
8. Within 30 minutes of blood collection, centrifuge balanced tubes for 15 minutes at 1500 RCF (x g). **It is critical that the tubes be centrifuged at the appropriate speed to ensure proper plasma separation.**
9. Remove the plasma by tilting the tube and placing the pipette tip along the lower side of the wall. **Use caution not to touch the buffy coat or packed red blood cells at the bottom of the collection tube so that the plasma is not contaminated** (see below).
10. Using a disposable pipette, aliquot 1.5 ml into each cryovial. Send 6 x 1.5 ml aliquots to BioSEND. If you cannot obtain the requested number of aliquots, please note “low volume draw” on the Sample Record and Shipment Notification form (Appendix I) under “Notification of Problems”. Each 10 ml EDTA tube should yield, on average, 4-5 ml of plasma.



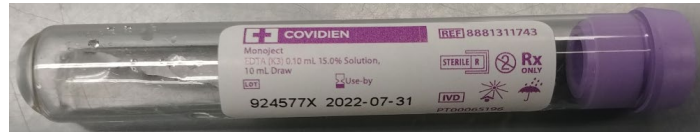
11. Complete the **Sample Record and Shipment Notification form (Appendix I)**.
12. Place the labeled cryovials in the 25 slot cryobox. Place the cryobox UPRIGHT on dry ice. Transfer to **-80°C freezer as soon as possible, within 2 hours of blood draw**. Store all samples at **-80°C until shipped** to BioSEND on dry ice.
13. Ship the frozen plasma aliquots to BioSEND according to **Appendix K – Frozen Shipping Instructions**.

Plasma Preparation –10 ml EDTA (Purple Top) Tube

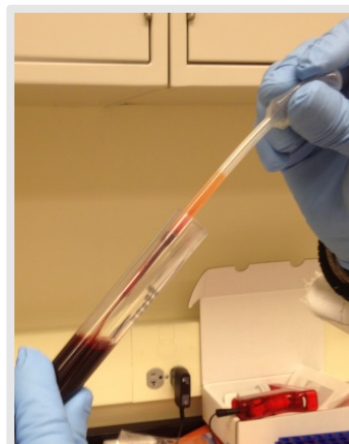
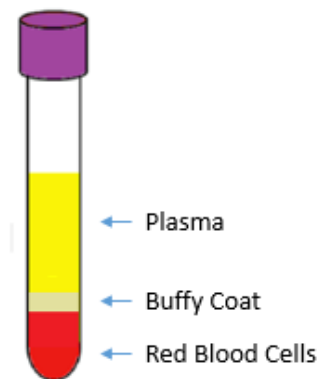


Appendix C –Whole Blood Collection for Isolation of Buffy Coat

Whole Blood Collection for Isolation of Buffy Coat: 10 ml Purple-Top EDTA tube(s) and cryovials are provided by BioSEND for the collection of the buffy coat.

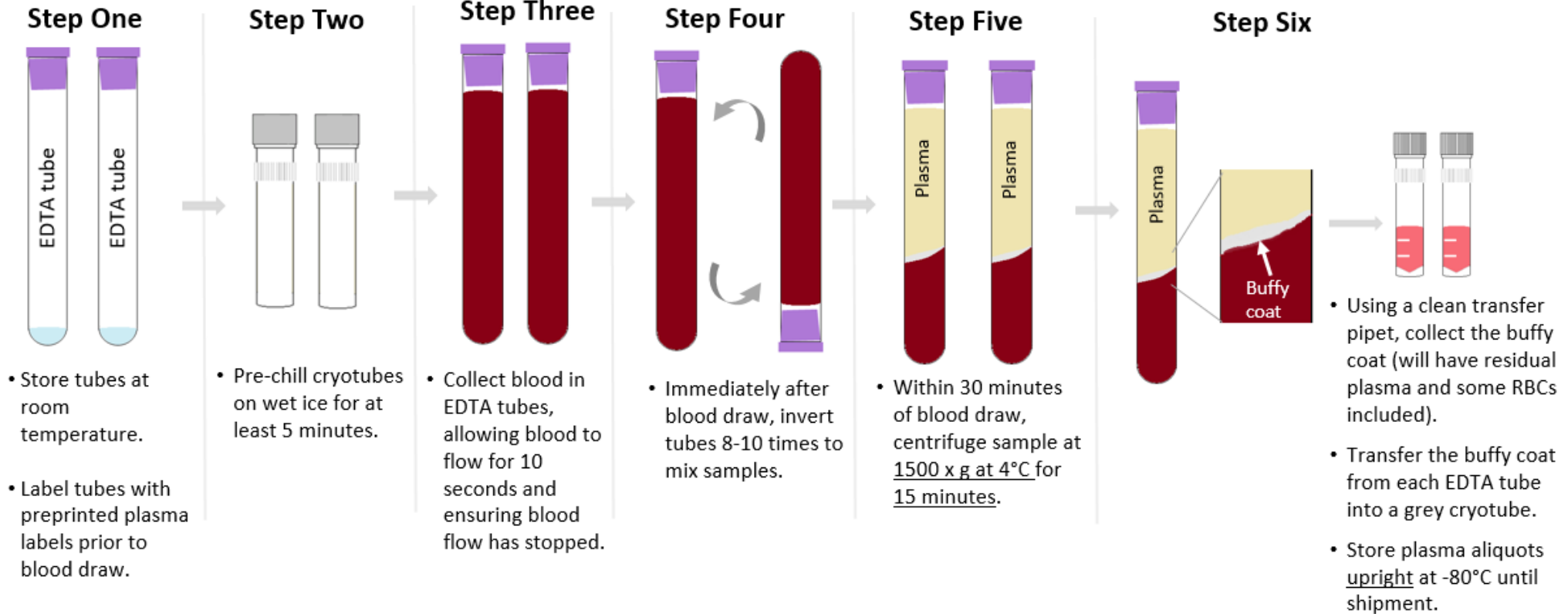
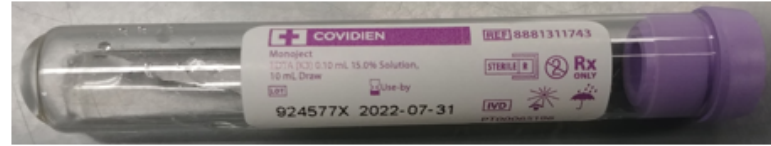


1. **CRITICAL STEP:** Store Purple-Top EDTA tubes at room temperature 64°F - 77°F (18°C to 25°C) before use.
2. Place grey aliquots pre-labeled with “Buffy Coat” to chill on wet ice for at least 5 minutes.
3. Set centrifuge to 4°C to pre-chill before use. Time needed to pre-chill the centrifuge will depend on your centrifuge model.
4. After plasma has been removed from the EDTA purple-top tube (see Appendix B), aliquot buffy coat layer (see figure below) into labeled cryovial with grey cap using a disposable graduated micropipette. All of the buffy coat from a single 10 ml purple-top EDTA tube will be placed into one cryovial. The buffy coat aliquot is expected to have a reddish color from the red blood cells.



5. Complete the **Sample Record and Shipment Notification form (Appendix I)**.
6. Freeze cryovial(s) in upright position on dry ice. Transfer to a **-80°C Freezer when possible**. Store all samples UPRIGHT at **-80°C until shipped** to BioSEND on dry ice.
7. Ship the frozen buffy coat aliquots to BioSEND according to **Appendix K – Frozen Shipping Instructions**.

Buffy Coat Preparation –10 ml EDTA (Purple Top) Tube



Appendix D – Whole Blood Collection (No Processing)

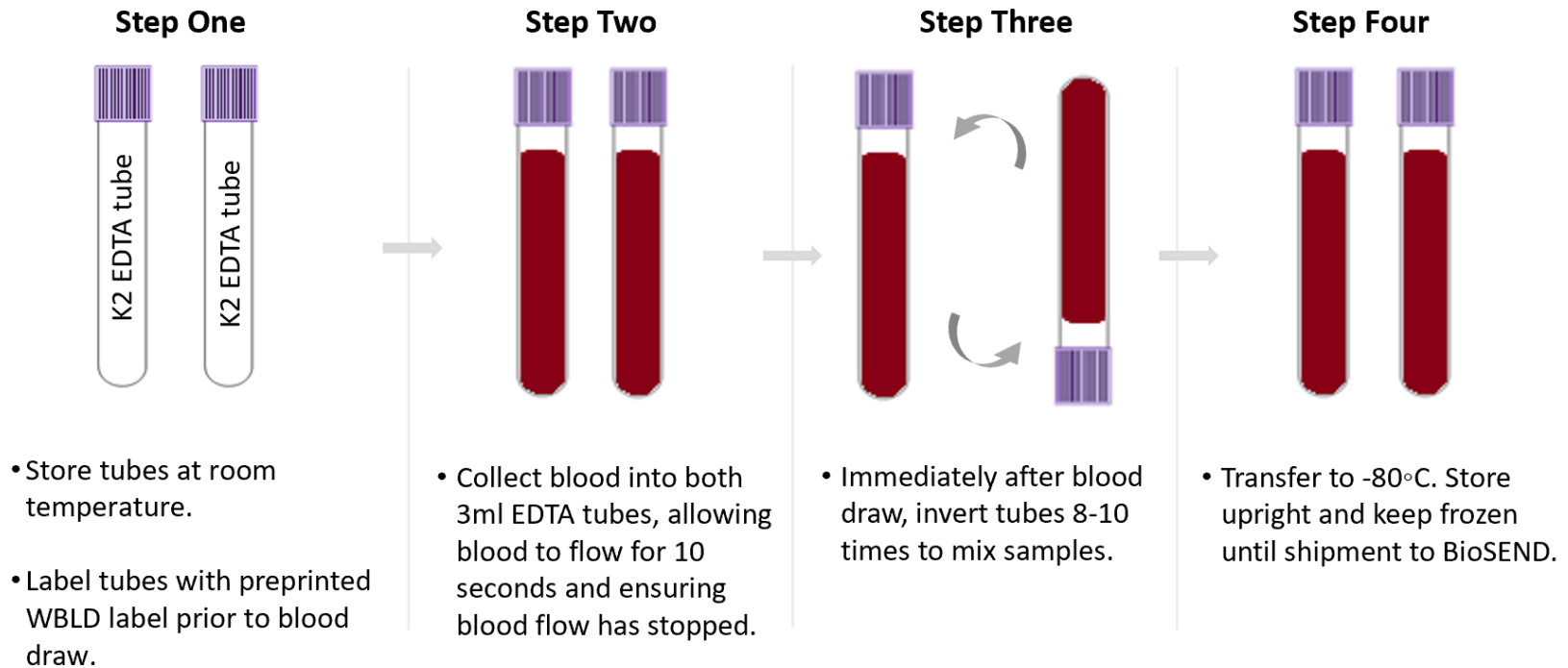
Two 3 ml Purple-Top EDTA Tube is provided by BioSEND for Whole Blood collection (to be shipped to BioSEND FROZEN; no processing required).

1. Store empty Whole Blood EDTA tubes at room temperature, 64°F - 77°F (18°C to 25°C) before use.
2. Place pre-printed specimen label (WBLD) on the **two 3ml purple top EDTA tube** prior to blood draw.
3. Using a blood collection set and a holder, collect whole blood into the tubes using your institution's recommended procedure for standard venipuncture technique.

The following techniques shall be used to prevent possible backflow:

- a. Place donor's arm in a downward position.
 - b. Hold tube in a vertical position, below the donor's arm during blood collection.
 - c. Release tourniquet as soon as blood starts to flow into tube.
 - d. Make sure tube additives do not touch stopper or end of the needle during venipuncture.
4. **Immediately after blood collection, gently invert/mix (180 degree turns) the EDTA tubes 8-10 times. Do not shake the tube!**
 5. Complete the Sample Record and Shipment Notification form (Appendix I).
 6. Place the Purple-Top EDTAs in a **WIRE** or **PLASTIC** rack. Do **NOT** use a Styrofoam rack. This will cause the Purple-Top EDTA tube to crack when frozen. Place the Purple-Top EDTA tubes immediately to a **-80°C Freezer**.
 7. Ship the whole blood tube to BioSEND according to **Appendix K - Frozen Shipping Instructions**.

WBLD Preparation – 2 x 3 ml K2 EDTA (Purple Top) Tube



Appendix I – Sample Collection and Processing Form

A Sample Collection and Processing Form must be completed for each subject-visit submitted to BioSEND. This form includes a Frozen Shipping Manifest that should be completed in advance of shipping to BioSEND also be physically included in the shipper. The form can be completed via REDCap by following the bellow link:

- **Link to Sample Collection and Processing Form:**

<https://redcap.link/CHANGEHDSampleForm>

Please note that there is a Save & Return option at the bottom of the survey. This may be used if, for example, you are ready to complete the Collection and Processing portion of the form, but not yet ready to complete the Frozen Shipping Manifest.

It is preferred that you complete the form online via the REDCap link above. However, a copy of the printed form is available on the following pages, should you need a back-up option. Please note that if you do not complete the form online, you will need to email a copy of the form directly to biosend@iu.edu prior to shipment.

CHANGE-HD Specimen Collection And Processing Form

Protocol: Growth and Development of Striatal-Cerebellum Circuitry in Subjects at Risk for Huntington's Disease (ChANGE-HD)

Please complete the Specimen Collection and Processing Form, below.

Study Site

- University of Iowa
- University of California-Davis
- University of Texas
- Columbia University
- Children's Hospital of Philadelphia
- Vanderbilt University

Email address of staff member completing this form

Note: A copy of the completed sample form and the shipping manifest will be sent to this address.

GUID:

Sex (used for DNA quality control)

- Male
- Female
- Other

Visit

- BL
- 12M
- 24M
- 36M
- 48M
- 60M
- 72M

ST Number/ Kit Number

Blood Collection and Processing

Date of venipuncture blood collection

Time of venipuncture blood collection

(Use 24 Hour clock)

Date participant last ate

Time participant last ate

1. PLASMA and BUFFY COAT (Purple-top EDTA tubes, 10 mL)

Was blood collected and processed for PLASMA EDTA?

- Yes
 No

Blood volume collected for PLASMA

(mL)

Reason volume was less than standard

- Difficult stick/poor veins
 Patient dehydrated
 Bad tube vacuum
 Other

Time of PLASMA EDTA tube centrifugation

(Use 24 Hour clock)

Duration of PLASMA EDTA tube centrifugation

(minutes)

Rate of PLASMA EDTA tube centrifugation

(x g)

Temperature of PLASMA EDTA tube centrifugation

(degrees Celsius)

Number of PLASMA EDTA aliquots created for BioSEND

(Each aliquot should be 1.5 mL)

Number of BUFFY COAT aliquots created for BioSEND

Date PLASMA EDTA and BUFFY COAT were placed in freezer

Time PLASMA EDTA and BUFFY COAT were placed in freezer

(Use 24 Hour Clock)

PLASMA EDTA and BUFFY COAT storage temperature

(degrees Celsius)

PLASMA EDTA notes

2. WHOLE BLOOD (EDTA tubes, 3 mL)

Was blood collected for WBLD?

- Yes
 No

Number of WBLD tubes collected

(Two 3ml EDTA tubes expected)

Date WBLD was placed in freezer

Time WBLD was placed in freezer

(Use 24 Hour clock)

WBLD storage temperature

(degrees Celsius)

WHOLE BLOOD notes

3. SALIVA

Was saliva collected?

- Yes
 No

Date of saliva collection

Time of saliva collection

(Use 24 Hour clock)

CHANGE-HD Frozen Shipping Manifest

Please verify/update the information below. When you click the "Submit" button below, a PDF copy of the Frozen Shipping Manifest will be emailed to you for Subject [subj_id].

Please print a copy of that document and include it in the Kit #[kit_num] shipping container.

Study Site:

GUID:

Visit:

ST Number/ Kit Number:

Date of blood collection:

PLASMA EDTA

Number of PLASMA EDTA aliquots shipped:

Number of BUFFY COAT aliquots shipped:

WHOLE BLOOD EDTA

Number of WHOLE BLOOD tubes shipped:

Shipping Information - Please complete.

Frozen shipments should be sent Monday-Wednesday only. Please check for holiday closures prior to shipping. Contact us at biosend@iu.edu if you are unsure whether or not it is safe to ship.

Date of shipment:

Did/will you use the IU UPS interface to generate the shipping label?

- Yes
 No

Which shipping service did you use?

- UPS
 FedEx
 World Courier
 Other

What is the shipment tracking number?

Appendix K – Frozen Shipping Instructions

IMPORTANT!

**FROZEN SAMPLES MUST BE SHIPPED MONDAY THROUGH WEDNESDAY ONLY
USING PRIORITY OVERNIGHT DELIVERY**

Please be aware of holidays and inclement weather, and plan your shipments accordingly.

Specimens being shipped to BioSEND are Category B UN3373 specimens and as such must be triple packaged and compliant with IATA Packing Instructions. *See the latest eEdition of the IATA regulations for complete documentation.*

Triple packaging consists of a primary receptacle(s), a secondary packaging, and a rigid outer packaging. The primary receptacles must be packed in secondary packaging in such a way that, under normal conditions of transport, they cannot break, be punctured, or leak their contents into the secondary packaging. Secondary packaging must be secured in outer packaging with suitable cushioning material. Any leakage of the contents must not compromise the integrity of the cushioning material or of the outer packaging.

IATA Packing and Labeling Guidelines

- The primary receptacle (cryovials or blood collection tubes) must be leak proof and must not contain more than 1 L total.
- The secondary packaging (plastic canister or biohazard bag) must be leak proof and if multiple blood tubes are placed in a single secondary packaging, they must be either individually wrapped or separated to prevent direct contact with adjacent blood tubes.
- Absorbent material must be placed between the primary receptacle (cryovials or blood collection tubes) and the secondary packaging. The absorbent material must be of sufficient quantity to absorb the entire contents of the specimens being shipped. Examples of absorbent material are paper towels, absorbent pads, cotton balls, or cellulose wadding.
- A shipping manifest listing the specimens being shipped must be included between the secondary and outer packaging.
- The outer shipping container must display the following labels:
 - ✓ Sender's name and address
 - ✓ Recipient's name and address
 - ✓ Responsible persons (shipper and recipient)
 - ✓ The words "Biological Substance, Category B"
 - ✓ UN3373
 - ✓ Class 9 label including UN 1845, and net weight of dry ice contained

BioSEND Packaging and Shipment Instructions – Frozen Shipments

1. Contact FedEx® to confirm service is available and schedule package to be picked up.
2. **Record the FedEx® tracking number (found at the top of the FedEx® airbill) onto the Sample Record and Shipment Notification form (Appendix I).**
3. Make a copy of the Sample Record and Shipment Notification form.



4. Place all frozen labeled 1.5 ml aliquots of plasma and buffy coat in the cryobox. Only include specimens from one subject in each cryobox.

5. Place the cryobox in the clear plastic biohazard bag. Leave the absorbent sheet in the biohazard bag and seal according to the instructions on the biohazard bag. Affix a Case Label to the outside of the biohazard bag.



6. Insert 6ml EDTA whole blood tube into the bubble wrap tube shuttle, and place the tube shuttle in the 2nd clear plastic biohazard bag. Seal the biohazard bag according to the instructions on the bag. Affix a Case Label to the outside of the biohazard bag.

7. Place approximately 2-3 inches of dry ice in the bottom of the Styrofoam® shipping container.
8. Place the biohazard bag containing the cryobox into the provided Styrofoam® shipping container on top of the dry ice. Please ensure that the cryobox is placed so that the cryovials are upright in the shipping container (as pictured).



9. Fully cover the cryobox with approximately 2 inches of dry ice. Please do not include more than two subjects' cases in a single box.

10. The inner Styrofoam® shipping container must contain approximately 10 lbs (or 4.5 kg) of dry ice. The dry ice should entirely fill the inner box and be placed on top of the cryoboxes to ensure the frozen state of the specimens.



11. Replace the lid on the Styrofoam® container. Place the completed Sample Record and Shipment Notification form in the package on top of the Styrofoam lid for each patient specimen, and close and seal the outer cardboard shipping carton with packing tape.

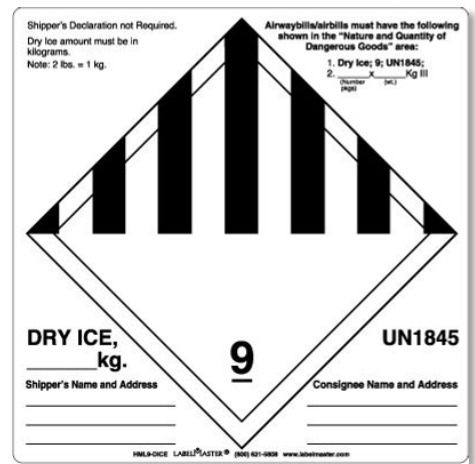
12. Complete the FedEx® return airbill with the following information:

- Section 1, “From”: fill in your name, address, phone number.
- Section 6, “Special Handling and Delivery Signature Options”: under “Does this shipment contain dangerous goods?” check the boxes for “Yes, Shipper’s Declaration not required” and “Dry Ice”. Enter the number of packages (1) x the net weight of dry ice in kg.

13. Complete the Class 9 UN 1845 Dry Ice Label (black and white diamond) with the following information:

- Your name and return address
- Net weight of dry ice in kg (this amount must match the amount recorded on the airbill)
- Consignee name and address:
 BioSEND
 IU School of Medicine
 351 W. 10th Street
 TK-217
 Indianapolis, IN 46202

- Do not cover any part of this label with other stickers, including pre-printed address labels.



IMPORTANT!
 Complete the required fields on the FedEx® return airbill and Class 9 Dry Ice labels, or FedEx® may reject or return your package.

14. Apply all provided warning labels (UN3373, Dry Ice Label and Fragile Label) as well as the completed FedEx® return airbill to the outside of package, taking care not to overlap labels.

15. Hold packaged samples in -80°C freezer until time of FedEx® pick-up/drop-off.

16. Specimens should be sent to the address below via **FedEx® Priority Overnight**. Frozen shipments should be sent Monday through Wednesday only to avoid shipping delays on Thursday or Friday. FedEx does not replenish dry ice if shipments are delayed or held over during the weekend.

BioSEND
 IU School of Medicine
 351 W. 10th Street
 TK-217
 Indianapolis, IN 46202

17. Notify BioSEND by email (biosend@iu.edu) that a shipment has been sent and attach the Sample Record and Shipment Notification form to your email. Alternatively, you can submit an online form through on the BioSEND website at https://biosend.org/sample_form.html. Do not ship until you've contacted and notified BioSEND staff about the shipment in advance.

18. Use FedEx® tracking to ensure the delivery occurs as scheduled and is received by BioSEND.

In addition to tracking and reconciliation of samples, the condition and amount of samples received are tracked by BioSEND for each sample type. Investigators and clinical coordinators for each project are responsible for ensuring that the requested amounts of each fluid are collected to the best of their ability and that samples are packed with sufficient amounts of dry ice to avoid thawing in the shipment process.

Appendix O – Low Fat Diet Menu Suggestions

Foods to avoid prior to blood collection:

Avoid: *All fats and nuts such as:*

- Butter
- Cream
- Bacon fat
- Lard
- All oils
- All margarine
- All nuts
- Peanut butter
- Coconut
- Whole seeds such as pumpkin and sunflower

Avoid: *All milk and dairy products such as:*

- All whole milk products
- All cheese
- All products containing cheese
- Sour cream
- All ice cream
- Milk chocolate

Avoid: *High fat prepared foods and foods naturally high in fat:*

All red meats or meats containing fat
 such as pork and:

- Fatty meats such as:
 - Luncheon meats
 - Organ meats
 - Bacon
- Fatty fish such as:
 - Salmon
 - Mackerel

-
- Salad dressing and mayonnaise
 - Fried foods
 - Fried snacks such as:
 - Chips
 - Crackers
 - French Fries
 - Buttered, au gratin, creamed, or fried vegetables
 - Gravies and sauces
 - Baked goods and frosting

Appendix Q - UPS ShipExec™ Thin Client Instructions

***** The shipment label in ShipExec should not be created until the day of shipment *****

- 1) Log in to the UPS ShipExec™ Thin Client website: <https://kits.iu.edu/UPS> or <https://kits.iu.edu/ups>.
 - a. To request an account, complete the following survey:
<https://redcap.uits.iu.edu/surveys/?s=88TTWY3KAF>
- 2) Find the “Shipping” dropdown menu in the top left corner of the screen and click on “Shipping and Rating”.
- 3) Once the Indiana University page loads, look for the “Study Group” dropdown menu under “Shipment Information” on the right side of the screen. Choose your study from the dropdown menu.
- 4) After selecting your study, click on the magnifying glass icon on the left side of the screen under “Ship From”.
- 5) An address book and filters will populate the screen. On the right side of the screen, a list of all the site addresses within the study you selected should populate.
 - a. Filter the list down more by looking to the left side of the screen and searching for their address by filling in the “Company”, “Contact”, or “Address 1” fields. Click on the Search button when ready.
 - b. Once you have found your site address, click on the “Select” button to the left of the address.
- 6) Make sure your address populated in the fields under “Ship From” on the main page.
 - a. If you accidentally selected the wrong address, click on the “Reset” button on the bottom right of the screen. After the page reloads and clears the information, select your study again from the “Study Group” menu and click on the magnifying glass icon again to search for your correct address.
 - b. To change the address for your site and study group, please complete the following survey:
<https://redcap.uits.iu.edu/surveys/?s=88TTWY3KAF>
- 7) Enter the total weight of your package in the “Weight” field on the right side of screen under the name of your study.
 - a. Leave the “Dry Ice Weight” field empty or enter “0” if shipping an ambient sample.
- 8) Enter the weight of the dry ice for frozen shipments in the “Dry Ice Weight” field.
 - a. The “Dry Ice Weight” field can *never* be higher than the “Weight” field.
 - b. **(Steps 9-10 can be skipped if you do not need to schedule a pickup)**
- 9) After entering the weights, click on the blue “Pickup Request” button.
- 10) When the Create Pickup Request box pops up, enter information into all the fields provided.
 - a. Enter the “Earliest Time Ready” and “Latest Time Ready” in 24-hour format.
 - i. Schedule pickup at a minimum 1 hour *before* the “Earliest Time Ready”
 - b. Choose a name and phone number that is the best contact if the UPS driver has question related to picking up your package
 - c. Entering the “Room Number” and “Floor” will help the UPS driver locate your package
 - i. The “Floor” field only allows numerical characters while the “Room Number” field is free text.
 - d. Click “Save” when done.
- 11) Once you are certain that all the correct information has been entered, click the “Ship” button in the bottom right corner of the screen.
- 12) If no red error messages pop up at the top of your screen after clicking on “Ship”, then you should have 2 downloaded PDF files: Shipment Receipt & UPS Package Label

- a. Shipment Receipt will list a “Pickup No.” that references your specific package if there is ever an issue with UPS picking up your package
- 13) Print out the UPS airway bill to any printer at your location.
- a. Fold the UPS airway bill and slide it inside the plastic UPS sleeve.
 - b. Peel the back off the plastic UPS sleeve and stick the sleeve to your package, making sure it is laying as flat as possible along the surface of the package.
- 14) Place your package in the spot designated in your pickup request, or wherever your daily UPS pickups occur.
- 15) If you need to reprint your airway bill or void your shipment, click on “History” at the top of the main screen.
- a. If your shipment does not automatically pop up, enter the date of shipment and then click “Search”.
 - b. To reprint your airway bill, click on the printer icon to the far left under “Action”
 - c. To void your shipment, click on the “X” icon to the far left under “Action”
 - i. If you created an airway bill that you no longer need, you must void the shipment to ensure your study will not be charged for the shipment.

Appendix R - Saliva Collection For DNA

Participant should not eat, drink, smoke, or chew gum for 30 minutes prior to giving your sample.

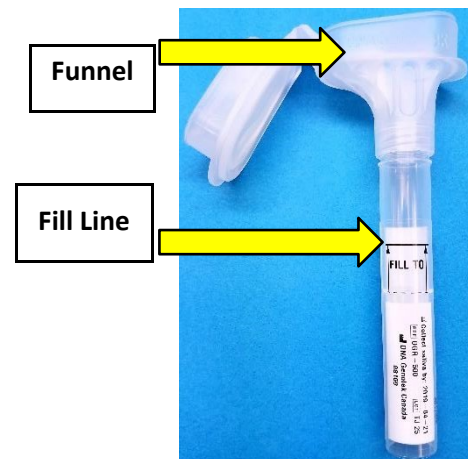
Give the following directions to the participant: Do not rinse your mouth prior to giving your sample. Most people take between 2 and 5 minutes to deliver a saliva sample following steps 1 through 7 below. Before spitting, have participant relax and rub your cheeks gently for 30 seconds to help create saliva. Please take care to use infectious PPE (mask, face shield, gown, gloves) while handling saliva samples. Provide a safe distance between yourself and the participant during collection. Please disinfect the exterior of the tube with alcohol wipes upon receiving the collected sample from the participant.

To review a video of the saliva collection procedure, please visit:

<http://www.dnagenotek.com/ROW/support/ciOG500.html>

STEP 1

- Do NOT remove the plastic film from the lid of the container.
- Have the participant spit directly into the funnel at the top of the tube until the amount of liquid saliva (not including bubbles) reaches the fill line shown in picture #1.
- **The saliva tube has a false bottom, so you will only need to provide 2 milliliters (less than ½ teaspoon) of saliva to reach the fill line.**
- Do NOT fill above the line.



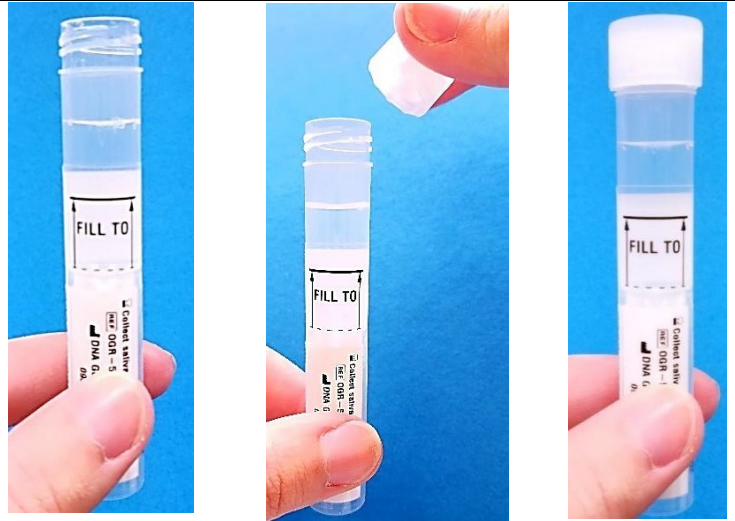
STEP 2

- Once the saliva level reaches the fill line, hold the tube upright with one hand.
- Close the lid with the other hand (as shown) by firmly pushing the lid until you hear a loud click.
- The liquid in the lid will be released into the tube to mix with the saliva. Make sure that the lid is closed tightly.



STEP 3

- Hold the tube upright.
- Unscrew the funnel from the tube.
- Pick up the small cap for the tube.
- Use the small cap to close the tube tightly.



STEP 4

- Shake the capped tube for 5 seconds.
- Discard or recycle the funnel.
- Place sample in provided specimen bag for shipment back to BioSEND.



STEP 5

- Peel off blue plastic liner at the top of the specimen bag to expose the adhesive.
- Seal bag by pressing down across the top of the bag.



STEP 6

- Put specimen (in the provided specimen bag) into this shipping envelope.



STEP 7

- Peel off the white paper at the top of the envelope to expose the adhesive, fold this flap down, and press firmly to seal envelope.
- Send the envelope via UPS Ground as soon as possible after sample collection.



Intended Use: This product is designed for the safe collection of human saliva samples.

Contents: The funnel lid contains 2 mL of Oragene•DNA liquid. The solution should be clear and colorless.

Warnings: Do not ingest the Oragene•DNA liquid. Wash with water if the Oragene•DNA liquid comes in contact with eyes or skin. Small Cap, choking hazard.

Storage: Store at room temperature 15-30°C (59-86°F).