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Doc. #:	SOP340567	Revision:	-	Effective Date:	10/08/2021

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LHTP Approval: Ralph E. Parchment Date: Ralph E. Parchment -S (Affiliate) Digitally signed by Ralph E. Parchment -S (Affiliate) Date: 2021.11.30 11:28:47 -05'00'

DCTD OD Approval: Toby Hecht Date: Toby T. Hecht -S Digitally signed by Toby T. Hecht -S Date: 2021.12.06 11:58:47 -05'00'

Change History

Revision	Approval Date	Description	Originator	Approval
--	10/08/2021	New Document	LL/RA/KFG	KFG

Please check for revision status of the SOP at

http://dctd.cancer.gov/ResearchResources/ResearchResources-biomarkers.htm

and be sure to use the current version.

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1.0 PURPOSE

Standardize the method for collecting, handling, and shipping frozen needle tumor biopsies to EET Biobank to enable measurement of pharmacodynamic (PD) markers following treatment with anticancer agents.

2.0 SCOPE

This procedure applies to all personnel involved in the collection and handling of frozen needle tumor biopsies for use in PD marker assays during clinical trials. The goal of this SOP and associated training is to ensure consistency in tumor needle biopsy collection and handling between clinical sites.

3.0 ABBREVIATIONS

DCTD	=	Division of Cancer Treatment and Diagnosis
EET Biobank	=	NCI Early-Phase and Experimental Clinical Trials Biospecimen Bank, also referred to as the Nationwide Biorepository or ETCTN Biorepository
FNLCR	=	Frederick National Laboratory for Cancer Research
ID	=	Identification / Identifier
IQC	=	Internal Quality Control
LHTP	=	Laboratory of Human Toxicology and Pharmacology
PADIS	=	Pharmacodynamics Assay Development & Implementation Section
PD	=	Pharmacodynamic
SOP	=	Standard Operating Procedure

4.0 INTRODUCTION

Specimen handling, shipping, and storage procedures (pre-analytical variables) can have a significant impact on the reliability of biomarker measurements in the laboratory. Following detailed steps for sample collection and handling procedures and recording any deviations from this procedure allow retrospective identification of artifactual changes in biomarker readout and increases the reliability of the data and validity of the analytical results.

5.0 ROLES AND RESPONSIBILITIES

Laboratory Director/Supervisor	The Laboratory Director/Supervisor directs laboratory operations, supervises technical personnel and reporting of findings, and is responsible for the proper performance of all laboratory procedures. Oversees the personnel who follow the SOPs in the laboratory and is responsible for ensuring the personnel are certified and have sufficient experience to handle clinical samples.

Certified Assay Operator and/or PK/PD Support Lab Personnel	An assay operator and/or PK/PD Support Lab personnel may be a Laboratory Technician/Technologist, Research Associate, or Laboratory Scientist who has been trained by DCTD personnel on this SOP. Working under the guidance of the Laboratory Director/Supervisor, this person performs laboratory procedures and examinations in accordance with the current SOP(s), as well as any other procedures conducted by a laboratory, including maintaining equipment and records and performing quality assurance activities related to performance.

5.1 It is the responsibility of the Laboratory Director/Supervisor to ensure that all personnel have documented training and qualification on this SOP prior to the actual handling and processing of samples from clinical trial patients. The Laboratory Director/Supervisor is responsible for ensuring the assay operator running the SOP has sufficient experience to handle and analyze clinical samples. To become proficient with this SOP, sites are highly encouraged to reach out to NCI_PD_Support@mail.nih.gov for additional training materials.

5.2 It is the responsibility of the assay operator to confirm scheduled specimen collection time points, pre-print all labels, request access to **NCI Medidata Rave** (ETCTN Specimen Tracking System), check documentation for accuracy, request sample shipping kits from the EET Biobank and verify that the required collection tubes, supplies, and equipment are available for successful collection and handling of biopsy samples.

5.3 It is the responsibility of the assay operator to conduct the specimen collection and handling procedures following this SOP and complete the required tasks and associated documentation. The Biopsy Collection Record (Appendix 1) must be completed for each patient sample collection and filed with the study patient's other records.

5.4 The responsible personnel are to check the DCTD Biomarkers Web site (http://dctd.cancer.gov/ResearchResources/ResearchResources-biomarkers.htm) to verify that the latest SOP version is being followed.

6.0 MATERIALS AND EQUIPMENT REQUIRED

6.1 Stopwatch, total time in minutes and seconds required

6.2 1.5-mL Sarstedt o-ring screw cap, conical bottomed tubes (Sarstedt, Cat#: 72.703.416)

6.3 Disposable, fine-tipped tweezers (e.g., VWR, Cat#: 83009-010). Tweezer tips need to easily fit to the bottom of a 1.5-mL Sarstedt tube

6.4 Printable microcentrifuge tube labels or BSI labeling system

6.5 81-place freezer boxes (e.g., Fisher Scientific, Cat#: 12-565-182)

6.6 Thermoflask cooler or polystyrene foam container

6.7 Ice bucket

6.8 Liquid nitrogen or dry ice/ethanol bath

6.9 -80°C freezer (or colder)

6.10 Specimen shipping kit from EET Biobank

7.0 OPERATING PROCEDURES

7.1 This SOP uses **NCI Medidata Rave** for sample tracking, please review the following training videos for **NCI Medidata Rave** before you start:

7.1.1 General RAVE training:
https://www.youtube.com/watch?app=desktop&v=ZRX0lSqs5zo

7.1.2 Label Printing training:
https://www.youtube.com/watch?app=desktop&v=9_Q6_k-KHHs

7.2 Sample Shipping Kits

Sample shipping kits should be requested prior to enrolling the first biopsy patient from EET Biobank by emailing BPCBank@nationwidechildrens.org. For current customers, the kits can be requested through the EET Biobank (kit management system: https://kits.bpc-apps.nchri.org/Auth/Login?ReturnUrl=%2f. Please allow 5-7 business days for kit shipment.

7.3 Labels

7.3.1 Prepare enough pre-printed specimen labels in **NCI Medidata Rave** by following steps 7.3.1.1- 7.3.1.5:

7.3.1.1 Log into **NCI Medidata Rave** and go to **Enrollment** folder and confirm the **Histology and Disease** form is complete.

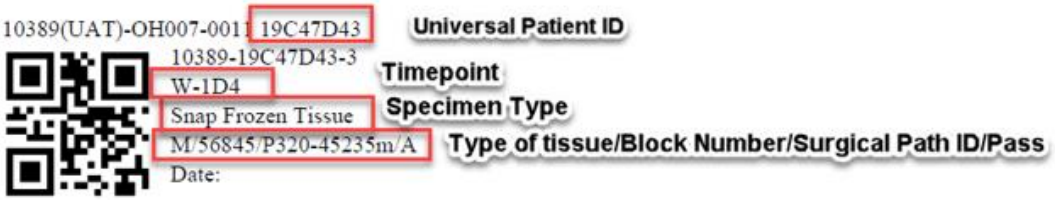
7.3.1.2 Go to **All Specimens** folder.

7.3.1.3 Complete the **Specimen Consent** form.

7.3.1.4 Complete the **Specimen Tracking Enrollment** form for each specimen.

7.3.1.5 Complete the **Print Labels** form. Labels will be sent to user's email address. For tissue specimens, apply appropriately coded label to each pass of the biopsy (see below).

Note: Five labels will be printed by default when you enter "**1**" in the "**How many labels are needed**" field. The first four will be designated with A, B, C and D to represent different passes of the biopsy procedure. Please use those accurately to label the specimens; pass A should be for the first pass, B for the second etc. The fifth label will have no pass designation and can be used on reports to be uploaded into RAVE. See an example of pre-printed label for frozen tissue biopsy below.



7.4 Tumor Needle Biopsy Collection and Handling

7.4.1 The research nurse is to notify the laboratory of scheduled PD sample collections, preferably giving at least 24 hours of notice. Arrive at the biopsy collection site early enough to allow sufficient time to set up laboratory supplies, collect relevant clinical information, and ensure rapid transport of frozen specimens from the procedure area to the laboratory, where they will be placed into storage at -80ºC (or colder).

7.4.2 Prior to biopsy, the lesion should be assessed as to whether or not the biopsy should be performed and yield a successful outcome. Fill out the **Pre-Biopsy Lesion Score** form in **NCI Medidata Rave** using inputs from interventional radiologists and/or oncologists.

7.4.3 Bring all necessary lab supplies to the biopsy collection site, including: disposable tweezers, a minimum of four 1.5-mL Sarstedt tubes pre-cooled on liquid nitrogen or dry ice/ethanol in an insulated bucket (Sarstedt tubes will be provided in the sample shipping kit from EET Biobank; please use one tube for each whole biopsy core), the label with no pass designation to give to the research nurse for the patient record, and a printout of Appendix 1.

Note: Pre-chill additional 1.5-mL Sarstedt tubes for specimen collection in case the interventional radiologist collects additional passes, or if one of the tubes is compromised prior to collection.

7.4.4 The total time elapsed between biopsy collection and placement into the pre-chilled tube is of **key importance** to biomarker analysis; this time should be documented in **NCI Medidata Rave** for each biopsy pass. **It is important to note that all biopsies should be frozen within 2 minutes of collection.** The interventional radiologist will eject the biopsy onto a sterile slide (for optimal analyte recovery the slide should be pre-chilled). Start a stopwatch at this point (or note the time in Appendix 1) and immediately walk the slide to the sample preparation table for transfer to the pre-chilled Sarstedt tube.

7.4.5 Immediately snap freeze the biopsy by placing the tube in liquid nitrogen or a dry ice/ethanol bath (stop the stopwatch at this point). **Note:** DO NOT let the tubes tip over in the liquid nitrogen or dry ice/ethanol bath.

7.4.6 Calculate the total time elapsed from biopsy collection to biopsy freezing and record the total number of **minutes and seconds** (Appendix 1).

7.4.7 Note the specific needle type used and location of each biopsy pass collected (*e.g.*, spleen, large left upper quadrant splenic mass) (Appendix 1).

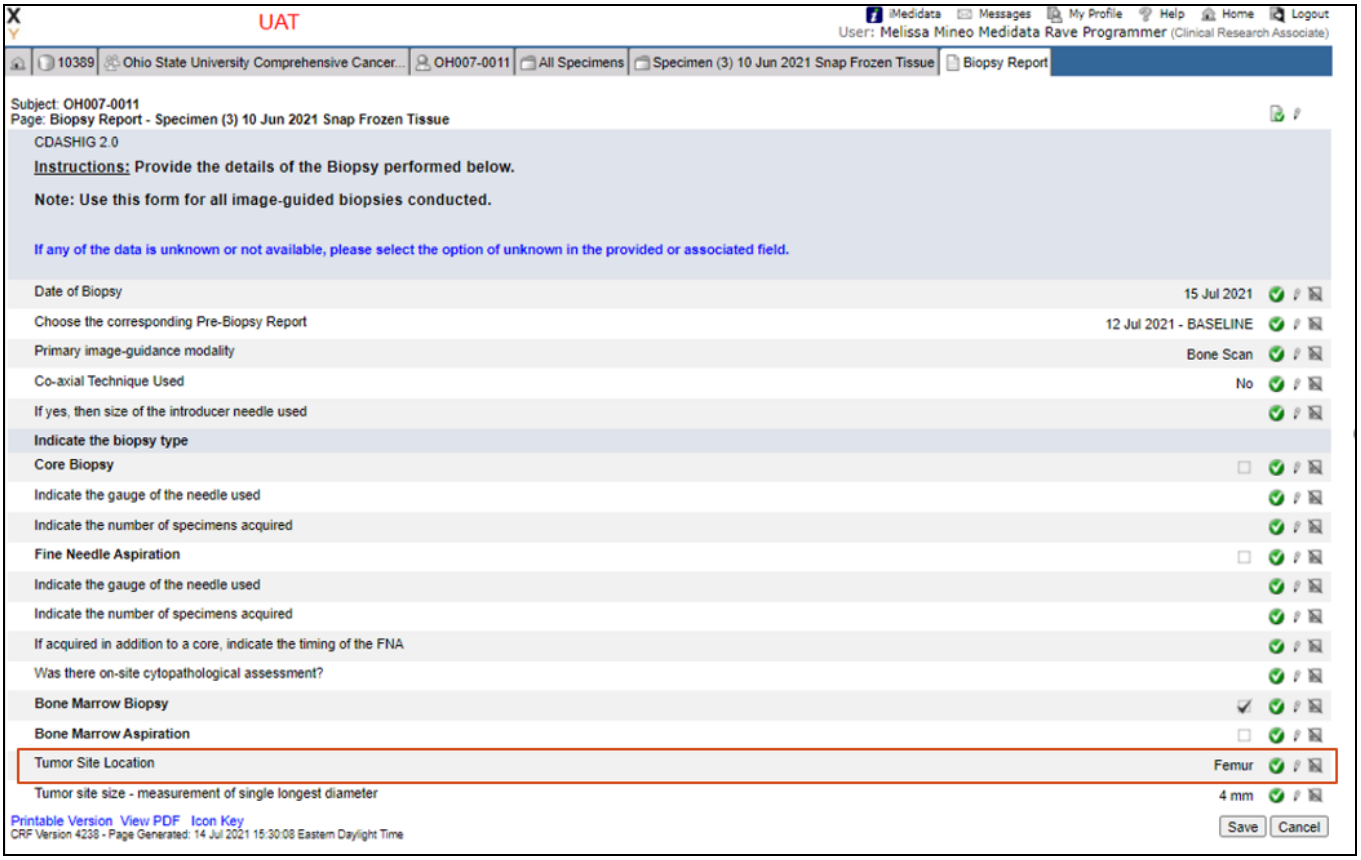
7.4.8 Note the protocol biopsy timepoint in Appendix 1.

7.4.9 Return to the sample processing laboratory and transfer the frozen biopsy specimen(s) to -80°C (or colder) for storage until shipment to the EET Biobank.

7.4.10 After biopsy collection, complete sample tracking documentation in **NCI Medidata Rave** according to notes recorded in Appendix 1.

7.4.11 Fill out **Biopsy Report** form in the **All Specimen** folder.

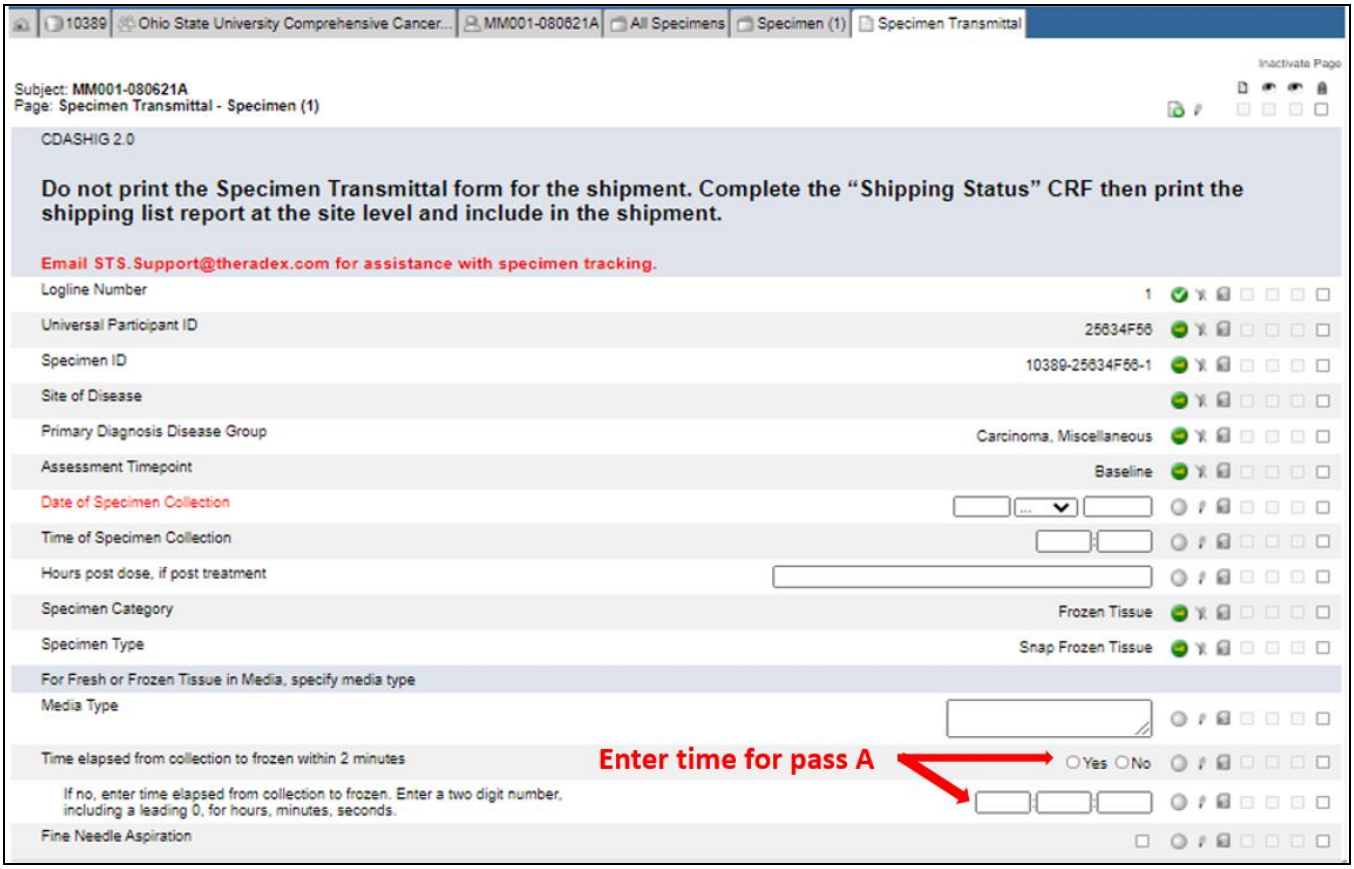
Note: It is very important to record the site of the biopsy to the **Tumor Site Location** field as shown below.



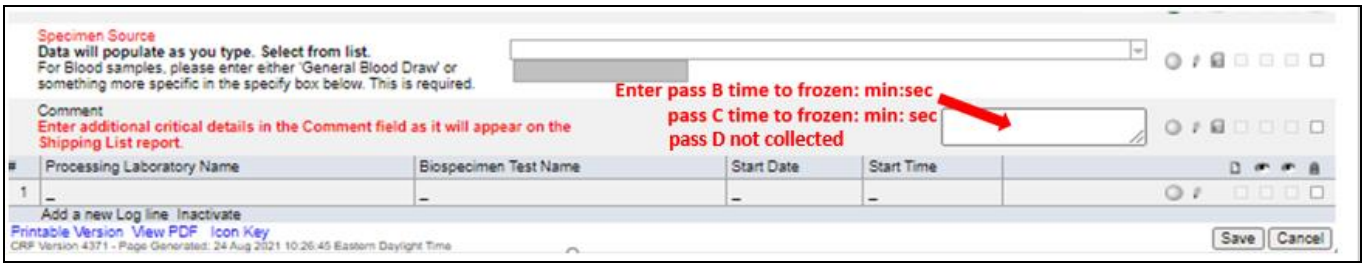
7.4.12 Complete the **Specimen Transmittal** form in the All Specimen folder.

Note: It is important to fill out the time from collection to frozen for each pass in the **Specimen Transmittal** form by following the instructions below.

Pass A time will be recorded in the appropriate fields as shown below:



Times elapsed for passes B, C and D will be recorded in the **Comment** field near the bottom of the Specimen Transmittal form as shown below. Biopsy passes not collected will also be recorded in the **Comment** field as shown below.



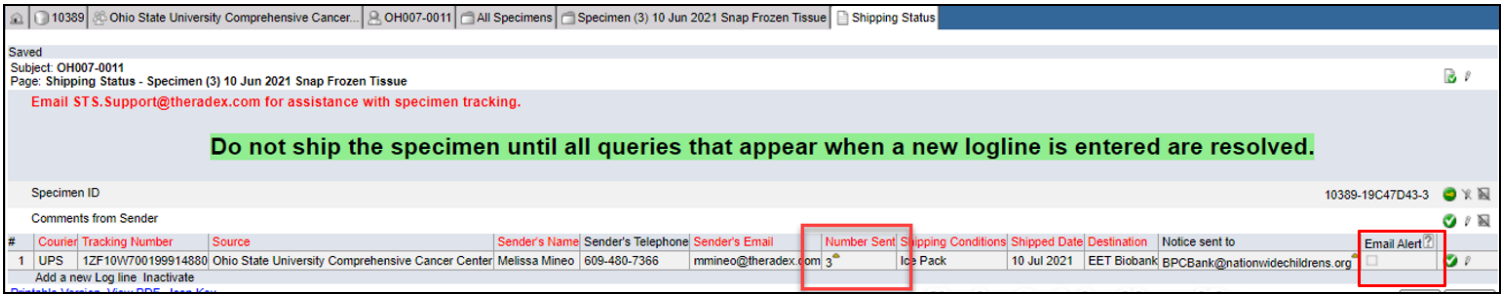
8.0 SHIP TO EET BIOBANK

8.1 When specimens are ready to be shipped, complete shipment documentation in **NCI Medidata Rave.**

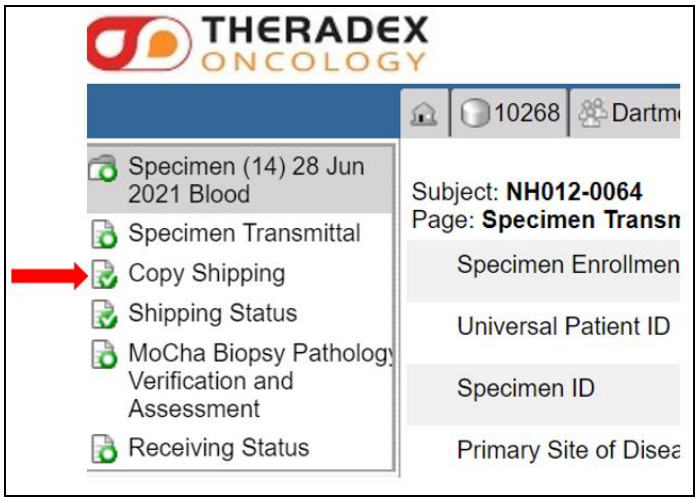
8.1.1 Complete the **Shipping Status** form.

8.1.1.1 Each field in the **Shipping Status** form should be completed as shown below and **Number Sent** (circled below) should equal the number of biopsy passes in the shipment.

8.1.1.2 **Email Alert** (circled below) is only checked for the last specimen in a shipment if multiple specimens are shipped together.

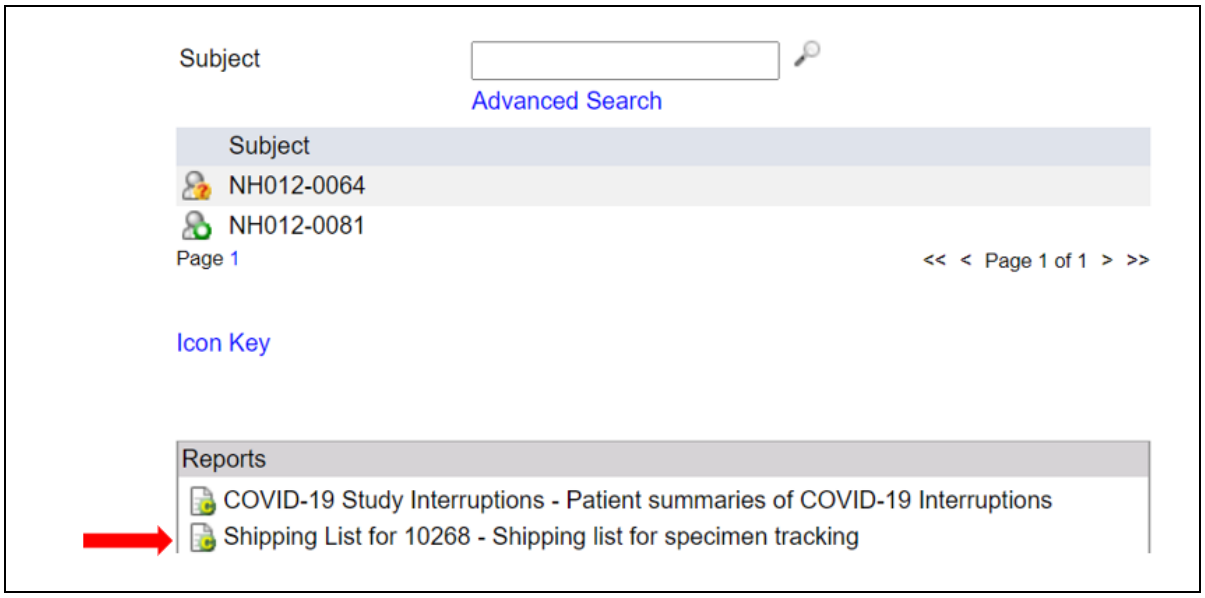


8.1.2 If there are other specimens to be shipped with the frozen biopsies, use the **Copy Shipping** utility form (shown below) in the other specimens' folder.



8.1.3 Print the **Shipping List** report and place it in the box with the specimens.

8.1.3.1 The **Shipping List** report is found in the report panel at the bottom of the window at the site level (an example shown below) since specimens from multiple patients can be included in a single shipment.



8.1.3.2 Shipment should include a hard copy (printed copy) of the **Shipping List**. An example is shown below.

Shipping List

Protocol: 10389 - UAT
Site: Ohio State University Comprehensive Cancer Center
Shipping Date: 10 Jul 2021
Tracking Number: 1ZF10W700199914880

Contact Info: Melissa Mineo
609-480-7366
mmineo@theradex.com

Please include a hardcopy of the pathology and any other relevant report in the shipment.

Protocol-Patient ID	TimePoint	Category	Samples Sent	Tissue	Sample Site	Collection Date/Time	Comments
Universal Pat. Id		Type				Processed Date/Time	
Specimen ID						Frozen in 2 min/Elapsed	
10389-OH007-0011 19C47D43 10389-19C47D43-1	Baseline	Blood Blood	1		General Blood Draw	21 Jun 202109:00 N/A	
10389-OH007-0011 19C47D43 10389-19C47D43-2	Archival	Formalin Fixed Paraffin Embedded Tissue FFPE Block	1	Metastatic	Esophagus	09 Jan 202115:00 N/A	
10389-OH007-0011 19C47D43 10389-19C47D43-3	Week -1 Day 4 (Expansion Cohort Only)	Frozen Tissue Snap Frozen Tissue	3	Metastatic	Esophagus	10 Jun 202111:10 N/A No/00:03:25	Pass B time to frozen: 02:20 ; Pass C time to frozen: 00:50

8.1.3.3 Shipment should also include a hard copy of the **TISSUE BIOPSY VERIFICATION** form found in the appendices of corresponding protocols.

8.2 Specimen shipment to EET Biobank

8.2.1 Follow the **Shipping Specimens from Clinic Site to the EET Biobank/ETCTN Biorepository** section of the clinical protocol for general instructions of sample shipment to EET Biobank.

8.2.2 Frozen biopsies should be shipped in kits provided by EET Biobank. The shipping container sent with kit contents should be used to ship specimens to EET Biobank. **Note:** It's important to include sufficient dry ice to keep the biopsy frozen for at least 96 hours.

8.2.3 Frozen specimens may be shipped on Monday through Thursday to the following address:

EET Biobank
The Research Institute at Nationwide Children's Hospital
700 Children's Drive, WA1340
Columbus, Ohio 43205
PH: (614) 722-2865
FAX: (614) 722-2897

Note: FedEx Priority Overnight service is the required shipping method. The EET Biobank FedEx account will not be provided to submitting institutions. Sites are responsible for all costs for shipments to the EET Biobank, so the overnight express shipment should be billed directly to the shipping institution/site.

8.3 Useful contacts for Specimen Collection, Handling and Shipment:

8.3.1 Send all questions related to this SOP or PD- assay support questions to: NCI_PD_Support@mail.nih.gov

8.3.2 Send all technical questions about the Specimen Tracking System to: STS.Support@theradex.com

8.3.3 EET Biobank queries (kit inquiries and sample shipping): BPCBank@nationwidechildrens.org

APPENDIX 1: BIOPSY COLLECTION RECORD

Note: This document lists important information to be recorded during the biopsy collection process for later documentation in **NCI Medidata Rave.** The completed document should be filed with the study patient's other records at a predetermined location according to local policy for managing clinical trial information. Please **do not** include the document in the shipment to EET Biobank**.**

Certified Assay Operator: _____

Facility/Clinic Collecting Specimens: _____

Clinical Protocol Number: _____

Patient ID: _____

1. Biopsy Collection Information:

Note: Information collected in the table below will be entered in Medidata RAVE.

Note: Record times using military time (24-h designation); for example, specify 16:15 to indicate 4:15 PM.

	Pass A	**Pass B**	**Pass C**	**Pass D**
Specimen ID				
Protocol timepoint of biopsy (Cycle, Day, and Hours post dose, if post treatment)				
Needle type				
Site of biopsy (complete for all passes or note "same" for replicate cores)				
Required: Time elapsed from collection to placement in tube	min sec	min sec	min sec	min sec
Date biopsy collected				
Time biopsy collected	:	:	:	:
Time biopsy placed in tube	:	:	:	:

2. Notes, including any deviations from the SOP: