



NLST- ACRIN REMNANT TISSUE MANUAL OF PROCEDURES SUMMARY OF CHANGES



Version: August 07, 2009

Reason:

The ACRIN NLST Remnant Tissue MOP was revised to reflect the NLST Site process to identify, request and procure all resected tissues for patients that are part of the NLST study for the Tissue Micro Array bank. The process for creating TMA's at UCLA Tissue Micro Array Core Laboratory was removed from the RT-MOP as the purpose of the RT-MOP is to serve as an instructional guide for the site RA in the collection of paraffin tissue blocks and not focus on creating the TMAs at UCLA.

Cover Page

Title change -

- From: ACRIN NLST REMNANT TISSUE MANUAL OF PROCEDURES, title now reads:

NLST-ACRIN REMNANT TISSUE MANUAL OF PROCEDURES

Logo change -

- ACRIN Logo formerly known as trademark [™] to current Registered [®]

Page numbering change -

- Numbering of Coversheet as page 1 removed.

Table of Contents

- Titles, page numbers and renumbering of sections were adjusted to match the current version.

Chapter 1, Page 4 – Introduction

Paragraph 1 -

- Paragraph one was reconfigured from: The National Lung Screening Trial is a multi-center, randomized, controlled trial in which low-dose spiral computed tomography (CT) will be compared with chest X-ray (CXR) to determine which screening test will result in fewer lung cancer deaths among individuals at high risk of lung cancer. The ACRIN-NLST has become a key national resource for lung cancer etiology and early molecular marker research because of the biospecimen collection that has been undertaken in roughly 10,000 of the cohorts in both the low dose CT and CXR screening arms; paragraph now reads:

The National Lung Screening Trial is a multi-center, randomized, controlled trial in which low-dose helical chest computed tomography (CT) will be compared with chest X-ray (CXR) to determine which screening test will result in fewer lung cancer deaths among individuals at high risk of lung cancer. The NLST-ACRIN specimen biorepository has collected specimens from roughly 10,000 participants in both the CT and CXR arms, and will be a key national resource for determining lung cancer etiology and the molecular markers of early lung cancer.

Paragraph 2 –

- Deleted “remnant” after “of”; deleted “ACRIN” after “the” in the first sentence; deleted “patients” after “all” and replaced it with “participants”; inserted new sentence “The NLST-LSS will similarly be collecting resected tissues from lung cancer participants” after the first sentence; changed “The” to “This”; deleted “of these tissues” after “collection” in the third sentence; deleted “status” and replaced it with “signatures” in the last sentence; paragraph now reads:

This collection provides increasing opportunities for the study of questions relevant to tumor molecular biology, and specifically, the contributions of genetic and proteomic factors that initiate or

sustain cancer and metastases, and for relating blood, urine, or sputum-based markers to the molecular signatures of the primary tumors.

Chapter 1, Page 4 – Section 1.1 Study Objectives

Sentence 1 -

- Deleted “ACRIN”; deleted “are” and replaced with “is”. Sentence now reads:

The main objective of the NLST remnant tissue collection is to answer critical questions about cancer etiology. This collection is unique because:

Bullet Points -

- First three bullet points were changed to sequential numbers.
- Bullet point two: deleted “of the” after Many; deleted “sequentially” after “obtained”; deleted “time” after “at the”; added “visits, potentially” after “screening”; added a comma after “cancer”. Bullet point 2 now reads:

Many participants will have other available biospecimens obtained at the screening visits, potentially prior to the diagnosis of lung cancer, on which ancillary and complementary studies can be performed.

Sentence 2 -

- Deleted “ACRIN”; pluralized effort. Sentence now reads:

The specific objectives of the NLST specimen collection efforts are:

Numbered Bullet Points –

- Bullet point one: deleted “To” at start of sentence and capitalize collect. Bullet Point 1 now reads:

Collect pathology samples to provide opportunities for research relating risk factors to histological and molecular-pathologic sub-types of lung cancer.

- Bullet point two: deleted “To” at start of sentence and capitalize study; deleted “pathological and clinical” after “different”.

Study tissues of different stage to enhance the understanding of markers for lung cancer etiology and early detection.

- Bullet point three: deleted “To” at start of sentence and capitalize study; deleted “related” after “tissue” and replaced it with “characteristics relative”. Bullet Point 3 now reads:

Study tissue characteristics relative to epidemiological observations.

- Bullet point four: deleted “To” at start of sentence and capitalize study; add “of” after Study. Bullet Point 4 now reads:

Study the influence of environmental exposures, hereditary factors, and other types of exposure on molecular lesions

Chapter 1, Page 5 – Section 1.2 Scientific Background

Paragraph 1 -

- Deleted first 2 sentences - On the 3rd sentence deleted comma after existing; deleted “time of” before screening and added “visits” after screening; Paragraph 1 now reads

The creation of an archive of resected lung cancers will richly augment the existing serial biosamples obtained on participants at the screening visits and will promote identification of the most significant molecular phenomena associated with lung cancer.

Paragraph 3 -

- Deleted “ACRIN” before NLST; deleted vertical line between clinical and pathological stage. Paragraph 3 now reads:

The major prerequisite for TMA construction is a large collection of well characterized tissues—as is the case with the NLST participants, in whom detailed demographic data, health information, smoking histories and exposures to other known carcinogens have been collected. All lung cancers will have been characterized by location, histology and grade, and clinical pathological stage at diagnosis. All treatments will be recorded as well as disease free interval and locations and kinds of tumor recurrence.

Paragraph 4 –

- Added colon at end of sentence.

Bullet Point 4 –

- Deleted semi colon and changed to comma after small.

Chapter 1, Page 6 – Section 1.3 Tissue Types and Methods for Selection for Sampling**Title –**

- Deleted “ for Selection for Sampling” after Methods, title now reads:

Tissue Types and Methods of Sampling Selection

Sentence 1 -

- Deleted “The tissue types that will be collected are the following:” - sentence now reads:

Representative tissue cores from resected surgical specimens will be obtained based on annotation of targets (regions of interest) on a representative slide of the tissue block by a lung pathologist. The following tissue types are of interest:

Bullet Point 1 -

- Deleted plural “s” from area; deleted “the” before tumor; deleted “including regions of highest grade, lowest grade, and sites of pre-malignancy, based on mapping by a pathologist on representative slides from the tissue block” - bullet point one now reads:

Primary lung cancer. Multiple cores will be obtained from each representative area of tumor histology and grade to capture the molecular heterogeneity within these regions.

Bullet Point 2 –

- Deleted “adjacent to the lung cancer will also be sampled, based on mapping by a pathologist on representative slides from the tissue block” - bullet point two now reads:

Adjacent normal (or non-tumor) lung tissue. Cores will be obtained from representative areas of non-malignant tissue, with the aims of sampling: normal adjacent lung parenchyma, non-tumorous proximal bronchus, non-tumor distal bronchiolar tissue, and pre-malignant lesions (such as dysplasia, atypical adenomatous hyperplasia).

Bullet Point 3 -

- Deleted “Resected regional malignant lymph nodes. It is estimated that up to 25% of all lung cancer cases undergoing resection may have involved intrathoracic lymph nodes resected as well. Every effort should be made to collect these resected, involved lymph nodes for purposes of creation of the TMAs. The molecular signatures of regional nodes may differ from that of the primary tumors and the collection of these specimens could yield important information about the spread of lung cancer.” – bullet point three now reads:

Malignant lymph nodes. Metastatic lymph nodes that have been resected should be included in the request for tissue blocks, since the molecular signatures of metastases may differ from the primary tumor. Multiple cores will be obtained from these individual lymph nodes.

Bullet Point 4 –

- Inserted bullet point four

Normal lymph nodes. Cores should be taken from uninvolved lymph nodes *if* cores taken from involved nodes (to capture germ line DNA).

Bullet Point 5 –

- Deleted “of metastatic disease” after resected sites; deleted “an extremely” before small, deleted entire phrase “(the vast majority of metastases are determined by clinical means or by percutaneous needle core or aspiration, which are not amenable to TMA processing)”; deleted “However,” from beginning of next sentence; deleted “in which there has been tissue resection; deleted “and obtained for TMA creation at end of last sentence.– bullet point five now reads:

Resected metastases will be available in a small percentage of participants. Any surgically resected metastatic lesions should be requested. Multiple cores will be obtained from these tumor metastases.

Paragraph 1 -

- Paragraph one was deleted

Numbered Bullet Points -

- Numbered bullet points 1-3 were deleted

Paragraph 2 –

- Deleted “reviewed”, “The pathologist will mark the slide with a wax (or other) marker to show the areas in which core samples should be obtained. Digital high-resolution scans of the annotated H&E”, “showing the regions for core sampling”, “obtained and”, “included in the archive”, paragraph now reads:

An H&E slide created from each paraffin block of resected tissue will be digitized on the Aperio system for annotation by a lung pathologist. The slide digitization system allows the pathologist to review the slide at low and high (20X to 40X) powers. Color-coded targets (regions of interest) will be digitally annotated on the slide, from which a thin film template can be created to guide the coring process. The digitized slides will be permanently archived. The anticipated duration of the tissue collection and building of the TMAs is 18 months.

Chapter 1, Page 7 – Section 1.4 Determining the Number of Cores – was deleted in its entirety**Chapter 2, Page 8 – Section 2.1 Selection Criteria****Sentence 1-**

- Add “all participants in NLST” at end of sentence. – sentence now reads:

The selection criteria for remnant tissue collection will include all participants in NLST:

Bullet points 1 and 2-

- Were changed from All participants in the ACRIN-NLST in whom the diagnosis of a primary lung cancer has been established and Lung cancer participants in whom there is remnant tissue available from a surgical resection of some form: New bullet points one and two now read:

Who have a documented primary lung cancer *and*
Whose primary lung cancer or lung cancer metastases have been resected.
Signed a Remnant Tissue Consent Form (See section 2.4 – “Informed Consent”)

Paragraph 1 -

- Deleted sentences two and three and replaced with new sentence- paragraph now reads:

The ACRIN BDMC (Biostatistics Data Management Center) will provide a list of all confirmed lung cancers in a Remnant Tissue Selection List to each individual NLST site. For each confirmed lung cancer case, the site should collect the following documentation:

Paragraph 2 -

- Deleted sentence and table with selection criteria: and replaced with 2 bullet points and sentence; it now reads:

Original pathology report. Procure ALL pathology reports, as there may be multiple reports if there were separate surgeries (e.g., initial mediastinoscopy for lymph node resection and thoracotomy for lung resection),

Operative report(s) corresponding to the pathology report.

It is possible that an NLST site will become aware of additional lung cancer cases that have not yet been recorded in the ACRIN database. In this case, consult with ACRIN Data Management and the lead administrator of the Resected Tissue Project before acting on these cases.

Chapter 2, Page 9 – Section 2.2 Confidentiality**Re-arrangement of section –**

- Section 2.2 Confidentiality is now section 2.3

Chapter 2, Page 9 – Section 2.3 Informed Consent**Re-arrangement of Section –**

- Section 2.3 Informed Consent is now section 2.4

Paragraph 3 –

- Inserted “for remnant tissue collection” after “consent” in the first sentence, sentence now reads:

If there are participants with potential remnant tissues who have *not* previously been approached to provided written informed consent for remnant tissue collection the site may approach their IRB to consider a waiver of consent under Title 21 CFR Part 56 section 56.109.

Chapter 2, Page 10 – Section 2.4 Contacting Pathology Departments/Laboratories**Rearrangement of sections -**

- Section was moved from section 2.4 to 2.2

Paragraph 1 –

- Deleted “original” after “The”; deleted “on participants with” after “Report” and replaced it with “documentation” in the first sentence; paragraph now reads:

The Pathology Report documenting the diagnosis of primary lung cancer will identify the source pathology laboratory. The site should contact the pathology laboratory to establish a relationship and to procure contact information, including: the name, phone number, e-mail address, fax number, and shipping address of a contact person at the laboratory for specimen collection.

Paragraph 2 –

- Paragraph two was reconfigured from: The Pathology Laboratories from which specimens are collected may have specific loan policy requirements regarding HIPAA authorizations, such as the use of a specific proprietary authorization form. It is strongly recommended that each laboratory be contacted prior to requesting participant authorization for specimen collection; paragraph now reads:

The lending pathology laboratories may require specific documentation before the release of surgical tissues, including:

- Signed informed consent
- Signed Authorization to Release Surgical Material
- HIPAA authorization (or equivalent form prior to HIPAA enactment)
- Their own institutional forms

- Any combination of the above
- No documentation

It is strongly recommended that sites contact the laboratories to determine exactly what they will require prior to making specific requests for tissues.

Paragraph 3 –

- Inserted “also” after “should”; deleted “comma” after “specimens”, deleted “that will be” after “period” in sentence one; deleted “insure” after “to” and replaced it with “ensure” in sentence two; paragraph now reads:

The site should also determine the pathology laboratory’s policies on specimen loans, costs for requesting specimens, whether the lab is willing to grant permanent retention of the specimens or, if not, the maximum loan period permitted. The site should inform the lab of the available reimbursement rate for processing and providing tissues and the minimum loan period of three (3) months required to ensure adequate time for shipping and processing. Payment for requests, if required by the pathology laboratory, should be managed by the site in agreement with the pathology laboratory

Chapter 2, Page 10 – Section 2.5 Participant Authorization and HIPAA

Title –

- Inserted “to Release Surgical Material” after Authorization, title now reads:

Participant Authorization to Release Surgical Material and HIPAA

Paragraph 1 –

- Deleted “The majority of” at the beginning of the sentence; inserted “at the time of randomization in accordance with their local IRB / institutional guidelines. Lending pathology laboratories may or may not accept this authorization when lending remnant tissue” to the end of the sentence – paragraph now reads:

ACRIN-NLST sites have administered a HIPAA authorization or notification (ACRIN template or local-IRB approved HIPAA release) to NLST participants at the time of randomization in accordance with their local IRB / institutional guidelines. Lending pathology laboratories may or may not accept this authorization when lending remnant tissue.

Paragraph 2 –

- Paragraph 2 was reconfigured from: However, participants who have not signed HIPAA authorization will need to do so prior to requesting remnant tissue, if required by the Pathology Laboratory. Participants selected for remnant tissue collection who have not signed an authorization should be mailed the following materials prior to making a request for remnant tissue. Please refer to your local IRB for guidance regarding requirements; paragraph(s) now reads:

Some lending pathology laboratories may request additional authorization from the participant in order to release remnant tissue. They may have a specific Authorization Form that they will send to you or, if permitted by the lending pathology laboratory, you may use the template provided marked as Appendix II “Authorization to Release Surgical Material Template”.

Participants selected for remnant tissue collection, where the lending pathology laboratory requires additional authorization, should mail the necessary materials to the participant prior to making a request for remnant tissue from the lending pathology laboratory. Please refer to your local IRB for further guidance regarding any additional requirements.

Sentence 1 -

- Inserted new sentence after last paragraph:

If applicable, mail the following to the participant and complete the following steps:

Numbered Bullet Points –

- Bullet point two – was reconfigured from: An Authorization Form, which requests participant permission for the named pathology laboratory to release pathology specimens and related health information and personal identifiers to the ACRIN-NLST (Appendix II) (if required by the pathology laboratory, the proprietary authorization form from the lab should be mailed instead); bullet point two now reads:

Authorization to Release Surgical Material (**Appendix II**), which requests participant permission for the named pathology laboratory to release pathology specimens and related health information and personal identifiers to the ACRIN-NLST or the proprietary authorization form from the lending pathology laboratory.

- Bullet point three – inserted “to Release Surgical Material or proprietary authorization form from the lending pathology laboratory” after Authorization and deleted “form” after “authorization” bullet point now reads:

A second duplicate Authorization to Release Surgical Material or proprietary authorization form from the lending pathology laboratory to be retained by the participant for their personal records.

- Bullet point five – was added:

Review signed authorization, store it in the participant’s ACRIN file, and document receipt in the remnant tissue tracking file with date of signature.

- Bullet point six –was added:

Send all necessary authorizations to the lending pathology laboratory for release of the remnant tissue.

Paragraph 3 –

- Inserted “to Release Surgical Material” after Authorization and deleted “form” in the last sentence; inserted “where necessary” at the end of the sentence - paragraph now reads:

ACRIN-NLST sites must abide by regulations established by their local IRB when dealing with cases in which the participant is deceased. These cases will need to be reviewed individually to establish the possibility of obtaining Authorization to Release Surgical Material for Remnant Tissue collection where necessary.

Paragraph 4 –

- Inserted “to Release Surgical Material” after Authorization and deleted “form” in two places; paragraph now reads:

If a participant is unable to sign and date the Authorization to Release Surgical Material because of illness or other problems, the Authorization to Release Surgical Material can be sent to the participant’s authorized representative or proxy for signature according to local IRB rules.

Paragraph 5 –

- Paragraph 5 was reconfigured from: The site will review each signed authorization, store it in the participant’s ACRIN file, and document receipt in the remnant tissue tracking file with date of signature. Participants for whom a signed Authorization Form is obtained will be included in the pathology specimen process; paragraph now reads:

Only Participants for whom a signed Authorization to Release Surgical Material is required and obtained will be included in the remnant tissue process.

Chapter 3, Page 12 – Requesting Specimens from Pathology Labs**Title –**

- Inserted “Lending” after from, title now reads:

Requesting Specimens from Lending Pathology Labs

Chapter 3, Page 12 – Section 3. 1 Request Packets**Paragraph 1 -**

- Paragraph one was reconfigured from: Once consent and authorization are obtained, if required, the NLST site coordinator will assemble a request packet for each pathology laboratory. Each request may include specimens from multiple participants. Each request packet will include the following items (which are also explained in detail in the following sections); new paragraph now reads:

Once participant consent and authorization is established, the NLST site coordinator should assemble a request packet for each pathology laboratory. Specimens from multiple participants may be requested from a single pathology laboratory in one packet. Each request packet will include the following items (which are included as appendices to this MOP and are explained in detail in the following sections):

Bullet Points -

- Bullet points were numbered.
- Bullet point one went from: Request cover letter signed by the NLST Site Principal Investigator (PI) or designee, new bullet point 1 now reads:

Pathology Request Cover Letter (Appendix IV) signed by the NLST Site Principal Investigator (PI) or designee.

- Bullet point two went from: Pathology Request Form (can be downloaded from the ACRIN Web site) to show requested specimens and used by the pathology laboratory to document release of the specimens or the reason specimens were not provided; new bullet point 2 now reads:

Pathology Specimen Collection—Request Form(s) (Appendix V) that specifies the requested histologies. This will be used by the pathology laboratory to document release of the specimens or the reasons for which specimens were not provided.

- Bullet point three went from: Copies of the participant’s written consent to remnant tissue collection, site-specific HIPAA authorization form (or Authorization Form if site-specific HIPAA release was not obtained), new bullet point 3 now reads:

Copies of the participant(s) **Authorization to Release Surgical Material (Appendix II)** or comparable authorization according to the pathology labs policies.

- Bullet point four: Pathology report is in bold and a period was added to the end, new bullet point 4 now reads:

Pathology report for all participants included in each pathology laboratory request.

- New sentence added after final bullet point:

These items are included as appendices to this MOP and are explained in detail in the following sections.

Chapter 3, Page 12 – Section 3.1.1 – Pathology Request Cover Letter**Paragraph 1 –**

- Paragraph one was changed from: The Pathology Request Cover Letter was designed to simplify the request process and to facilitate rapid retrieval of specimens. It is formatted and styled as a routine request from “ACRIN-NLST Specimen Collection.” The request briefly explains the purpose of the request, how loaned specimens will be processed and returned to the originating pathology laboratory, and asks that specimens be mailed to the ACRIN-NLST site in the enclosed pre-addressed, postage-paid shipping containers. A Pathology Request Cover Letter is included as Appendix IV; paragraph now reads:

The Pathology Request Cover Letter (**Appendix IV**) briefly explains the purpose of the request, how loaned specimens will be processed and returned to the originating pathology laboratory, and asks that specimens be mailed to the NLST site in the pre-addressed, postage-paid shipping containers.

Chapter 3, Page 12 – Section 3.1.2 – Pathology Request Form

Title–

- Inserted Specimen Collection after Pathology, title now reads:

Pathology Specimen Collection—Request Form

Paragraph 1 –

- Paragraph one was reconfigured from: The Pathology Request Form is enclosed with the Cover Letter and will be used by pathology departments to indicate authorization for release of specimens, or to indicate problems associated with fulfilling the request. The form will be returned by pathology laboratories to NLST sites along with specimens, or will be returned alone to indicate barriers or reasons for refusal to provide tissues. A template Pathology Request Form is included as Appendix V ; paragraph now reads:

The Pathology Specimen Collection—Request Form (**Appendix V**) will be used by lending pathology departments to indicate the release of specific specimen types and their unique paraffin block identification, or to indicate problems associated with fulfilling the request. The NLST Site coordinator will be responsible for filling out the pertinent participant information at the top of the form and the date of procedure for each block that is being requested before sending the form to the lending pathology laboratory. The form should be returned by the lending pathology laboratory to NLST sites along with specimen blocks, or returned alone to indicate barriers or reasons for refusal to provide tissues.

Paragraph 2 –

- Paragraph two was reconfigured from: Note that multiple Pathology Request Forms may be included in a request packet if specimens from multiple participants are being requested at one time. Also, a pathology laboratory may receive additional request packets through the year as the NLST site continues to identify participants with new lung cancer diagnoses; paragraph now reads:

Note that a Pathology Specimen Collection—Request Form should be provided for *each* individual participant. Multiple forms may be included in a request packet if specimens from multiple participants are requested at one time. Also, a pathology laboratory may receive additional request packets through the year as the NLST site continues to identify participants with new lung cancer diagnoses. If a pathology laboratory does not return a filled out Pathology Specimen Collection Form, the site RA is responsible for filling out a “Note to File”. Please document if you received specimen(s) or not and the reason for not getting a returned form. A copy of the Note to File” should be retained in the participants chart.

Chapter 3, Page 12 – Section 3.1.3 – Remnant Tissue Consent

Title –

- Deleted entire title. title now reads:

Authorization to Release Surgical Material

Paragraph 1 –

- Paragraph one was reconfigured from: A copy of the remnant tissue consent or IRB waiver of consent will be attached to the Cover Letter, unless specifically not required by a pathology laboratory. The original remnant tissue consent or IRB waiver of consent should be stored in the participant's ACRIN-NLST file; paragraph now reads:

The signed Authorization to Release Surgical Material (**Appendix II**) should be attached to the Pathology Request Cover Letter, if specifically required by the pathology laboratory.

Chapter 3, Page 13 – Section 3.1.4 – HIPAA Authorization or Authorization Form

Paragraph 1 –

- Paragraph one was reconfigured from: A copy of the HIPAA Authorization or the Authorization Form (included as a template for execution by participants that have not signed a HIPAA authorization) will be attached to the Cover Letter, unless specifically not required by a pathology laboratory. The original HIPAA Authorization or the Authorization Form should be stored in the participant's ACRIN-NLST file; paragraph now reads:

A copy of the site's HIPAA Authorization should be attached to the Pathology Request Cover Letter, if specifically required by the pathology laboratory. Keep a copy of the site's HIPAA Authorization and/or the original Authorization to Release Surgical Material in the participant's NLST site file.

Chapter 3, Page 13 – Section 3.1.5 – Pathology Report

Paragraph 1 –

- Paragraph was reconfigured from: A copy of the pathology report that confirms and describes the primary cancer of interest from which specimen samples will be collected will be attached to the request letter. The pathology report should be stored in the participant's ACRIN-NLST file ; paragraph now reads:

A copy of the pathology report that describes the tissue(s) of interest should be attached to the Pathology Specimen Collection—Request Form. Keep the original pathology report in the participant's NLST site file.

Chapter 3, Page 13 – Section 3.1.6 – Shipping Materials

Title –

- Inserted “for Pathology Laboratories” after Material, title now reads:

Shipping Materials for Lending Pathology Laboratories

Paragraph 1 –

- Paragraph 1 was reconfigured from: NLST sites should obtain and include the appropriate shipping materials in the request packet to facilitate shipment of specimens from pathology laboratories. The shipping materials to be included in the request packet are; paragraph now reads:

NLST sites should include all appropriate shipping materials in the request packet to facilitate shipment of specimens from pathology laboratories. If a site should need shipping material or shipping labels, send a request by e-mail to the Remnant Tissue coordinator at rmedina@acr-arrs.org. Please put “request for shipping material in the subject line. The shipping materials to be included in the request packet are:

Sentence 1 -

- Deleted entire sentence before list of materials.

Deleted List of shipping material –

- Deleted complete list of shipping list:

Storage boxes for blocks (Bell Metal Specialty, dimensions 5” x 5” x 2”).
Multi-purpose insulated bio-shippers (Polyfoam Packers part, dimensions 11 5/8” x 9 7/8” x 7”).
M3 carton sealing tape.
Styrofoam peanuts and bubble wrap.

Cold Packs (to use in shipments with <70°degrees weather temperature) - inserted new list of shipping materials:

Storage boxes for blocks (dimensions 5" x 5" x 2")
 Multi-purpose insulated bio-shippers (dimensions 14" x 10" x 14")
 Biohazard bags
 M3 carton sealing tape
 Styrofoam peanuts and/or bubble wrap
 Cold Packs (to use for all shipments in climates with >70°F temperature)
 Shipping labels to indicate: "Fragile-Handle With Care" and Diagnostic Specimens – Not restricted, Packed in Compliance wit IATA Packing Instructions 650"

Chapter 3, Page 13- Section 3.2 Non-Response Follow-Up for Specimen Request

Title -

- Inserted "Pathology Laboratory" before Non-response, title now reads:

Pathology Laboratory Non-Response Follow-Up for Specimen Request

Paragraph 1 –

- Deleted "ask" after and, replaced it with "inquire"; deleted "they need" after if, replaced it with clarification and added is needed at the end of the sentence; inserted a comma after response; deleted "or lend" after release; inserted Pathology Laboratory before Non-response; put in bold Appendix VI; paragraph now reads:

In the event that requested specimens are not received within three weeks of submitting the request, the NLST site coordinator will contact the local pathology department/laboratory and inquire if the laboratory received the request packet and if clarification or any further assistance is needed. If after two follow-up attempts, there is still no response, or if the pathology laboratory refuses to release any materials, the NLST site PI or designee will pursue negotiations with the pathology laboratory staff to gain access to these materials. The result of each follow-up effort will be documented on a hard copy Pathology Laboratory Non-Response Log: Request for Specimen(s) (**Appendix VI**). Non-response Logs should be stored in the participant's chart.

Chapter 4, Page 14- Collecting Specimens at Study Centers

Paragraph 1 -

- Inserted "lending" before pathology; deleted "is willing" and replaced it with "agrees"; inserted "Specimen Collection" after Pathology; deleted "bubble wrap lined mailer" and replaced it with "shipping container". deleted "they will" after "tissue" and replaced it with " it should"; inserted Specimen Collection after Pathology; paragraph now reads:

The lending pathology laboratory will receive the request packet and review the letter and accompanying form. If the pathology laboratory is willing to release the requested tissue, it will return the Pathology Request Form and the tissue to the NLST site in a pre-addressed, postage paid, shipping container. If the pathology laboratory is not willing to release the tissue, they should indicate the reason for refusal on the Pathology Request Form and fax or mail it back to the NLST site.

Chapter 4, Page 14 – Section 4.1 Receipting Specimens from Lending Pathology Laboratories

Title –

- Deleted "Receipting" and replaced it with "Receiving" and Inserted "Lending" before Pathology; title now reads:

Receiving Specimens from Lending Pathology Laboratories

Paragraph 1 –

- Deleted first word “receiving” and replaced it with “receiving”; inserted “Pathology Specimen Collection” before “Form” (capitalized Request Form); deleted “ing” from “receiving” and inserted “of” before “specimens”; paragraph now reads:

Receiving specimen materials at the NLST site involves review of both the completed Pathology Specimen Collection—Request Form and the specimens. The NLST site will implement the following procedures for receipt of specimens:

Point number 1 –

- Point one was reconfigured from: Check to see that a completed Request Form was returned. If the form is missing or incomplete, correspond with the pathology laboratory to obtain a completed form; point number 1 now reads:

Verify that a completed Request Form was returned. If the form is missing or incomplete, request that a completed form be provided. Note: if a request form is not returned, fill out a “Note to File” and store it in the participants chart.

Point number 2 –

- Inserted (s) after tissues; deleted “fill out” after “and” and replaced it with “complete”; put in bold Appendix VII; point number 2 now reads:

Verify that each specimen corresponds to the tissue(s) requested. If there are any discrepancies, contact the pathology laboratory and complete a Discrepancy Notification Form (**Appendix VII**).

Point number 3 –

- Point three was reconfigured from: Check each specimen for damage. If a block is damaged, contact the pathology department to report the damage and to request a replacement block if needed and available. Damaged blocks should be returned to the pathology lab. If you are uncertain about the viability of a block, forward the specimen to UCLA and they will determine if the block can be processed; point number 3 now reads:

Inspect each specimen for damage. If a block is damaged, report the damage to the pathology department and request a replacement block if available. Extremely damaged blocks (i.e. melted, severely punctured, cut in half, severely smashed) should be returned to the pathology lab. If you are uncertain about the viability of a block, forward the specimen to UCLA Tissue Microarray (TMA) Core Facility and they will determine if the block can be processed.

Point number 4 –

- Point four was reconfigured from: The NLST coordinator labels each specimen with the ACRIN-NLST ID label and attaches identical labels to the participant’s pathology report. The NLST coordinator will ensure that any protected health information is de-identified prior to sending the specimens to the UCLA Tissue Array Core Facility; point four now reads:

The site coordinator should label each block with the NLST ID label supplied by ACRIN HQ and attach identical labels to the RT-Form in the row that corresponds to that particular block. The site coordinator should insure that any protected health information is de-identified prior to sending the specimens to the UCLA TMA Core Facility.

Point number 5 –

- Deleted “ACRIN” after “The”; deleted last sentence “problem codes, such as for damage, are also entered during receipt”; point number 5 now reads:

The NLST ID for each specimen is then entered into the NLST Remnant Tissue Tracking excel file.

Chapter 4, Page 14 - Section 4.2 Labeling and Storing Specimens from Pathology Labs

Title –

- Inserted “Lending” before Pathology – title now reads:

Labeling and Storing Specimens from Lending Pathology Labs

Paragraph 2–

- Deleted “write urgent and Attn: Rosa Medina at the top of the form.” after “specimens”; deleted “(6654 Data Forms link)” after web site and inserted “(Under Administration Menu, click on Administrative Resources, it is located under Documents); paragraph 2 now reads:

ACRIN will send pre-printed labels for all cases identified on the Remnant Tissue Case Selection List. If an NLST site identifies additional cases determined to be eligible for remnant tissue collection, the site coordinator should submit a ‘Request for Case Specific Labels’ form to ACRIN Headquarters. Indicate on the form that the labels will be used for NLST remnant tissue specimens. The ‘Request for Case Specific Labels’ form can be downloaded from the ACRIN Web site: <http://www.acrin.org> (Under Administration Menu, click on Administrative Resources, it is located under Documents).

Paragraph 3–

- Deleted “ACRIN” before “NLST”; inserted “uniquely” after “will”; deleted “belonging to a specimen” after “block” and replaced it with “of a participant”; deleted “sample” after “The”; paragraph now reads:

The NLST ID number printed on each label will uniquely identify each tissue block of a participant. The ID numbers have the following format: (NNNN-NNNNN-NN)

NNNN: four-digit ACRIN site number

NNNNN: five-digit case number (case numbers range from 2 digits up to 5 digits)

NN: two-digit sequence number (starting at 01 and ending at 10)

Paragraph 4–

- Inserted “ACRIN site number and” after “same”; deleted “and” after “number” and inserted “followed by”; inserted ‘and to prepare blocks for shipping.’ after “blocks”; paragraph number 4 now reads:

If multiple blocks are obtained for a single specimen, each will have the same ACRIN site number and case number followed by an incremental sequence number. Follow the instructions below to label the tissue blocks and prepare blocks for shipping.

Numbered Bullet Points –

- Bullet point one – deleted first word “Peel” and capitalized attach; deleted “ACRIN” before “NLST”; point number 1 reads:

Attach the NLST ID label to the side edge of the paraffin block cassette.

- Bullet point two – deleted “pathology report” and replaced it with “row on the RT-Form”, point number 2 now reads:

Attach the duplicate label to the corresponding row on the RT-Form.

- Bullet point three – inserted “personal” after “cover”, bullet number 3 now reads:

Use blank labels to cover personal identifiers elsewhere on the cassette.

- Bullet point four - was added

Place a copy of the pathology report in the biohazard bag form slot.

- Bullet point five (was 4); deleted “a small (2” x 3”) zip-lock plastic bag” and replaced it with “the zip lock portion of the biohazard bag; point number 5 now reads:

Place the cassette in the zip lock portion of the biohazard bag.

- Bullet point six (was 5); deleted 5 ½" x 5 ½" x 2 and inserted the correct box dimensions: 5" x 5" x 2" ; deleted (or 3"); inserted "(Note: a box may fit 1-2 bagged specimens)" at the end of the sentence - point number 6 now reads:

Place each bag in a 5" x 5" x 2" storage box. (Note: a box may fit 1-2 bagged specimens)

- Bullet point seven (was 6); deleted Tissue Array after UCLA and replaced it with "TMA"; added "see below" at the end; bullet point 7 now reads:

Store in ambient temperature with cool ventilation until the next scheduled shipping date to UCLA TMA Core Facility (see below).

Chapter 5 – page 16 Shipping Specimens to UCLA Tissue Micro Array Core (TMA) Facility

Title –

- Inserted "Maintaining and" in front of "Shipping", title now reads:

Maintaining and Shipping Specimens to UCLA TMA Core Facility

Paragraph 1 –

- Deleted "collected for this effort" after "specimens"; ended sentence with a period after "blocks" and deleted " by the pathology laboratories"; paragraph now reads:

The pathology specimens are preserved in paraffin blocks. Prior to shipment, they should be stored in a cool, dark container and be protected from excessive light and temperature to prevent deterioration of the wax and embedded tissue.

Paragraph 2 –

- Paragraph two was reconfigured from: Weather problems, holiday schedules, and end-of-week shipping may cause specimen shipment delays, which the study coordinator should work to avoid. Shipping methods should take seasonal temperatures into account, and include use of extra insulated packaging, overnight delivery, and a cooling agent (cold packs), as needed. The standard shipping package for a specimen will include a zipper bag inside a storage box, inside a foam-insulated shipping box (bio-shipper); paragraph now reads:

Shipping methods should take seasonal temperatures into account, and include the use of extra insulated packaging and a cooling agent (cold packs), as needed. The standard shipping package for a specimen should include the biohazard bag, placed in a storage box, which is then placed inside a foam-insulated shipping box (bio-shipper).

Paragraph 3 –

- Paragraph three was reconfigured from: All non-problematic specimens obtained from pathology departments will be shipped every two weeks to the UCLA Tissue Array Core Facility via overnight courier. Specimens will be shipped with the RT Form (Appendix VIII) and appropriate pathology report(s). A copy of the RT Form should be faxed to ACRIN DM and filed in the NLST participant chart. Shipment days are limited to Monday through Wednesday to avoid specimen receipt on Fridays, weekends, or holidays.); paragraph now reads:

Sites have pre-assigned shipment days (see below, Section 5.4). Shipment days are limited to Monday, Tuesday and Wednesday to avoid specimen receipt on Fridays, weekends, or holidays.

Paragraph 4 –

- Paragraph four was reconfigured from: On the day of shipment, the study coordinator will notify the UCLA Tissue Array Core Facility via e-mail of the upcoming shipment with estimated date of arrival and shipment tracking information. Upon receipt of the specimens, UCLA will reconcile the materials and notify the NLST site regarding missing or damaged specimens. The UCLA Tissue Array Core Facility will contact the appropriate study coordinator to resolve any problems.; paragraph now reads:

Specimens should be shipped on a weekly basis by overnight FedEx to the UCLA TMA Core Facility. The original RT Form (ACRIN website | Protocol 6654 Forms) and copies of the corresponding pathology report(s) should be included with the specimens. A copy of the pathology report should be faxed to ACRIN DM and the original retained in the NLST participant chart. On the day of shipment, the study coordinator will notify the UCLA TMA Core Facility via e-mail (stze@mednet.ucla.edu) or Fax (310-267-2940) of the upcoming shipment. Include the estimated date of arrival and the FedEx tracking number.

New Entry after paragraph 4 -

- Inserted: **NOTE:** The subject line of the email/FAX should include the following so that the UCLA TMA Core Facility staff can distinguish between blocks sent by ACRIN versus LSS sites:

ACRIN Specimen Block Shipment--Site [Name or ID].

Upon receipt of specimens, the UCLA TMA Core Facility will reconcile the materials and notify the NLST study coordinator of missing specimens, damaged specimens, or any concerns to be addressed.

Chapter 5 – page 16 Section 5.1 Shipping Materials

Title -

- Inserted “and Process” after “Materials”, title now reads:

Shipping Materials and Process

Sentence 1 –

- Deleted “ACRIN” after “for”; sentence now reads:

The appropriate shipping materials for NLST specimens are the following

Numbered bullet points -

- Numbered bullet points were changed to bullet points
- Deleted list of materials:
Storage boxes for blocks (Bell Metal Specialty, dimensions 5” x 5” x 2”).
Multi-purpose insulated bio-shippers (Polyfoam Packers part, dimensions 11 5/8” x 9 7/8” x 7”).
M3 carton sealing tape.
Styrofoam peanuts and bubble wrap.
Cold Packs (to use in shipments with <70°degrees weather temperature
Notification Shipping labels (Fragile – handle with Care, IATA label) and inserted new list of materials:

Storage boxes for blocks (Fisher; dimensions 5” x 5” x 2”)
Multi-purpose insulated bio-shippers (Thermosafe Bio-Shippers; dimensions 14” x 10” x 14”).
Biohazard bags
Shipping labels
M3 carton sealing tape.
Styrofoam peanuts and bubble wrap.
Cold Packs (to use for all shipments in climates with > 70°F temperature).
Shipping labels to indicate: “Fragile—Handle With Care” and “Diagnostic Specimens – Not restricted, Packed in Compliance with IATA Packing Instruction 650”

New Entry after shipping list –

- Inserted “The packing process for shipments includes the following:”

Place a copy of the pathology report(s) for a single participant inside one biohazard bag in the form slot, place the block(s) for that participant in the zip lock slot, then place the biohazard bag inside the white storage box (5” x 5” x 2”).
Pack the storage boxes containing the specimens in the shipping container (14” x 10” x 14”).

Place packing materials such as Styrofoam peanuts and/or bubble wrap in and around the storage boxes to prevent them from shifting during transit.
 Place the RT Form(s) log inside a zip-lock bag and place the bag inside the insulated shipping container on top of the filler material.
 Close the lids and seal the shipping container with tape.
 Maintain a copy of the transmittal log at the site.

Chapter 5 – page 17 Section 5.2 Shipping Task List

Re-arrangement of Section –

- Section 5.2 Shipping Task List is now section 5.3

Title -

- Inserted “Summary” in front of “Shipping”; title now reads:

Summary Shipping Task List

Section-

- Entire section went from:

The following is a list of the tasks to be completed on the day of a scheduled shipment:

- Select specimens to be shipped and prepare transmittal paperwork. Copy all paperwork for the local file.

Prepare and send a notification e-mail or fax to UCLA listing the items being sent, including the number of storage boxes being sent, courier tracking number, total count of blocks included in the shipment, and the expected date of arrival. Please note “NLST Shipment Notification” in the e-mail ‘Subject’ line.

- The requested and selected tissue blocks will be shipped at room temperature or with cold packs during warmer weather conditions.
- Place the RT Form log and pathology reports inside a zip-lock bag and place the bag inside the bottom of the corrugated fiberboard shipping container box (8” x 8” x 41/4”).
- Pack the storage boxes containing the specimens in the shipping container.
- Place the packing materials such as styrofoam peanuts and bubble wrap in and around the storage boxes to prevent them from shifting during transit.
- Seal the shipping container with carton sealing tape.
- Label each shipping container with an express courier label and return address label.
- Send the package using FedEx. You may charge the shipping expenses to the 3rd Party ACRIN Account # 3374-3966-7.
- File a copy of the transmittal log. Section now reads:

The following summarizes the tasks to complete by the site for a scheduled shipment:

- Prepare transmittal paperwork and retain copies at the NLST site.
- Send a notification e-mail | Fax to the UCLA TMA Core Facility listing the items being shipped, including: the number of storage boxes, FedEx tracking number, total number of blocks in the shipment, and the expected date of arrival. Please note “**ACRIN Specimen Block Shipment-- Site [Name or ID].**” in the e-mail | Fax ‘Subject’ line.
- Pack the blocks according to instructions above.
- Label each shipping container with the FedEx shipping label as well as the labels indicating fragile contents and diagnostic specimens.
- Maintain a copy of the transmittal log at the site.

Chapter 5 – page 17 Section 5.3 Labeling Shipping Containers

Renumbered section -

- Section 5.3 is now section 5.2

Sentence 1 –

- Deleted “shipping” after “each”; inserted “FedEx shipping label to include the” after “the”, deleted “information” after the “following”; sentence now reads:

Label each shipping container with the FedEx shipping label to include the following:

Numbered bullet points -

- Point number two - inserted e-mail address and fax number to end of shipping address.

Sentence 2 –

- Inserted sentence “Charge the shipping expenses to the 3rd Party ACRIN Account # 337439667 and remnant tissue reference number 6839” after numbered bullet points.

Chapter 5 – page 18 Section 5.4 Scheduled Shipping Dates

Paragraph 1 –

- Entire paragraph was reconfigured from: Refer to the table below for the scheduled shipping dates for each study coordinator. Shipping to the UCLA Tissue Array Core Facility is scheduled for every two weeks for each site. If no specimens are to be shipped on a scheduled day because there are no specimens to send, the study coordinator should notify the UCLA Tissue Array Core Facility. If no specimens are to be shipped on a scheduled day for any other reason such as holiday or office closure, the study coordinator should ask UCLA’s preference for a make-up shipping day. Shipping should be limited to Monday, Tuesday, and Wednesday in order to minimize the chance of an over-weekend delivery delay; paragraph now reads:

Refer to the table below for the scheduled shipping days for each site. Shipping to the UCLA TMA Core Facility should occur only on the assigned day, on a weekly basis. If a scheduled shipping day falls on a holiday or day of office closure, contact the UCLA TMA Core Facility to determine a make-up shipping day. Shipping should be limited to Monday, Tuesday, and Wednesday in order to minimize the chance of an over-weekend delivery delay.

Sentence 1 –

- Deleted “dates” after shipping and replaced it with “days”; deleted “ tissue Array” after UCLA and replaced it with “TMA”; sentence now reads:

Shipping days for NLST Site to the UCLA TMA Core Facility

Chapter 6 – pages 19 -21 Specimen Processing at UCLA TMA Core Lab -Deleted Chapter 6 in its entirety

- It was relative to UCLA’s Tissue Micro Array Core Lab’s Scope of Work. Therefore, it was removed from the RT-MOP.

Chapter 7 – pages 22 Returning Loaned Specimens

Chapter renumbered -

- chapter 7 is now section 6

Paragraph 1 -

- Paragraph 1 was reconfigured from: A specimen obtained for permanent retention will be stored at the UCLA Tissue Array Core Facility after processing. A loaned specimen will be returned, via the NLST screening center, to the originating pathology laboratory within the loan period. Prior to return to the screening center, a processed specimen will be checked out of the UCLA Tissue Array Core Facility database inventory, packed in original packaging and shipped to the NLST screening center with advance notification including courier tracking number; paragraph now reads:

Tissue blocks that do not need to be returned to the originating pathology laboratory will be maintained at the UCLA TMA Core Facility. Loaned blocks will be mailed to the NLST site for return shipment to the originating pathology laboratory.

Paragraph 2 –

- Paragraph 2 was reconfigured from: The NLST screening center receipts each returned specimen and, if needed, contacts the UCLA Tissue Array Core Facility to resolve any discrepancy or problem with the shipment. The screening center batches and ships specimens to originating pathology

laboratories as needed to meet loan period deadlines. Transmittals for returns to pathology laboratories are generated by the NLST site. Materials are packaged as described for specimen shipments to the UCLA Tissue Array Core Facility. ACRIN-NLST ID labels, and any blank masking labels, are removed just prior to packaging for return.; paragraph now reads:

The site should contact the UCLA TMA Core Facility to resolve any discrepancy or problem with return shipments. The NLST site is responsible for returning blocks within the timeframe specified by the lending pathology laboratory. If possible, loaned blocks can be batch-shipped to the lending pathology laboratories.

Paragraph 3 -

- Paragraph 3 was reconfigured from: The NLST screening center is responsible for returning the block within the timeframe required by the lending Pathology Laboratory. paragraph now reads:

Transmittals for returns to pathology laboratories are generated by the NLST site. Materials are packaged as described for specimen shipments to the UCLA TMA Core Facility. NLST ID labels and blank masking labels should be removed prior to packaging for return

Appendix I – page 23 Authorization Cover Letter Template

Formatting -

- Date was switched to the left side
- A line was added under the logos
- Deleted old logo and inserted new logo
- Appendix I is in bold
- Font was changed to 11

Paragraph 1 –

- Deleted “medical” in the first sentence after “related” and replaced it with “surgical”; paragraph now reads:

Our records show that since the time you started with the NLST, you have had a lung-related surgical procedure. We would like to obtain a small amount of the surgical material (also known as a pathology specimen) that was removed and preserved after your procedure. This will help future cancer research.

Paragraph 2 –

- Deleted “of it” in the second sentence after “copies” and replaced it with “of the form”; paragraph now reads:

To allow us to obtain the material from the pathology lab, please sign the <<Authorization Form(s)>> included with this letter. We have enclosed two copies of the form. Please read, sign, and return one copy to us in the enclosed postage paid envelope. The other copy is for your records.

Paragraph 3 –

- Deleted “now” after “but”; deleted “the” after “of”; deleted “new” after “important”; deleted quotation marks around authorization; deleted “a” after “obtain” and replaced it with “portion of the”; paragraph now reads:

As you know, you have already given us consent for your involvement in NLST, but because of important HIPAA laws that are designed to protect the privacy of your medical information, we are asking for this additional authorization to obtain a portion of the pathology specimen from the pathology lab.

Enclosures –

- Added “self-addressed, stamped” to return envelope

Appendix II – page 24 Authorization to Release Surgical Material Template**Formatting -**

- A line was added under the logos
- Deleted old logo and inserted new logo
- Appendix II is in bold
- Font was changed to 11

Paragraph 1 –

- Inserted “the” after “and” in the first sentence; paragraph now reads:

Your signature below gives permission to staff at << Pathology Lab Name >> to release surgical material (also known as pathology specimen) and the related pathology report obtained during your diagnosis or treatment of lung cancer or related condition. The pathology specimen will be used for research in lung cancer detection, prevention and treatment by the ongoing National Lung Screening Trial (NLST), in which you are a participant.

Paragraph 2 –

- Deleted “It” and replaced it with “ This authorization” in the beginning of the paragraph; added “we” after “will”; added a period at the end of the sentence after ‘form’; inserted “ACRIN” after “NLST”; inserted “the” after “at”; inserted “Micro” after “Tissue”; deleted “to use” after “confidence” and replaced it with “will use”; inserted “will” after “and”; deleted “to” after “not”; paragraph now reads:

This authorization is required by law to protect your health information. The pathology specimen and pathology report will be released to your local NLST screening center, identified at the top of this form. Any identifying information attached to the pathology specimen and pathology report such as your name, specimen ID or medical record number will be removed or blanked out before being sent to the NLST-ACRIN Central Laboratory located at the University of California at Los Angeles Tissue Array Core Facility. By signing this document, you authorize << Pathology Lab Name >> to release your pathology specimen and pathology report for this research. Your local NLST screening center will hold your health information in confidence, will use it only for study purposes, and will not release it to anyone other than the study team unless required by law. Only the screening center and Central Laboratory staff involved with NLST research will have access to your pathology specimen and pathology report for this research.

Paragraph 4 –

- Deleted “take back” and replaced it with “revoke”; deleted “have” after actions; paragraph now reads:

You may change your mind and revoke this Authorization at any time, except to the extent that any actions have already been taken based on this Authorization. To revoke this Authorization, contact your local NLST screening center or write to << Pathology Lab Name >>, << Pathology Lab Contact >>, << Pathology Lab Address >>. This authorization does not have an expiration date.

Signature line –

- 4th signature line - Deleted “to sign for participant” after “authority”

Appendix III – page 25 Non-Response Log: Request for Authorization**Title -**

- Inserted “Participant” in from of “Non-Response”, title now reads:

PARTICIPANT NON-RESPONSE LOG: REQUEST FOR AUTHORIZATION

Formatting -

- A line was added under the logos
- Deleted old logo and inserted new logo
- Appendix III is in bold

Table –

- Section 1 – deleted “ACRIN NLST Inst#”
- Section 2 – deleted all “2008” and replaced with “2009”

Appendix IV – page 26 Pathology Request Cover Letter Template

Formatting –

- A line was added under the logos
- Deleted old logo and inserted new logo
- Appendix IV is in bold
- Letterhead of NLST Screening Center is in bold
- Date was added above Director, Pathology Department
- Font was changed to 11

Paragraph 1 –

- Deleted “study” after “this” and added “trial” in the second sentence; inserted new sentence “The lung cancers found by NLST screening are likely to represent earlier stages of disease.” after the third sentence; deleted “Pathology” and replaced it with “These specimens” at the beginning of the fourth sentence; deleted “for” after “potential” and replaced it with “to” ; deleted “ing” from “increase”; paragraph now reads:

We are writing to request your participation in a pathology specimen collection for the National Lung Screening Trial (NLST). << NLST Screening Center >> is collaborating with the National Cancer Institute (NCI) on this trial. The purpose of the study is to determine the effects of imaging-based screening on lung cancer-related deaths. The lung cancers found by NLST screening are likely to represent earlier stages of disease. These specimens offer great potential to increase our understanding of lung cancer and its genetic and environmental causes as well as for improving lung cancer prevention and treatment efforts.

Paragraph 2 –

- Inserted “from the NLST” after “collected”; inserted in parenthesis (“4um thick), inserted a comma after “staining”; deleted “Based upon this slide, up to twelve 0.6 mm cores from different sites of the tumor and up to twelve 0.6 mm cores of adjacent normal tissue will be removed for TMA construction. In addition, three 0.6 mm triplicate cores of the lymph node will be taken, if available “. If multiple blocks are obtained for a single tissue, cores may be distributed from among the blocks for improved capture of heterogeneity, selection of tumor and normal tissue, and core preservation.” and replaced it with “from which regions representative of a histology of interest for coring will be determined by a lung pathologist. The representative tissues of interest include:” ; paragraph now reads:

The specimens collected from the NLST will be used to construct tissue microarrays. Collected paraffin tissue blocks will have one slide (4 μm thick) cut for H&E staining, from which regions representative of a histology of interest for coring will be determined by a lung pathologist. The representative tissues of interest include:

- The predominant and secondary histologies or grades of the primary lung cancer
- Normal (non-tumor) lung, including the distal airspaces, proximal bronchus, and peripheral bronchiolar tissues
- Metastases in lymph nodes or resected metastases from other organ sites.

If multiple blocks are provided for a single histology, cores may be distributed among the blocks for improved capture of histologic and molecular heterogeneity.

Paragraph 3 –

- Deleted “pathology material from” after “collect” and replaced it with “these”; deleted “procedures during this trial” after “related” and inserted “pathologies”; deleted “are attached along with the” after “forms” and inserted “as well as a”; inserted are provided after material at the end of the paragraph; paragraph now reads:

The NLST participant listed on the attached Request Form has given signed consent and authorization to collect these lung cancer-related pathologies. These forms as well as a copy of the pathology report pertinent to this pathology material are provided.

Paragraph 4 –

- Deleted “primary” after “of” and replaced it with “the” ; deleted “with” after “tumor” and replaced it with “ (include all representative histologies or grades) as well as”; deleted sentence “Please indicate on the Request Form your preferred loan period for the material and any problems in fulfilling our request”; inserted new sentence “Blocks that include non-tumor involved central bronchus, peripheral bronchiolar tissue and lung parenchyma are also requested” ; – paragraph now reads:

The Pathology Request Form specifies the material we are requesting. For tumors, we are requesting the most representative specimen(s) of the tumor (include all representative histologies or grades) as well as tumor-free margin. Blocks that include non-tumor involved central bronchus, peripheral bronchiolar tissue, and lung parenchyma are also requested. A minimum 3-month loan period will be required by the Pathology Core to process this specimen block.

Signature –

- Deleted extra PI signature line.

Appendix V – page 27 Pathology Specimen Collection Request Form

Formatting –

- A line was added under the logos and appendix heading
- Deleted old logo and inserted new logo
- Appendix V is in bold

Paragraph –

- Deleted “representative” after “with”; deleted second sentence “We have provided *possible* representative blocks based on the attached pathology report. If there are more representative blocks, please provide the information in the table below on Procedure Date, Tissue type, Accession #, Block ID, and Block Section” and replaced it with “For each block, please record the date of procedure, explicit block identification, and provide any additional comments as appropriate.” paragraph now reads:

The NLST participant listed above reported resection of a lung cancer at your institution. We are requesting that you provide us with **buffered formalin-fixed paraffin blocks** of the tissue types listed below. For each block, please record the date of procedure, explicit block identification, and provide any additional comments as appropriate.

Table –

- Deleted columns: “Accession #”; “Block Section”; and “Pathology Department: Specimen Shipping Status”.
- Block ID Column - inserted “ Unique” in front of “Block” and expanded ID
- Tissue Type Column–
 - inserted “1st histology and grade” after “Primary Lung Tumor” to row one and two
 - inserted “Non-tumor involved proximal bronchus” to row six
 - inserted “Non-tumor involved distal bronchioles” to row seven

Contact information –

- Inserted “phone #” under “City, State, Zip code”

Appendix VI – page 28 Non-Response Log: Request for Specimen(s)

Title –

- Inserted Pathology Laboratory in front of Non-response, title now reads:

PATHOLOGY LABORATORY NON-RESPONSE LOG: REQUEST FOR SPECIMEN(S)

Formatting -

- A line was added under the logos
- Deleted old logo and inserted new logo
- Appendix VI is in bold

Section 1-

- Inserted a grid

Section 2-

- Inserted a grid

Section 3-

- Inserted lines for dates of mailing and calling
- outcome of call, reason for refusal, level of refusal and comments are in bold
- deleted all 2008 and replaced it with 2009

Appendix VII – page 29 Discrepancy Notification Form

Formatting –

- A line was added under the logos and appendix heading
- Deleted old logo and inserted new logo
- Appendix VII is in bold

Text -

- All text is now is bold
- Inserted “of” after Date

Appendix VIII RT Form (Remnant Tissue Transmittal Form) – was removed from the RT-MOP

The latest version of the RT Form can be found on the ACRIN website 6654 forms page.

Appendix IX RT Form Instructions – was removed from the RT-MOP

The latest version of the RT Form instructions can be found on the ACRIN website 6654 forms page.