

DCTD Standard Operation Procedure (SOP)

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Doc. #:	LHTP003.08.03	Revision:	004	Effective Date:	1/27/2015

Pharmacodynamic Assay Development and Implementation Section

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LHTP Approval:	<u>Ralph E. Parchment</u>	Date:	<u>27-Jan-2015</u>

Change History

Revision	Approval Date	Description	Originator	Approval
--	6/1/2011	New Document	LW	RJK
001	6/15/2011	Allow for Thursday shipments with prior approval.	LW	RJK
002	12/12/2012	Updated contact information for specimens	LW, TP	RJK
003	6/12/2013	Updated contact information for specimens, expanded Responsibilities section, and updated Specimen Submission Form.	LW	RJK
004	1/27/2015	Updated information related to prepared shipping kits, updated contact information for specimen shipments.	KFG	RJK

**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

The purpose of this SOP is to describe the procedures for collection, preparation, and shipment of 10-mL human blood specimens in CellSave tubes from Clinical Centers. The CellSave tube collections will be used for enrichment of circulating tumor cells (CTCs) on the CellSearch device.

### 2.0 SCOPE

This SOP applies to all Clinical Center personnel responsible for collecting, preparing and shipping blood specimens from patients participating in clinical trials to PADIS, LHTP, Frederick National Labs for analysis.

### 3.0 ABBREVIATIONS

CRT	=	Controlled Room Temperature
CTC	=	Circulating Tumor Cell
DCTD	=	Division of Cancer Treatment and Diagnosis
FNLCR	=	Frederick National Laboratory for Cancer Research
LHTP	=	Laboratory of Toxicology and Pharmacology
NCI-F	=	National Cancer Institute at Frederick
PADIS	=	Pharmacodynamic Assay Development and Implementation Section
RT	=	Room Temperature, 18°C - 25°C
SOP	=	Standard Operating Procedure

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## 5.0 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**

A Certified Assay Operator and/or PK/PD Support Lab personnel may be a Laboratory Technician/ Technologist, Research Associate, or Laboratory Scientist who has been certified through DCTD training on this SOP and works 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.
- 5.2 It is the responsibility of the Certified Assay Operator and/or PK/PD Support Lab personnel to confirm scheduled sample collection time points, pre-print all labels and data collection sheets in advance, check documentation for accuracy, and verify that the required collection tubes, supplies, and equipment are available for successful collection and handling of blood samples.
- 5.3 It is the responsibility of the Certified Assay Operator to ensure timely transport and processing of the samples, enter and review all of the required collection and processing data, and archive all data sheets in the appropriate files.
- 5.4 Certified Assay Operators following this SOP are required to be certified in working safely with bloodborne pathogens in research laboratories in accordance with OSHA Bloodborne Pathogen Standard (29 CFR 1910.1030).
- 5.5 A Specimen Submission Form ([Appendix 1](#)) should be prepared for each batch of patient samples prior to shipping to the processing laboratory for PD analysis. All samples must be shipped **within 24 h of collection.**
- 5.6 The responsible personnel are to check the DCTD Biomarkers site (<http://dctd.cancer.gov/ResearchResources/ResearchResources-biomarkers.htm>) to verify that the latest SOP version is being followed.

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## 6.0 MATERIALS AND EQUIPMENT REQUIRED

### 6.1.1 Blood shipment container provided by NCI-F – store at room temperature

- 6.1.1.1 Controlled room temperature (CRT) gel packs
- 6.1.1.2 Styrofoam box
- 6.1.1.3 Shipping cardboard box (red/white)

### 6.1.2 Specimen collection kits provided by NCI-F – store at room temperature

- 6.1.2.1 CellSave Preservative Tubes, 10.0-mL draw capacity (Veridex, Cat#: 7900005). **Do not** use CellSave tubes after expiration date.
- 6.1.2.2 50-mL Falcon tube containing absorbent paper (secondary holding tube)
- 6.1.2.3 Zip lock bag – to protect Specimen Submission Form (Appendix 1) upon return
- 6.1.2.4 FedEx Priority Overnight return label; pre-addressed with NCI account information

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## 7.0 OPERATING PROCEDURES

### Important:

- Processing limitations: a minimum volume of 8.0 mL of blood in the CellSave tube is needed for processing.
- Blood specimens **MUST** be stored, transported, and processed at 18°C to 25°C.
- All samples **MUST be shipped within 24 h of collection** to ensure quality results.

### 7.1 Order Shipping Kits and Blood tubes

**Important: Blood shipment containers (SOP Section 6.1) and specimen collection kits (SOP Section 6.2) are shipped separately.**

**7.1.1** Blood shipment containers can be requested by e-mail to [NCI\\_PD\\_Support\\_CellSearch@mail.nih.gov](mailto:NCI_PD_Support_CellSearch@mail.nih.gov). Specify the number of shipment containers you will need.

- Allow at least six business days for receipt of the blood shipment containers.
- A confirmation e-mail with the expected shipping date will be sent.

**7.1.2** Specimen collection kits can be requested by e-mail to [NCI\\_PD\\_Support\\_CellSearch@mail.nih.gov](mailto:NCI_PD_Support_CellSearch@mail.nih.gov). Specify the number of specimen collection kits you will need.

- Allow at least six business days for receipt of the specimen collection kits.
- A confirmation e-mail with the expected shipping date will be sent.

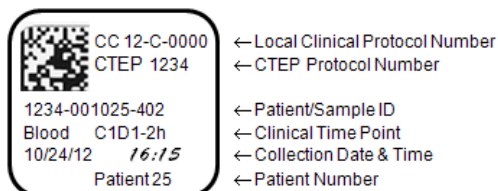
### 7.2 Preparation

**7.2.1** Store the blood shipment containers and the specimen collection kits at 18°C to 25°C (RT).

**7.2.2** Do not use CellSave tubes after their **expiration date**.

**7.2.3** Print specimen labels for the CellSave tubes to be collected including the Patient/Sample ID, CTEP/clinical protocol number, and collection date and time.

**7.2.3.1** Patient/Sample IDs for blood samples collected at the NCI include the CTEP number followed by a unique patient identifier and a sequential specimen ID; NCI blood samples for CTC PD sampling are series 400 (see example label).



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#### 7.4 Collection into CellSave Tubes

**Important:** If blood samples are collected by a second party (nursing staff, phlebotomist, etc.), remove all clinical and personal identifiers from tube when received and replace with the pre-printed specimen label. **Do not** just place specimen label on top of clinical label.

**7.4.1** Place a pre-printed specimen label on the CellSave tube.

**7.4.2** Collect whole blood aseptically by venipuncture or from a venous port into a CellSave tube.

- Note: If the patient is on doxorubicin therapy, allow at least 7 d following administration of a dose of doxorubicin before blood draw.

**7.4.3** Fill the CellSave tube with a minimum of **8-mL volume for a 10-mL capacity tube** until the blood flow stops to ensure the correct ratio of sample to anticoagulant and preservative. If < 8-mL blood volume is collected, make a note on the Specimen Submission Form ([Appendix 1](#)) for that sample so the processing laboratory is aware of the deviation.

**7.4.4** Immediately mix the specimen tube by **gently inverting** the tube 8-10 times; tube inversion prevents clotting. **Do no shake** the tube, vigorous mixing can cause hemolysis. Inadequate or delayed mixing may result in inaccurate test results.

**7.4.5** **Do not** refrigerate or freeze specimens; keep tubes at 18°C to 25°C (RT).

**Important:** Do not place sample(s) on ice. If the clinical staff placed the CellSave tube on ice, make a notation on the Specimen Submission Form ([Appendix 1](#)) and bring the tube to 18°C to 25°C (RT) before proceeding with sample processing.

**7.4.6** Label each tube with Patient/Sample ID, collection date and time, and clinical trial time point (i.e., cycle, day, hour: C1D1-2h).

**7.4.7** Blood specimens should be shipped **within 24 h of collection**, preferably on the day of collection to ensure quality results. Packaging and shipping instructions are in SOP Section 9.0.

**7.4.7.1** Blood specimens may be stored or transported in CellSave Tubes for up to 96 h at 18°C to 25°C (RT) prior to processing, but processing **must** begin within 96 h of collection.

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## 8.0 SHIPMENT OF SAMPLES

### Important:

- All samples **MUST be shipped within 24 h of collection** to ensure quality results.

**8.1** Complete a **Specimen Submission Form** ([Appendix 1](#)) for all samples in the shipment.

**8.1.1** For each sample record the Patient/Sample ID, Clinical Protocol/CTEP number, collection date and time, clinical trial time point, and clinical diagnosis if known. Inclusion of the clinical diagnosis allows the specimen processing laboratory to more efficiently enrich CTCs from the blood sample.

**8.1.2** In the comments field, record any deviations during blood collection (e.g., < 8.0-mL blood).

### 8.2 Packaging Instructions

**8.2.1** Store CRT packs at 18°C to 25°C (RT). **DO NOT** refrigerate or freeze CRT packs.

**8.2.2** Place an 18°C to 25°C (RT) CRT pack in the bottom of a Styrofoam shipping container.



**8.2.3** Wrap absorbent paper around the specimen-filled CellSave tube and place in a 50-mL Falcon centrifuge tube or blood shipping tube.





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- 8.2.1** Place the tube in the Styrofoam box on top of the CRT pack, put a second 18°C to 25°C (RT) CRT pack on top of the tube, and insert the completed Specimen Submission Form ([Appendix 1](#)) into a Zip lock bag and place on top of the CRT gel pack.



- 8.2.2** Close the Styrofoam box and place it inside a cardboard shipping box.



### 8.3 Shipping Instructions

- 8.3.1** Seal the cardboard box and attach the return shipping label to the outside of the box; do not cover the UN3373 (Biological substance, Category B) sticker with the shipping label. Specimens should be shipped to:

Attention: Dan Danner  
 NCI-F/FNLCR  
 1073 Beasley Street, Building 1073  
 Fort Detrick  
 Frederick, MD 21701  
 Phone: 301 846-5748

- 8.3.2** Send an e-mail on the day of shipment to [NCI\\_PD\\_Support\\_CellSearch@mail.nih.gov](mailto:NCI_PD_Support_CellSearch@mail.nih.gov) to ensure timely receipt and processing of the samples.

8.3.2.1 The **subject line** should state: "PD Clinical Shipment Notification"

8.3.2.2 For each specimen being shipped include the following information:

- Patient/Sample ID (s)
- FedEx Tracking Number (s)
- Your Site Name

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## APPENDIX 1: PD SPECIMEN SUBMISSION FORM AND CHAIN OF CUSTODY

If submitting more than 10 specimens, attach an additional copy of the Specimen Submission Form. Include a copy of the submission form and signed, chain of custody section with every shipment.

### 1. Specimen Submission Form

**NOTE:** Record times using **military time** (24-h designation); e.g., specify 16:15 to indicate 4:15 PM. If submitting more than 10 specimens, attach an additional Specimen Submission Form.

Total No. Specimens:		Shipment Date:					
Item No.	Patient/Sample ID	Protocol/CTEP No.	Collection Date	Collection Time	Cycle/Day/Hour	Clinical Diagnosis	Comments
<i>Ex:</i>	<i>1234-001025-402</i>	<i>1234</i>	<i>10/24/2012</i>	<i>16:15</i>	<i>C1D1-2h</i>	<i>sarcoma</i>	
1							
2							
3							
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**2. Chain of Custody Signatures**

Prior to shipping the Clinical Center Specimen Handling personnel should verify contents of and sign and date on line 1 below to verify contents of container.

Task	Responsible Party	Signature	Date
1. Shipment of blood tubes (22°C ± 3°C controlled temperature gel packs)	Clinical Center		/ /
2. Receipt of specimen: log receipt, verify specimen(s), and verify shipping conditions.	NCI-F/FNLCR		/ /
3. Receipt of specimen for research use.	NCI-F/FNLCR		/ /