

DCTD Standard Operation Procedure (SOP)

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Pharmacodynamic Assay Development and Implementation Section

Laboratory of Human Toxicology & Pharmacology

Applied/Developmental Research Directorate, Leidos Biomedical Research, Inc.

Frederick National Laboratory for Cancer Research

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Change History

Revision	Approval Date	Description	Originator	Approval
--	6/5/2019	New Document	AP/RA	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 Streck blood collection tubes from clinical centers. The Streck blood tube collections will be used for enrichment and analysis of circulating tumor cells (CTCs).

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 Pharmacodynamic Assay Development and Implementation Section (PADIS), Laboratory of Human Toxicology and Pharmacology (LHTP), and Frederick National Laboratory for Cancer Research (FNLCR) for analysis.

3.0 ABBREVIATIONS

CRT	=	Controlled Room Temperature
CTC	=	Circulating Tumor Cell
CTEP	=	Cancer Therapy Evaluation Program
DCTD	=	Division of Cancer Treatment and Diagnosis
FNLCR	=	Frederick National Laboratory for Cancer Research
LHTP	=	Laboratory of Human Toxicology and Pharmacology
OD	=	Office of the Director
OSHA	=	Occupational Safety and Health Organization
PADIS	=	Pharmacodynamic Assay Development and Implementation Section
PD	=	Pharmacodynamic(s)
PK	=	Pharmacokinetic(s)
RT	=	Room Temperature, 18-25°C
SOP	=	Standard Operating Procedure

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4.0 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 that 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.

- 4.1** 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.
- 4.2** 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.
- 4.3** It is the responsibility of the Certified Assay Operator and/or PK/PD Support Lab Personnel to ensure timely transport and processing of the samples, enter and review all the required collection and processing data, and archive all data sheets in the appropriate files.
- 4.4** Certified Assay Operators and/or PK/PD Support Lab Personnel 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).
- 4.5** 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 via FedEx Priority Overnight on the same day as collection.
 - 4.5.1** Note: if a sample is collected after the FedEx pickup for that day, it should go out on the first available pickup the next day (via FedEx Priority Overnight).
- 4.6** 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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5.0 MATERIALS AND EQUIPMENT REQUIRED

5.1 All blood shipment containers and specimen collection kits will be provided by PD Central Receiving. See [Section 6.1](#) for ordering instructions.

5.2 Required blood collection and shipping supplies:

Blood Shipment Containers

- Cardboard Apocell shipping box (red/white)
- Two controlled room temperature (CRT) gel packs
- Insulating Styrofoam container

Specimen Collection Kits

- Streck Cell-Free DNA BCT® blood collection tubes, 10.0 mL draw capacity (Streck, Cat# 218962)
- 50.0 mL Falcon tube containing absorbent paper (secondary holding tube)
- 6" × 9" biohazard specimen bag
- Zip-lock bag – to protect Specimen Submission Form ([Appendix 1](#)) upon shipment
- FedEx Priority Overnight return label(s); pre-addressed with NCI account and address information ([Section 7.3.1](#))

Note: AccuCyte® Cell-Free DNA blood collection tubes, 10.0 mL draw capacity (RareCyte, Cat# 20-1069-004), can be used in place of Streck blood collection tubes.

Note: Do not use blood collection tubes after the expiration date, which is printed on each individual tube. Tubes must be used as specified by the manufacturer.

6.0 OPERATING PROCEDURES

Important:

- **Processing limitation:** A *minimum* volume of 8.0 mL of blood in the Streck blood collection tube is required for processing.
- Blood samples **MUST** be stored, transported, and processed at RT (18-25°C).
- All samples **MUST be shipped within 24 hours of collection** to ensure quality of the results.
- Processing of blood CTC samples must be completed **within 48 hours** from initial collection.
- Blood collections and sample shipments on Fridays, and/or any business day prior to a Federal holiday are **not permissible**, due to **48-hour processing restrictions**.
- Store CRT gel packs between 18°C and 25°C (RT). **Do not refrigerate or freeze** CRT gel packs.

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- PD Central Receiving Support needs to be notified as soon as possible of all protocol deviations or issues, prior to shipment of sample(s); in addition, the deviations or issues must be noted on the Specimen Submission Form ([Appendix 1](#)).

6.1 Ordering Blood Shipment Containers and Specimen Collection Kits

6.1.1 Blood shipment containers and specimen collection kits can be requested by sending an e-mail to:

NCI_PD_Support@mail.nih.gov

- Specify in the request the *number* of shipment containers needed.
- Allow at least **six business days** for receipt of the blood shipment containers and supplies.
- A confirmation e-mail with the expected shipping date will be sent from PD Central Receiving Support.

6.2 Preparation

6.2.1 Store the blood shipment containers and the specimen collection kits at RT (18-25°C).

6.2.2 **Do not** use Streck blood collection tubes after the **expiration date**, which is printed on each individual tube and is specified by the manufacturer.

6.2.3 Create specimen labels for each Streck blood collection tube, including the following information:

- Patient/Sample ID
- Clinical Protocol/CTEP number
- Collection date
- Collection time
- Timepoint – which includes the treatment cycle, day, and hour (*i.e.* C2, D1, 2hr)

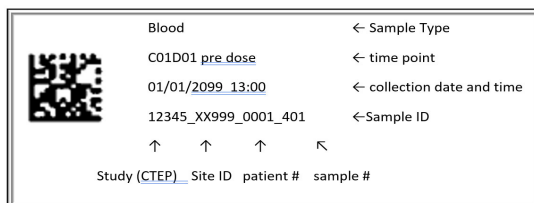
Note: All required information must be *clearly* labeled and *legible*.

6.2.3.1 Patient/Sample IDs for blood samples collected at the NCI contain:

- Clinical Protocol/CTEP number
- a unique patient identifier
- a sequential specimen ID in series (NCI samples for CTC blood PD are numbered as part of a 400-series [see example label below]).

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Example Specimen Label for a Sample Collected at NCI



The image shows a specimen label with a QR code on the left. To the right of the QR code, the following information is displayed with arrows indicating the corresponding fields on the label:

- Blood ← Sample Type
- C01D01 pre dose ← time point
- 01/01/2099 13:00 ← collection date and time
- 12345_XX999_0001_401 ← Sample ID

Below this information, there are four upward-pointing arrows and a rightward-pointing arrow, followed by the text: Study (CTEP) Site ID patient # sample #

6.3 Collection and Storage of Blood Samples

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 (see example in [Section 6.2.3.1](#)). **Do not** place specimen label on top of clinical label.

- 6.3.1** Place a pre-printed specimen label, containing all of the required information indicated in [Section 6.2.3](#), on the Streck blood collection tube.

Note: AccuCyte[®] Cell-Free DNA blood collection tubes, 10.0 mL draw capacity (RareCyte, Cat# 20-1069-004), can be used in place of Streck blood collection tubes.

- 6.3.2** Collect whole blood aseptically into a Streck blood collection tube by venipuncture or from a venous port.

Note: If the patient is on doxorubicin therapy, allow *at least* 7 days following administration of a dose of doxorubicin before drawing blood.

- 6.3.3** Fill the Streck blood collection tube with a *minimum* volume of **8.0 mL** for a **10.0 mL capacity tube**, to ensure the correct ratio of sample to anticoagulant and preservative.

Processing limitation: A minimum blood volume of 8.0 mL in the Streck blood collection tube is needed for processing. If <8.0 mL blood volume is collected, make a note of this protocol deviation on the Specimen Submission Form ([Appendix 1](#)) for that sample.

- 6.3.4** Immediately mix the specimen tube by *gently inverting* the tube 8-10 times. Tube inversion prevents clotting. **Do not** shake the tube, as vigorous mixing can cause hemolysis. Inadequate or delayed mixing may also result in inaccurate test results.

- 6.3.5** Blood samples must stay consistently between 18°C and 25°C (RT).

Important: **Do not** freeze or place blood sample(s) on ice.

If clinical staff accidentally place the Streck blood collection tube(s) on ice or refrigerate, make a notation on the Specimen Submission Form ([Appendix 1](#)) and bring the tube to RT before proceeding with sample processing or shipping.

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6.3.6 Check to make sure each tube is *clearly* labeled with patient/sample ID, CTEP/clinical protocol number, collection date, collection time, and time point ([Section 6.2.3](#)). This should always be done prior to collection, but this quality check is to ensure proper labeling and helps eliminate collection errors.

6.3.7 Blood specimens should be shipped **within 24 hours of collection**, to ensure good quality results. Packaging and shipping instructions are in [Section 7.0](#).

Note: Blood specimens in Streck blood collection tubes are required to be analyzed up to a **maximum of 48 hours** from collection at RT (between 18°C and 25°C).

7.0 SHIPMENT OF SAMPLES

Important:

- All samples must be **shipped within 24 hours of collection** to ensure quality of the results.
- Blood collections and sample shipments on the last business day of the week (typically Fridays), and/or any business day prior to a Federal holiday or weekend, are ***not permissible***, due to 48-hour processing restrictions.
- For all Saturdays, Sundays, and all Federal holidays or weekends, the FNLCR CTC laboratory is not in operation; sample shipments will not be delivered until the following business day. FedEx holds these sample packages at their local facility until the next operational day.
- Samples shipped on Fridays and/or any business day prior to a Federal holiday or weekend cannot undergo the necessary testing within the required 48-hour window following blood sample collection and are therefore unanalyzable.

Note: Please contact PD Central Receiving Support as soon as possible if there are any issues with meeting shipping requirements (see [Section 6.1](#) for e-mail contact).

7.1 Specimen Submission Form Instructions

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

7.1.1 For each sample collected, *clearly* record each piece of information on the Specimen Submission Form:

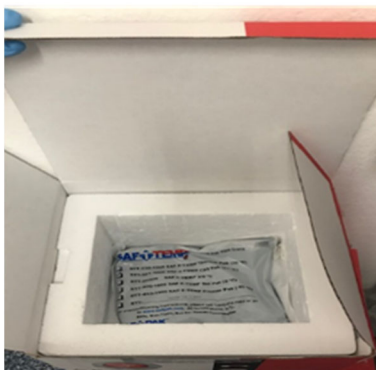
- Patient/Sample ID
- Clinical Protocol/CTEP number
- Collection date
- Collection time
- Time point
- Clinical diagnosis (if known) - Inclusion of the clinical diagnosis allows the specimen processing laboratory to more efficiently enrich CTCs from the blood sample.

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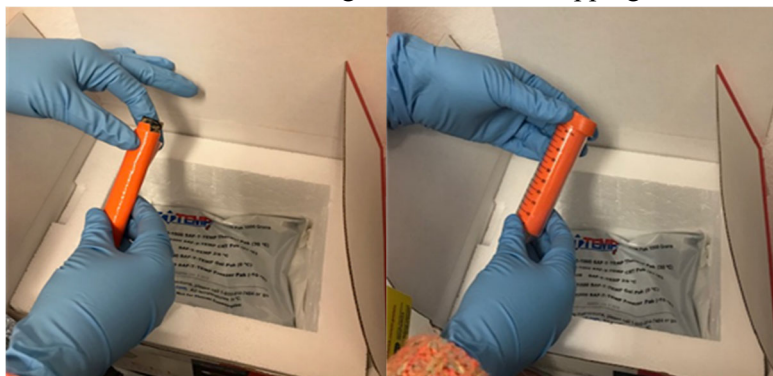
- Comments: Any protocol issues and deviations must be noted in the comments field (e.g., <8.0 mL blood collected, sample not shipped with proper ambient gel packs, etc.).

7.2 Packaging Instructions

- 7.2.1 Store CRT gel packs at RT. **Do not** refrigerate or freeze CRT gel packs.
- 7.2.2 All blood shipping containers and specimen collection kits should be held at RT.
- 7.2.3 The insulating Styrofoam container should be placed inside the cardboard Apocell shipping box.
- 7.2.4 Place one of two CRT gel packs at the bottom of a Styrofoam shipping container.



- 7.2.5 Wrap absorbent paper around the specimen-filled Streck blood collection tube and place in a 50.0 mL Falcon centrifuge tube or blood shipping tube.

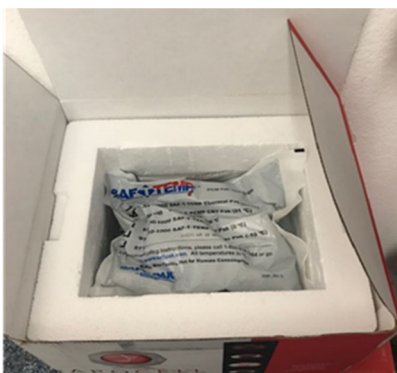


- 7.2.6 Place the Falcon tube containing the Streck blood collection tube in the biohazard specimen bag and seal securely.
- 7.2.7 Place the biohazard bag with the collection tube in the Styrofoam box, directly on top of the CRT gel pack.

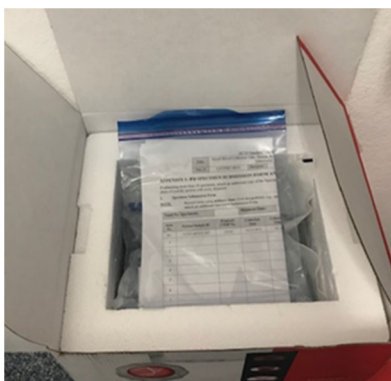
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7.2.8 Put a second CRT gel pack on top of the sample.

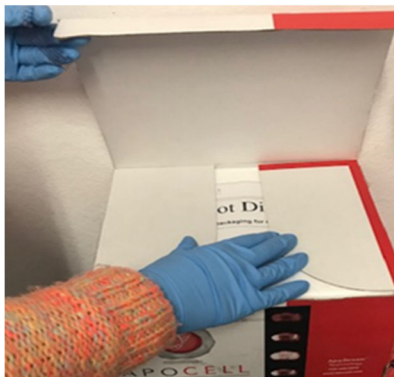


7.2.9 Insert the completed Specimen Submission Form ([Appendix 1](#)) into a zip-lock bag on top of the second CRT gel pack.



7.2.10 Close the insulating Styrofoam container with the accompanying lid and close the cardboard Apocell shipping box.

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7.3 Shipping Instructions

- 7.3.1** Seal the cardboard Apocell shipping box securely with adhesive shipping tape and attach the return shipping label to the outside of the box. **Do not** cover the **UN3373 (Biological substance, Category B)** sticker with the provided FedEx Priority Overnight shipping label (see [Section 6.1](#)).

Specimens should be shipped to the following address:

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

- 7.3.2** Before making the shipment, send a shipment notification by e-mail to NCI_PD_Support@mail.nih.gov, to ensure timely receipt and processing of the samples.
- 7.3.2.1** The *subject line* of the e-mail notification should state: "PD Clinical Shipment Notification".
- 7.3.2.2** For *each sample* being shipped, include the following information in the body of the e-mail message:
- Clinical Protocol/CTEP number
 - 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 a signed chain of custody section with every shipment. **Any protocol issues and deviations must be noted in the Comments field.**

1. Specimen Submission Form

NOTE: Record times using **military time** (24-hour 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>12345-001025-402</i>	<i>12345</i>	<i>10/24/2012</i>	<i>16:15</i>	<i>CID1-2h</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 the contents of the shipping container and sign and date on Line 1 below.

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.	FNLCR		/ /
3. Receipt of specimen for research use.	FNLCR		/ /