Biological Testing Branch, Developmental Therapeutics Program

National Cancer Institute at Frederick, and

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

Frederick National Laboratory for Cancer Research

Clinical and QA Reviewer: Michelle A. Eugeni

BTB Approval: Melinda Hollingshead

NCI PDM Repository Approval: Yvonne A. Evrard

SOP Developed in Collaboration with:

University of Nebraska Medical Center - Eppley Institute Rapid Autopsy Program, Drs. Michael Hollingsworth, and Paul Grandgenett

Change History

Revision	Approval Date	Description	Originator	Approval
--	2/1/2017	New Document	MAE, YAE	YAE
A	9/25/2017	Revision of text to reflect use of disposable & non-disposable instruments; minor text revisions regarding timeline for shipment and data provision	MAE	YAE
B	5/14/2018	Revised shipping days for viably cryopreserved specimens; general SOP text revisions to correspond with current practice and with revised Shipping Manifest; Shipping Manifest updated; Appendix 3 added.	MAE	YAE
C	2/19/2020	Collaborator details updated. Clarification of timeline for submission of limited data in Section 3.7. Appendix 3 Box map layout updated. General text language revisions throughout for consistency not altering processes or procedures.	MAE	YAE
D	11/19/2021	General text language revisions throughout for consistency not altering processes or procedures	MAE	YAE
E	6/12/2024	Cover page Contacts updated and redundant group email address for PDM receiving team eliminated; all other changes made were for consistency with current processes, procedures, and administrative text.	MAE	YAE
F	1/31/2025	Update to Shipping Manifest patient data header. SOP is retired, no longer actively updated.	YAE	MAE
xx	3/10/2025	Adapted internal-use SOP-PDM10108 for posting to public website for general recommendations on use of post-mortem specimens for patient-derived model development. Removed specific references for communication with the NCI PDMR. SOP is retired, no longer actively updated.	YAE	MAE

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1.0 PURPOSE

Standardize the method for collecting, preparing, and shipping viably cryopreserved autopsy/post-mortem material for use in patient-derived model (PDM) generation. Ideally these tissues will be from both the primary tumor site and metastatic lesions so PDXs from multiple locations can be developed for study. The tissue collections will be used for direct implantation into immune-compromised mice to generate patient-derived xenografts (PDX) and/or to culture in media to generate primary tissue-derived in vitro cell models. SOP was developed for models that are distributed through the NCI PDM Repository (PDMR).

Methodology and procedures described in this SOP and utilized by the Biological Testing Branch (BTB, DTP, DCTD, NCI-Frederick) to generate models for the NCI PDMR are provided to serve as general guidance and recommendations. We have performed a limited comparison of carcinoma PDX take-rates developed from matched non-cryopreserved and cryopreserved tissues. This data set demonstrated that development of PDXs from cryopreserved primary tissue specimens have decreased cell viability resulting in a significantly lower take rate than those attempted utilizing non-cryopreserved primary tissue specimens. This SOP has been developed to provide general standards and procedures for rapid autopsy/post-mortem (RAP) tissue specimen collection, cryopreservation, and shipment to be used when collection of non-cryopreserved specimens is not feasible due to any number of circumstances. Whenever possible, non-cryopreserved primary tissue specimens are always preferred for use in the development of PDXs.

2.0 ABBREVIATIONS

BTB	=	Biological Testing Branch
DCTD	=	Division of Cancer Treatment and Diagnosis
FNLCR	=	Frederick National Laboratory of Cancer
HBSS	=	Hank’s Balanced Salt Solution
NCI-F	=	National Cancer Institute at Frederick
PBS	=	Phosphate Buffered Saline
PDM	=	Patient-Derived Models
PDMR	=	Patient-Derived Models Repository
PDX	=	Patient-Derived Xenograft
PDX ID	=	Randomly generated ID assigned to PDX specimens of registered patients and used for internal tracking at Receiving Laboratory; it assists in the delinking process and minimizes the chance of PII issues
PII	=	Personally Identifiable Information
RAP#	=	Enrolling site Rapid Autopsy/Post-Mortem Identifier (not linked to patient medical record ID)
SOP	=	Standard Operating Procedure

3.0 ROLES AND RESPONSIBILITIES

Clinical PI/Project Leader — The Clinical PI/Project Leader, directs specimen collection operations, supervises technical personnel, and is responsible for the proper performance of all specimen collection and shipping procedures. Oversees the personnel who follow the SOPs and is responsible for ensuring the personnel have sufficient experience to handle clinical specimens.

Clinical Specimen Support Lab Personnel — Clinical Specimen Support Lab personnel work under the guidance of the Clinical PI/Project Leader. These people ensure specimen collection and shipping are performed in accordance with the current SOP(s), as well as any other procedures conducted by a clinical site.

3.1 It is the responsibility of the Clinical Specimen 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 specimens.

3.2 It is the responsibility of the Clinical Specimen Support Lab Personnel to ensure timely transport and processing of the specimens, enter and review all of the required collection and processing data, and archive all data sheets in the appropriate files.

3.3 Clinical Specimen 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).

3.4 The Clinical Specimen Support Lab Personnel responsible for conducting the specimen collection and handling procedures are to follow this SOP and complete the required tasks and associated documentation.

3.5 **Viably cryopreserved specimens should NOT be shipped the same day as collection** as they need to go through the freezing procedure.

3.6 Confirm FedEx Priority Overnight shipping has been arranged for **the date of choice for shipment Monday - Wednesday**; specimens can be held at -80°C for several days before shipping if the next shipping day would result in receiving laboratory receiving the specimens on a weekend.

3.7 A completed Shipping Manifest and signed Specimen Chain of Custody sheet must be included with each shipment (Appendix 1).

3.8 Provision of associated Patient Limited Medical Information (Appendix 2) or redacted autopsy report should be received within 10-14 days of shipment of the specimens.

4.0 MATERIALS REQUIRED

Note: As much as is reasonably possible, separate sets of sterile disposable or non-disposable instruments and petri dishes should be used for excision and manipulation of excised tissue from each separate anatomic site. This will help to minimize the risk of potential bacterial cross-contamination as well as the risk of intermingling of cells from different resection sites.

4.1 Autopsy Suite

4.1.1 Sterile instruments – disposable or non-disposable

4.1.1.1 Ideally multiple sets:
- one for the initial external to internal incision,
- preferably one set for each separate site of tumor excision.

4.1.2 Sterile, one-time use tweezers and scalpels (one set per tumor/metastatic site).

4.1.3 Sterile drapes/surgical fields
Optional: Sterile petri dish for manipulation of individual excised tissues

4.1.4 Hydrogen peroxide (H_2O_2) solution 1.4% (e.g., Clorox Part# 30829)

4.1.5 Sterile saline, 1X PBS, or HBSS

4.1.6 2-mL cryovials

4.1.7 Laboratory marker and tube labels (e.g., Sigma-Aldrich, Cat# Z359122)

4.1.8 Tube holder

4.1.9 Microcentrifuge tube labels

4.1.10 Freezing media, held on wet ice (stored at 4°C)
- RPMI-1640 media containing 20% fetal bovine serum and 10% DMSO
  - Ideally made the same day as use.
- Alternatively, make RPMI-1640 + FBS only ahead of time and store at 4°C, then add DMSO same day as use.

4.1.11 Ice bucket with wet ice for transportation of specimen jars

4.2 Laboratory (freezing of specimens)

4.2.1 Mr. Frosty Freezing container (Nalgene, Cat# 5100-0001)

4.2.2 Isopropanol

4.2.3 -80°C freezer

4.3 Shipping

4.3.1 Tube box

4.3.2 ZipLock bag to protect Shipping Manifest upon return

4.3.3 Sufficient dry ice for 3-d shipment

4.3.4 Styrofoam box

4.3.5 Shipping cardboard box

4.3.6 FedEx Priority Overnight return label

5.0 OPERATING PROCEDURES

5.1 General limitations:

5.1.1 Please do not collect autopsy/post-mortem specimens from patients known to actively have or have a documented history of having the following bloodborne pathogens: human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV).

- NOTE: This is a safety restriction applied at NCI-Frederick/FNLCR, consult with your institution to determine allowable bloodborne pathogens.

5.1.2 The goal is to be as sterile as possible within the limitations of the autopsy suite/pathology laboratory setting and minimize post-mortem interval time (time of death to time of tissue collection).

- Wherever possible sterile technique should be used to limit environmental contamination post-mortem including sterile preparation of the body, use of a sterile field, and single use sterile disposable instruments for sample collection and handling or multiple set of non-disposable sterile instruments and containers for the rinse solutions (i.e., PBS, HBSS, etc.).

5.1.3 It is recognized that systemic infections present in the participant pre-mortem, diagnosed or undiagnosed, may contribute to down-stream contamination and cannot be anticipated.

- If the collecting site is aware of the pre-mortem infection, it is helpful for notification to be provided so that appropriate antibiotic coverage can be implemented once the specimens are received for implant and culture.
- Any signs of contamination that occur once the specimens are in culture or implanted will be addressed and managed as they present in the collected specimens and preclinical models

5.1.4 Shorter post-mortem interval to collection (time of death to time of tissue collection) will help improve tissue viability and minimize post-mortem bacterial contamination.

5.1.5 Components of the abdominal viscera (especially the large and small intestine) should be the last portion of the trunk that is autopsied, as permitted per institutional standards and procedures, to minimize cross-contamination with microbes that replicate within these organs pre- and post-mortem.

5.2 Processing limitations:

5.2.1 Specimens can be collected from both primary and metastatic tumors.

- Please collect each site into a separate media jar.
- Details on the Shipping Manifest should correspond exactly to the labeling on the cryovials.
- If matched fresh and viably cryopreserved specimens are collected, the site of resection details should correspond between the fresh specimen and the matched cryopreserved specimen.

5.2.2 Autopsy suite/tissue handling procedures listed in this SOP are for "best" conditions; depending on individual site set-up for tissue acquisition not all may be achievable.

5.2.3 The maximum size for individual pieces for shipping should be ~1-2 mm3 each; 3-5 pieces of this size can be placed in an individual cryo-vial for freezing.

5.2.4 Each shipping container should contain its own Shipping Manifest and Chain of Custody sheet (Appendix 1). Important: Each shipping box should contain tumor specimens from only one patient.

5.3 Notification of "On-call" for Upcoming Autopsy/Post-Mortem Specimens for Receiving Laboratory

5.3.1 Email the receiving laboratory at the earliest possible time if informed in advance of a potential procedure, even if the window is 2-3 weeks.

- It is understood that the availability of detailed information will be limited by the level of interaction of the site's rapid autopsy/post-mortem team with the hospital, hospice, or care providers but any amount of advance notice that can be provided is helpful.

Note: When possible, the plan to send both fresh and cryopreserved material should be included in the on-call notification email.

- Include pertinent information in the email to assist in laboratory preparation, such as the approximate time window (e.g., 1-2 weeks), general patient diagnosis (e.g., pancreatic adenocarcinoma), and sex.

Important: On the day of shipment an email must be sent with the FedEx shipping notification (SOP Section 7.3) and the completed Worksheet A (Appendix 2) so the receiving laboratories can prepare for specimen receipt. **Important:** Specimens should not be processed until the attestation of patient consent i.e., Worksheet A, is received (consult with your local IRB on timing of consent and processing requirements).

5.4 Day of Specimen Collection

5.4.1 Prepare specimen tube labels including the in-house rapid autopsy/post-mortem identifier (RAP#). **Important:** PDM specimens should never be labeled with PII, including but not limited to medical record numbers, date of birth, or patient initials.

5.4.2 Have screw-capped 2-mL cryo-vials and labels ready for collected tissue; place freeze medium on ice; multiple tubes can be collected for each tissue collection location.

5.4.3 Viably cryopreserved specimens should **NOT** be shipped the same day as collection as they need to go through the freezing procedure.

- Arrange FedEx Priority Overnight shipping for **the following day or the date of choice for shipment Monday – Wednesday.**
- Specimens can be held at -80°C for several days before shipping if the next shipping day would result receiving laboratory receiving the specimens on a weekend.

5.5 Autopsy/Post-Mortem Tissue Specimen Collection Process for PDM Development

Note: The following steps should be followed to the extent feasible based on the institutional policies and procedures of the enrolling site.

5.5.1 Set-up containers with H2O2 solution and sterile saline, PBS or HBSS to facilitate the process flow once the autopsy/post-mortem procedure begins (details in Step 5.5.5).

5.5.2 Set-up a sterile field and/or sterile petri dishes for placement of the post-dipped, excised tissue (details in Step 5.5.6).

5.5.3 Clean and/or sterilize the exterior of body before opening with sterile instruments.

5.5.4 Use sterile instruments for tissue excision. A separate set of instruments, disposable, or non-disposable should be used for each primary/metastatic lesion collected. Areas of obvious necrosis or hemorrhage should be avoided.

5.5.5 Dip excised tissue into the H2O2 solution and hold for 1 minute, then dip twice in sterile saline, PBS, or HBSS and place on a sterile surgical field or petri dish. Sterile 50-mL tubes or 6-well plates can be used for these washes.

- Two separate containers per resection site can be used: 1 with H2O2 and 1 with sterile saline, PBS, or HBSS. These would be used in a production line fashion with a separate set of containers used for each resection site.
- Alternatively, one sterile container can be used for each resection site.
  - Initially fill the container with H2O2 for the 1-minute dip.
  - The H2O2 can then be disposed of and the same container filled with sterile saline, PBS, or HBSS for the rinses.
  - A different container should be used for each resection site.
- Maintaining separate containers for each resection site minimizes the risk of cross-contamination of tumor cells and/or bacteria that may be present.

5.5.6 With a new set of sterile instruments on the sterile field or petri dish, cut the tumor tissue into 2-3 mm^3 fragments (~30 mg).

5.5.6.1 Place the number of cryovials needed for the available fragments (3-5 fragments/tube) into a tube rack; keeping the rack and vials on wet ice.

5.5.6.2 Add the 3-5 fragments to each tube.

5.5.6.3 Add 1-mL of freeze medium to each tube without exceeding the tube fill volume.

5.5.7 Seal the cryovials well, wipe with disinfectant, and place into wet ice.

5.5.8 Label vials with RAP# and tissue source.

- For example, if 10 fragments are collected from the same colon anotomical location of RAP#123 and split into two vials, both vials would be labeled "RAP#123, colon". The shipping manifest would note that 2 vials are being shipped for the colon resection.

6.0 CRYOPRESERVING RAP MATERIAL

6.1 If using a step-rate freezer:

6.1.1 Follow the manufacturer's instructions to operate stepped rate freezer. The Biological Testing Branch (DCTD, NCI-Frederick), who generates models for the NCI PDMR, current parameters are:

- 1°C/minute down to -4°C
- -25°C/minute down to -40°C
- +15°C/minute up to -12°C
- -1°C/minute down to -40°C
- -10°C/minute down to -90C

6.1.2 Vials can be held up to 3 days at -80°C before shipping or transferred to the vapor phase of a liquid nitrogen storage tank if there will be a longer time gap before shipping.

6.2 If using a slow rate freezing container, such as a Mr. Frosty:

Note: Follow manufacturer's instructions exactly paying close attention to whether the container should be pre-chilled or held at room temperature before loading.

6.2.1 For isopropanol-based devices (e.g., Mr. Frosty) it is important the isopropanol be replaced regularly, and the container be filled to the manufacturer's fill line.

6.2.2 Room-temperature isopropanol should be placed in the base of the cryo-container and the tube holder placed on top.

6.2.3 Transfer the specimen-containing cryovials from the ice-bucket into the cryo-container, screw on container lid, and place at -80°C overnight. Vials can be held up to 3 days at -80°C before shipping or transferred to the vapor phase of a liquid nitrogen storage tank if there will be a longer time gap before shipping.

7.0 PACKAGING OF TUMOR SPECIMENS

7.1 Complete a Shipping Manifest (Appendix 1) for each set of specimens collected.

7.1.1 At the top of the Shipping Manifest, enter the RAP# for the patient. The PDX ID box (gray text) will be completed by the receiving laboratory upon receipt for internal tracking.

7.1.2 The cryovial numbers and location of tissue collection should be clearly identified. In the below example, specimens from 2 different liver lesions have been obtained (ff and B) and 2 vials for each are being shipped. In Vial Label row three, a pancreas specimen (Pancreas A) has been obtained and only 1 vial is being shipped.

- If only one 81-slot box of freezer specimens is being sent, then column 4 (Box) would indicate 1 of 1.
- The Vial Position in the Box is based on a standard 81-Slot Box layout (Appendix 3)

Rapid Autopsy Material (viably cryopreserved)					
Vial Label (exactly as written on label)	**Vial Contents**	**# Vials**	**Box**	**Vial Position in Box**	**Tissue Type**
RAP 199 Liver ff	Cryopreserved fragments of Originator material from liver Section ff, patient #199	2	1 of 2	A1-A2	☐ Primary Tumor Site ☒ Metastatic Site ☐ Unknown
RAP 199 Liver B	Cryopreserved fragments of Originator material from liver, Section B, patient #199	2	1 of 2	A3-A4	☐ Primary Tumor Site ☒ Metastatic Site ☐ Unknown
RAP 199 Pancreas A	Cryopreserved fragments of Originator material from pancreas, Section A, patient #199	1	1 of 2	A5	☒ Primary Tumor Site ☐ Metastatic Site ☐ Unknown
RAP 199 Lung E	Cryopreserved fragments of Originator material from lung, Section E, patient #199	2	1 of 2	A6-A7	☐ Primary Tumor Site ☒ Metastatic Site ☐ Unknown
RAP 199 Lung F	Cryopreserved fragments of Originator material from lung, Section F, patient #199	1	1 of 2	A8-A9	☐ Primary Tumor Site ☒ Metastatic Site ☐ Unknown

7.2 Packaging Instructions

7.2.1 Place sufficient dry ice inside the internal styrofoam box to last 3 days. Ensure box is clearly marked that it contains dry ice per institutional guidelines and that there is a UN3373 label on the outside.

7.2.2 The cryotubes can be placed in a 50-mL conical and nested inside the dry ice for shipping. Alternatively, place them in a cryotube box and nest the box in the dry ice for shipping.

7.2.3 Close the styrofoam container.

7.2.4 Seal the completed Shipping Manifest with the Chain of Custody section signed on line #1 (Appendix 1) in the clear zip lock bag and place it on top of the styrofoam lid to protect it from condensation.

7.3 Shipping Instructions

7.3.1 Ship specimens on dry ice by FedEx Priority Overnight. Once the cardboard box is sealed, attach the provided return FedEx Priority Overnight shipping label to the outside of the box for shipment; **do not obscure the UN3373 label.**

7.3.2 Send an e-mail on the day of shipment to the receiving laboratory.

7.3.2.1 The **subject line** should state: "PDM Autopsy/Post-Mortem Material Shipment Notification"

7.3.2.2 For each shipping box being sent include the following information:

- FedEx Tracking Number(s)
- RAP#
- Number of individual cryo-vials with tissue from the patient included.
- If not previously sent, a finalized copy of Worksheet A. This is needed to verify patient consent was received by the institution for the collection.
- Scanned copy of the final Shipping Manifest(s) for the specimens.

APPENDIX 1: SHIPPING MANIFEST AND CHAIN OF CUSTODY

RAP number

PDX ID (Completed by Receiving Lab)

1. Shipping Manifest

Include a copy of the signed manifest, chain of custody section with every collection. If tissue specimens from >5 locations from one patient are being sent, complete an additional separate shipping manifest; both will be labeled with the same RAP#.

Basic Patient Information					
Collection Date	**Ischemic Time** (Approx. Time Elapsed from Death to Collection)	**Freeze Date**	**Patient Sex**	**Diagnosis/Disease Code** (standardized disease code)	**Histological Diagnosis/ Sub-Type**
			☐ Male ☐ Female		

Rapid Autopsy/Post-Mortem Specimens (viably cryopreserved)					
Vial Label (Exactly as written on label)	**Vial Contents** (Site of Resection)	**# Vials**	**Box** (e.g., 1 of 1, 1 of 2, etc.)	**Vial Position in Box** (A1, B2, etc.)	**Tissue Type**
					☐ Primary Tumor Site ☐ Metastatic Site ☐ Unknown
					☐ Primary Tumor Site ☐ Metastatic Site ☐ Unknown
					☐ Primary Tumor Site ☐ Metastatic Site ☐ Unknown
					☐ Primary Tumor Site ☐ Metastatic Site ☐ Unknown
					☐ Primary Tumor Site ☐ Metastatic Site ☐ Unknown

APPENDIX 1 - CONTINUED

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	Number of Vials	Signature	Date
1. Shipment of tumor specimens (dry ice)	Clinical Center	Total # Shipped: _____		/ /
2. Portion of specimens received by in vivo lab for implantation. Mark N/A if not provided to lab.	Receiving Personnel	Total # Received: _____		/ /

Important: If multiple **different** patient specimens are being sent in the same cryovial box, separate shipping manifests must be completed for each patient. Remember to leave one empty row in the cryovial box between the different patient specimens.

APPENDIX 2: REGISTRATION FOR RAPID AUTOPSY/POST-MORTEM SPECIMEN COLLECTION FOR <NAME OF EFFORT>

Worksheet A (page 1 of 1)		
Documentation of Consent and Registration		
☐ I confirm that the patient has signed an informed consent allowing collection of autopsy/post-mortem specimens for distribution to <RECEIVING LABORATORY> allowing for its use in creation of preclinical models, genetic characterization, and distribution of any derived materials and de-identified medical information to the research community. **Local Protocol #: _____** ***PI or designee name (please print):***		
PI or designee signature:		
Clinical Center:		
Date of signature *(mm/dd/yyyy)**:***		
Rapid Autopsy/Post-Mortem Identifier (RAP#):		
Registration Information		
Specimen Collection Date:	**Biological Sex:** ☐ Male ☐ Female	
Date of Primary Pathological Diagnosis:	**Age at Time of Primary Diagnosis:**	**Age at Collection:**
Detailed Diagnosis or Diagnosis code*: ***For example:*** • ***CTEP Simplified Disease Classification (SDC)*: http://ctep.cancer.gov/protocolDevelopment/docs/SDCv10_M10.xls** • ***OncoTree code*: http://oncotree.mskcc.org/** • ***WHO International Classification of Disease in Oncology***		
Tumor Stage/Grade (if applicable, e.g., Stage III, T3N0M1, Gleason score, Fuhrman Grade)		
Location of known metastases:		
Tumor Biomarker Information (if available and permitted per patient consent, local IRB and/or HIPAA policy, e.g., IHC results [ER+], genetic screening [BRAF-V600E], FISH analysis [nuc ish 8q24(MYCx2)]):		

RAP#: _____

Complete this form to the best of your ability. Any information unavailable in the patient record should be marked as "Don't Know," "Unknown" or write-in "Unknown."

Worksheet B (page 1 of 2)

Previous Tobacco Exposure

Was the subject a:

- ☐ Current Smoker
- ☐ Former Smoker
- ☐ Never Smoked
- ☐ Information not available

If 'Current or Former smoker, please complete the following based on the information available.

Total pack/years*: _____

*This is calculated by multiplying the number of packs smoked per day by the number of years the person has smoked (most US packs contain 20 cigarettes)

Occupation, Race and Ethnicity

Racial Categories (select one or more, as applicable)

- □ American Indian/ Alaska Native
- □ Asian
- □ Native Hawaiian or Other Pacific Islander
- □ Black or African American
- □ White
- □ Unknown
- □ Subject declined to provide

Ethnicity (select one):

- □ Hispanic or Latino
- □ Not Hispanic or Latino
- □ Unknown
- □ Subject declined to provide

RAP#: _____

Complete this form to the best of your ability. If any of the following information is not be available in the patient record, simply write-in "Unknown." If the patient was not on therapy at time of death or had no previous therapies, indicate "No Current Therapy" or "No Previous Therapy" in the appropriate sections.

Worksheet B (page 2 of 2)

Systemic treatments (include chemoradiation related to current diagnosis. Include radiotherapy related to current diagnosis only if administered to area of collected tissue). If unable to list specific agent names, list by agent class, mechanism of action or indicate 'Clinical Trial', as appropriate.

Therapy	Date Therapy Started (MM/YYY or YYYY)	Best Response* (SD/CR/PR/ PD, Non-Evaluable, Not Assessed)	Treatment Duration (months or cycles)	Prior or Current** Treatment	Comments
1				□ Prior □ Current	
2				□ Prior □ Current	
3				□ Prior □ Current	
4				□ Prior □ Current	
5				□ Prior □ Current	
6				□ Prior □ Current	
7				□ Prior □ Current	

* Best Response as assessed by RECIST; Indicate "N/A" if patient not assessed or it was not documented. If Best Response is assessed by other criteria, please indicate criteria used in Comments.

**Current Treatment includes any treatment received within 2 weeks prior to patient death.

APPENDIX 3: 81-SLOT BOX LAYOUT

A1	A2	A3	A4	A5	A6	A7	A8	A9
B1	B2	B3	B4	B5	B6	B7	B8	B9
C1	C2	C3	C4	C5	C6	C7	C8	C9
D1	D2	D3	D4	D5	D6	D7	D8	D9
E1	E2	E3	E4	E5	E6	E7	E8	E9
F1	F2	F3	F4	F5	F6	F7	F8	F9
G1	G2	G3	G4	G5	G6	G7	G8	G9
H1	H2	H3	H4	H5	H6	H7	H8	H9
I1	I2	I3	I4	I5	I6	I7	I8	I9