



**ACRIN Protocol 6668**  
**SUMMARY OF CHANGES**

July 11, 2008

Amendment # 6

In addition to the minor changes and edits that typically accompany protocol amendments which are listed below, we have revised the protocol to make clarifications in the following sections: Site Selection, Drug Therapy, and Eligibility Checklist. Web page URLs have been updated to reflect the new ACRIN Web site. Please see below all the changes made to the protocol.

**COVER PAGE**

Contact information for the **Thoracic Radiology Co-chair**, Reginald Munden, M.D., has been changed from:

“Univ Texas M.D. Anderson Cancer Center” to “University of Alabama at Birmingham”;  
 “1515 Holcombe Blvd., Box 57” to “619 19th Street South”;  
 “Houston, TX 77030” to “Birmingham, AL 35249”;  
 (phone) “713-792-5585” to “205-934-9577”;  
 (fax) “713-745-1399” to “205-934-8110”; and  
 (email address) “[Rmunden@di.mdacc.tmc.edu](mailto:Rmunden@di.mdacc.tmc.edu)” to “[rmunden@uabmc.edu](mailto:rmunden@uabmc.edu).”

The version date has been changed from “August 15, 2007” to “July 11, 2008.”

“Including Amendments: 1-5” has been changed to “Includes Amendment 1 - 6.”

**5.0 PARTICIPANT SELECTION (PAGE 9)**

Section 5.1.7, “... a RTOG clinical trial ...” has been revised to “... an RTOG clinical trial ...” in the second sentence NOTE.

**6.0 SITE SELECTION (PAGE 10)**

The parenthetical “(see Section 6.1)” has been revised for consistency of capitalization.

Sections 6.1 and 6.1.1, page 10, the URL for ACRIN 6668 content online has been updated in 3 locations. It now reads: “[www.acrin.org/6668\\_protocol.aspx](http://www.acrin.org/6668_protocol.aspx).”

Section 6.3, first paragraph, the text “on the following page” has been revised to read “below.”

**7.0 ONLINE REGISTRATION SYSTEM (PAGE 12)**

In Section 7.1, the final sentence referring to the ACRIN Procedure Manual has been deleted.

In Section 7.2.2, “ACR” is now “ACRIN” in three locations of the paragraph.

**8.0 DATA COLLECTION AND MANAGEMENT (PAGE 13)**

In Section 8.2.2, the final sentence was corrected to read: “The case is closed when all data have been received and reviewed, and no outstanding data query exists for the case.”

In Section 8.2.5, final sentence, the reference to “ACR” has been changed to “ACRIN.”

In Sections 8.4 and 8.6, several changes were made for clarity and consistency, including:

- “Complimentary” has been corrected to read “Complementary” in the fourth sentence.
- The acronyms “BC” and “DMC” have already been spelled out so are used in this section.
- The term “DMC RA” or “DMC research associate” has been replaced with simply “DMC” to avoid confusion between ACRIN DMC personnel and site RAs.

In Section 8.6.2, the parenthetical "(QA)" has been added to the first sentence to precede the use of "QA" in the second sentence.

### **9.0 DATA COLLECTION FORMS (PAGE 16)**

The URL has been updated to "[www.acrin.org/6668\\_protocol.aspx](http://www.acrin.org/6668_protocol.aspx)."

### **10.0 IMAGE SUBMISSION (PAGE 16)**

In Section 10.1 and 10.2, contact information has been revised from Rex Welsh and Tim Welsh to Cyndi Fenerty and Anthony Levering throughout:

- Last sentence of Section 10.1 is now: "...contact Cyndi Fenerty ([cfenerty@phila.acr.org](mailto:cfenerty@phila.acr.org); 215-940-8863) or Anthony Levering ([alevering@phila.acr.org](mailto:alevering@phila.acr.org))."
- Section 10.1.1, last sentence: "Contact Cyndi Fenerty ([cfenerty@phila.acr.org](mailto:cfenerty@phila.acr.org)) ...".
- Section 10.1.2, last sentence: "... contact Cyndi Fenerty ([cfenerty@phila.acr.org](mailto:cfenerty@phila.acr.org); 215-940-8863), ...".
- Section 10.2, last sentence: "... to Cyndi Fenerty ([cfenerty@phila.acr.org](mailto:cfenerty@phila.acr.org); 215-940-8863)."

Section 10.5 on page 17 contains the updated URL "[www.acrin.org/6668\\_protocol.aspx](http://www.acrin.org/6668_protocol.aspx)."

### **11.0 DIAGNOSTIC EVALUATION OF STUDY PARTICIPANTS (PAGE 18)**

In Section 11.2.1, the URL has been updated to "[www.acrin.org/6668\\_protocol.aspx](http://www.acrin.org/6668_protocol.aspx)."

### **12.0 RADIATION THERAPY (PAGE 25)**

The following Section 12.6.2 has been added to address the use of Proton Therapy:

#### **12.3.6 Proton Therapy**

*Proton therapy is discouraged, since it is not currently approved for RTOG therapeutic clinical trials. However, it is recognized that several RTOG member institutions have invested large amounts of scientific resources toward developing programs in proton beam radiotherapy for thoracic malignancies. It is also recognized that the relative biological effect (RBE) of proton beam radiotherapy is similar to that for conventional photon irradiation. Thus, in selected circumstances, selected institutions (subject to Dr. Machtay's approval) may use proton beam radiotherapy if it is deemed in the patient's best interest (for example in order to prevent overdose of normal lung tissue irradiation). Ideally, proton beam radiotherapy should be performed on a (separate) in-house clinical trial rather than ad hoc. Patients treated with proton beam radiotherapy must still be treated with concurrent chemotherapy as well.*

*If you are planning proton therapy, contact Dr. Machtay (e-mail: [mitchell.machtay@mail.tju.edu](mailto:mitchell.machtay@mail.tju.edu); phone: 215-955-6702). Centers who use proton therapy without consent of the PI will have to submit protocol violation paperwork and may face additional consequences.*

### **14.0 PATHOLOGY/TRANSLATIONAL RESEARCH (PAGE 27)**

The name of the RTOG Biospecimen Resource (formerly RTOG Tissue Bank) has been updated in Sections 14.0, 14.1, and 14.2.4.

Section 14.5 contains new mailing and other contact information for the RTOG Biospecimen Resource:

- 14.5** *Submit materials for Tissue Banking, Central Review, or Translational Research as follows:*

***Mailing Address: For Non-frozen Specimens Only***  
*RTOG Biospecimen Resource  
 University of California San Francisco  
 Campus Box 1800  
 1657 Scott Street, Room 223  
 San Francisco, CA 94143-1800*

**Courier Address (FedEx, DHL, etc.): For Frozen Specimens**  
 RTOG Biospecimen Resource  
 University of California San Francisco  
 1657 Scott Street, Room 223  
 San Francisco, CA 94115

**Questions:** (415) 476-RTOG (7864)/FAX (415) 476-5271; [mRTOG@ucsf.edu](mailto:mRTOG@ucsf.edu)

Because the location of the RTOG Specimen Resource has moved from LDS Hospital to UCSF, the language in Section 14.6, the first sentence, has been revised to: "...will be performed at University of California, San Francisco."

### **15.0 STATISTICAL CONSIDERATIONS (PAGE 29)**

The name of the RTOG Biospecimen Resource (formerly RTOG Tissue Bank) has been updated in Section 15.2, sixth sentence.

### **16.0 ADVERSE EVENT REPORTING (PAGE 32)**

In Section 16.2, the first sentence ("Adverse events are classified as serious or non-serious.") has been deleted and the bullet points have been revised to be grammatically correct after the semicolon.

In Section 16.2 on page 33, the final sentence contains updated contact information: "...it should be treated as serious and reported to the ACRIN SAE dedicated phone line at 215-717-2763."

Section 16.3 contains reference to the CTCAEv3.0 for details of AE grading: "... based on CTCAEv3.0 descriptions."

In Section 16.3, two spaces were added between "3 – Severe:" in the grading description for consistency.

In Section 16.4, two instances of "PET-FDG" have been revised to read "the FDG-PET scan."

The numbering from Section 16.5 through the end of the section (16.11) has been revised.

Section 16.5 on page 33 has three revisions: "toxicity" is now "adverse event" in the first sentence, and two instances of "PET" are now "FDG-PET" in the second sentence.

The header for Section 16.6 is now "FDG-PET" instead of "PET" scans.

In Section 16.7, "PET NSCLC trial" has been changed to "FDG-PET scan" in the second sentence.

Section 16.8, page 34, has been extensively revised:

- The first paragraph contains two additional sentences, "*Anyone uncertain about whether a particular adverse event should be reported should contact the ACRIN headquarters at (215) 574-3150 and ask for the ACRIN AE Coordinator for assistance. However, an adverse event report should be submitted if there is a reasonable suspicion of the imaging procedure.*"
- The third paragraph now references the NCI TRI system in the first sentence, "...immediate notification of National Cancer Institute's Cancer Imaging Program (NCI/CIP) via TRI (Technical Resources International, Inc.) and ACRIN per section 16.8 and 16.9."
- The fourth paragraph, second sentence, "PET NSCLC Trial" has been changed to "FDG-PET scan."
- The fifth paragraph, first sentence, "PET Scan and FDG" has been changed to "the FDG-PET scan" and "CRFs" has been spelled out at first mention to read "case report forms (CRFs)."
- The final paragraph before the table has been added on page 35:  
*"All unresolved adverse events should be followed by the investigator until the events are resolved, the subject is lost to follow-up, or the adverse events are otherwise explained. Any death or adverse event occurring at any time after a participant has discontinued or terminated study participation that may be reasonably related to the study imaging effect should be reported."*

- Above the table, “PET NSCLC Trial” has been revised to “FDG-PET scan.”
- In the table, across the first row, “days” has been defined as “Working Days” and “NCI-CIP” has been changed to “NCI/CIP via TRI.”
- The footnote for the table has been changed from “...with attribution of possible, probable, or definite” to read: “...considered possibly, probably, or definitely related to the FDG-PET scan.”

In Section 16.9, page 35, the header has been changed from “To NCI” to “to NCI/CIP.”

In Section 16.9.1, first sentence, “...with attribution of possible, probable, or definite” has been changed to “...considered possibly, probably, or definitely related to the FDG-PET scan.” In the second and third sentences, “NCI’s Cancer Imaging Program” and “CIP” have been changed to “NCI/CIP via TRI.” In the third sentence, “IRB” is no longer spelled out since it has been previously defined in the protocol.

In Section 16.9.2, first sentence, “PET NSCLC Trial” has been changed to “FDG-PET scan”; “NCI’s Cancer Imaging Program (CIP)” has been changed to “NCI/CIP via TRI”; and “IRB” is no longer spelled out.

In Sections 16.9.3 and 16.9.4, “PET NSCLC Trial” has been changed to “FDG-PET scan” in the first sentence of each section.

Sections 16.10 and 16.11 have been extensively altered:

#### **16.10 How to Report to the NCI/CIP via TRI and to ACRIN**

**16.10.1** *All unexpected fatal adverse events with attribution of possible, probable, or definite and unexpected life-threatening/disabling unexpected adverse events with attribution of possible, probable, or definite should be reported by telephone to NCI/CIP via TRI and ACRIN within 24-hours of the first knowledge of the adverse event.*

#### **16.10.2 Expedited Telephone Reporting to NCI/CIP via TRI and to ACRIN**

**16.10.2.1** *To make an expedited telephone reports to NCI/CIP, contact TRI staff at (301) 897-1704, available 24 hours a day (recorder after hours from 7:30 PM to 7:30 AM Eastern Time).*

**16.10.2.2** *To make a telephone report to ACRIN, call (215) 717-2763, available 24 hours a day (recorder after hours from 4:30 PM to 8:00 AM Eastern Time).*

#### **16.10.3 Expedited Written Report Submission to NCI/CIP via TRI and ACRIN**

**16.10.3.1** *An expedited adverse event report requires submission to the NCI/CIP via TRI and ACRIN using the paper templates “Adverse Event Expedited Report—Single Agent” (AdEERS) available on the CTEP home page, <http://ctep.info.nih.gov>.*

**16.10.3.2** *Protocols involving only imaging procedures must be submitted using a paper version. (Do not try to send the form via the web site; it will not accept a form without those fields filled in.) Investigators following those protocols should omit the “Course Information” section and the “Protocol Agent” section, even though the template indicates those as mandatory.*

**16.10.3.3** *General questions regarding completion of the AdEERS report or submission can be sent to [CIPSAEReporting@tech-res.com](mailto:CIPSAEReporting@tech-res.com). The AdEERSMD helpline is available for any questions via phone at (301) 897-7497.*

**16.10.3.4** *An expedited adverse event report must be sent with the above-mentioned timeframe to NCI/CIP by fax at (301) 897-7402. All fatal adverse events should be reported by telephone within 24-hours of the event.*

**16.10.3.5** *A copy of all expedited adverse event reports should be sent to ACRIN by fax at (215) 940-8819, AND the original (signed and dated) report must be sent to ACRIN headquarters.*

**ACRIN 6668 Adverse Event  
Attn: ACRIN Adverse Event Coordinator  
1818 Market Street, 16<sup>th</sup> Floor  
Philadelphia, PA 19103**

**16.11 Adverse Event Reporting and Local IRB**

*All expedited adverse event reports should be sent to your local IRB per your local IRB policies and procedures. Adverse events not requiring expedited reporting are normally reported to the local IRB in an annual report and/or continuing review report. **Please refer to your local IRB's policies regarding adverse events/serious adverse events and safety reports.***

**17.0 INSTITUTIONAL AUDITS (PAGE 37)**

In Section 17.1, the URL for the protocol-specific page of the ACRIN Web site has been updated to "[www.acrin.org/pdrc.aspx](http://www.acrin.org/pdrc.aspx)" in the final sentence.

In Section 17.3, second paragraph, first sentence, "case report forms (CRFs)" is now "CRFs" since they have been previously defined.

In Section 17.4, second paragraph, first sentence, "case report forms (CRFs)" is now "CRFs" since they have been previously defined.

**APPENDIX I: SAMPLE INFORMED CONSENT FORM (PAGE 49)**

Under "About Using Tissue for Research," second paragraph, first sentence, the location of the central storage facility for pathology has been revised from "Latter-Day Saints Hospital in Salt Lake City, Utah" to "University of California, San Francisco."

Further down the same page, the second sentence under "WHAT SIDE EFFECTS OR RISKS CAN I EXPECT FROM BEING IN THIS STUDY?" has been revised to read:

*"The tissue-sample information provided to the University of California, San Francisco should be de-identified (that is, your name, address, phone number and other personal identifying information should be removed) to protect your privacy."*

**APPENDIX III: ACRIN CREDENTIALING PROCEDURES FOR PET IMAGING (PAGE 56)**

The first sentence contains the updated URL "[www.acrin.org/6668\\_protocol.aspx](http://www.acrin.org/6668_protocol.aspx)."

**APPENDIX IV: PET IMAGING QUALITY CONTROL STANDARDS (PAGE 57)**

The first sentence contains the updated URL "[www.acrin.org/6668\\_protocol.aspx](http://www.acrin.org/6668_protocol.aspx)."

**APPENDIX VI: CT ACQUISITION PARAMETERS (PAGE 59)**

The first sentence contains the updated URL "[www.acrin.org/6668\\_protocol.aspx](http://www.acrin.org/6668_protocol.aspx)."

**APPENDIX VII: ACRIN 6668 PROTOCOL-SPECIFIC APPLICATION INFORMATION (PAGE 60)**

The last sentence contains the updated URL "[www.acrin.org/6668\\_protocol.aspx](http://www.acrin.org/6668_protocol.aspx)."